12. Yang QQ, Zhou JW. Neuroinflammation in the central nervous system: symphony of glial cells. Glia. 2019;67(6):1017–35. doi: 10.1002/glia.23571.
13. Zhou L, Liang J, Xiong T. Research progress of mesenchymal stem cell-derived exosomes on inflammatory response after ischemic stroke. J Zhejiang Univ Med Sci. 2022;51(4):500–6. doi: 10.3724/zdxbyxb-2022-0077.
14. Zhu ZH, Jia F, Ahmed W. Neural stem cell-derived exosome as a nano-sized carrier for BDNF delivery to a rat model of ischemic stroke. Neural Regen Res. 2023;18(2):404–9. doi: 10.4103/1673-5374.346466.

Conflict of interest. The authors have no conflicts of interest to declare.

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Article received: 14.03.2025.

DOI 10.26724/2079-8334-2026-1-95-219-224
UDC 611.12–053.13:546.48'131:546.461.4:616–091.8–092.9

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EXPERIMENTAL STUDY OF THE EMBRYO- AND CARDIOPROTECTIVE ROLE OF ZINC SUCCINATE IN RELATION TO CADMIUM CHLORIDE TOXICITY

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Cardiovascular diseases remain the leading causes of mortality worldwide and in Ukraine. The current direction of modern morphological research is to determine the changes that occur in vivo under the influence of cadmium compounds on the fertilization process, embryogenesis, and formation and development of the heart. The aim of the experiment was to determine changes in heart morphogenesis and the main indicators of embryogenesis under conditions of chronic daily exposure to cadmium chloride with isolated administration and in combination with zinc succinate. The data obtained demonstrated a complex, dose-dependent nature of the interaction of cadmium chloride with the essential trace element zinc succinate. In the heart tissues of adult female rats and its embryos, the level of cadmium accumulation decreased with the combined administration of the studied substances. Also, the simultaneous administration of zinc succinate with cadmium chloride significantly reduced the effects of embryo- and cardiotoxicity of cadmium, which allows us to consider zinc succinate as a potential protector or bioantagonist of the toxic properties of cadmium chloride in the studied doses and method of administration in the experiment on rats.

Key words: rats, heart, embryo, cardiotoxicity, cadmium, zinc, succinates, experiment.

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ЕКСПЕРИМЕНТАЛЬНЕ ДОСЛІДЖЕННЯ ЕМБРІО- ТА КАРДІОПРОТЕКТОРНОЇ РОЛІ СУКЦИНАТУ ЦИНКУ ВІДНОСНО ТОКСИЧНОСТІ ХЛОРИДУ КАДМІЮ

Серцево-судинні захворювання залишаються лідерами причин смертності в усьому світі та в Україні. Актуальним напрямком сучасних морфологічних досліджень є визначення змін, що виникають in vivo під впливом сполук кадмію на процеси запліднення, ембріогенез та формування і розвиток серця. Метою експерименту було визначення змін морфогенезу серця та основних показників ембріогенезу за умов хронічного щоденного впливу хлориду кадмію при ізольованому введенні та в комбінації з сукцинатом цинку. Отримані дані продемонстрували складний, залежний від тривалості надходження та дози характер взаємодії хлориду кадмію з есенціальним мікроелементом сукцинатом цинку. У тканинах серця дорослих самиць та у ембріонах щурів знижувався рівень накопичення кадмію при комбінованому надходженні досліджуваних речовин. Також одночасне надходження сукцинату цинку з хлоридом кадмію достовірно знижувало ефекти ембріо- та кардіотоксичності кадмію, що дозволяє розглядати сукцинат цинку як потенціальний протектор або біоантагоніст токсичним властивостям хлориду кадмію в досліджуванних дозах та способі введення в експерименті на щурах.

Ключові слова: щури, серце, ембріон, кардіотоксичність, кадмій, цинк, сукцинати, експеримент.

Funding. *The study is a fragment of the research projects "Biological foundations of organ and tissue morphogenesis under the influence of microelements and ultramicroelements in an experiment", state registration No. 0118U006635, and "Biological aspects of organ and tissue morphogenesis under the influence of xenobiotics and under experimental correction conditions", state registration No. 0125U004298.*

Cardiovascular diseases (CVD) remain the leading causes of mortality worldwide and in Ukraine. According to the State Statistics Service of Ukraine in 2021 the mortality rate in Ukraine due to CVD was 60 % of the total number of deaths. In addition, CVD significantly affects not only the duration, but also the quality of life; therefore, the treatment and prevention of CVD remain one of the key tasks of the World Health Organization (WHO) and the Ministry of Health of Ukraine. For decades, basic clinical, biological, and statistical studies have identified among the causes of CVD the age component, heredity, gender, bad habits (smoking and excessive alcohol consumption), stress, nutrition, physical inactivity, obesity, diabetes and environmental pollution. Some studies have found

that particles in the air containing an increased amount of heavy metals are potentially dangerous for the cardiovascular system [6]. Among the etiological factors, heavy metal compounds in the environment are increasingly being considered by researchers as reproductive toxicants, and their acute and chronic effects can cause changes in gametogenesis, disrupt implantation and embryogenesis and cardiogenesis, change the micro- and macroelement balance of the body, which provokes the formation of dyselementosis. Even in low doses, cadmium has a toxic effect on the nervous system, immune system, reproductive system and cardiovascular system [7, 10, 11, 14, 15].

Cadmium is widely known as a toxic element. The main problems associated with this element in humanity are caused by environmental pollution and its toxicity to living organisms even at low concentrations. Cadmium easily enters plants from the soil and atmosphere [3]. In terms of phytotoxicity and the ability to accumulate in plants, it ranks first among heavy metals: Cd>Cu>Zn>Pb [2]. Cadmium enters the human body through the consumption of vegetables, grains and meat [4]. The half-life and excretion period is from 10 to 30 years. That is why cadmium was identified as a class I carcinogen (International Agency for Research on Cancer, 2012) and its use is limited by international legislation. Heavy metal ions that enter the body from the environment can bind to many molecules in body tissues, including proteins and polysaccharides [9, 12]. In addition, many of these metals are biologically active and participate in a variety of physiological and pathophysiological reactions. Exposure to these metals promotes oxidative stress and inflammation, disrupts endothelial function and lipid metabolism, and alters ion homeostasis and gene regulation in vascular cells [8].

However, the effect on the body and embryo of the combination of heavy metal salts with biogenic metals in order to identify possible bioantagonism remains poorly studied [1, 13]. A relevant direction of modern morphological research is the determination of changes that occur in vivo under the influence of cadmium compounds: the chronic effect of cadmium salts on the fertilization process, embryogenesis and formation and development of the heart [5].

The purpose of the study was to determine changes in heart morphogenesis and the main indicators of embryogenesis under the influence of cadmium chloride with isolated administration and in combination with zinc succinate, to determine the effect of zinc succinate with simultaneous chronic administration on the level of cadmium accumulation in embryos and hearts of pregnant female rats.

Materials and methods. Experimental work was carried out from November 2023 to March 2024 in the vivarium of the Dnipro State Medical University on 64 certified young female rats (2.5–3 months) of the "Wistar" line weighing 150–180 g, which were obtained from the nursery "Dali 2001" (Kyiv). Rats kept in standard plastic cages of 3-4 individuals in each on a standard diet. The scientific research was conducted in compliance with international and national ethical standards, taking into account the General Ethical Principles of Animal Experiments, adopted by the 1st National Congress on Bioethics.

To achieve the purpose was necessary to obtain pregnant females with a dated gestation period. All pregnant female rats were divided into 3 groups: the first group – control; the second group – isolated administration of cadmium chloride solution at a dose of 2.0 mg/kg; the third group – combined administration of cadmium chloride solution at a dose of 2.0 mg/kg and zinc succinate solution at a dose of 5 mg/kg (16 females in each group). Solutions of cadmium chloride and zinc succinate were obtained by aquananotechnology using the patented domestic method "erosion-explosive nanotechnology for obtaining aquachelates of nanometals" according to the agreement on scientific cooperation with the Scientific Research Institute of Nanobiotechnologies and Resource Saving of Ukraine (Patent of Ukraine No. 29856. 2008). The experiment was chronic and lasted the entire period of pregnancy of the females – 20 days.

Surgical slaughter and collection of embryonic material took place on the 13th and 20th days of embryogenesis under thiopental anesthesia in accordance with the ethical standards for the treatment of laboratory animals. To determine the accumulation of trace elements and the effect of the studied substances on the state of the cardiovascular system in females, hearts and embryos were removed, which were subject to fixation and further histological examination.

In accordance with the purpose of determining the level of embryotoxicity of the studied substances, the following calculations were performed: total embryonic mortality, preimplantation mortality, postimplantation mortality, number of fetuses per 1 female, average value in the group (M±m); fetal weight (g) (M±m).

Determination of the features of the accumulation of cadmium and zinc in the heart of pregnant female rats and embryos of the 13th and 20th days with isolated administration of cadmium chloride and under conditions of correction with zinc succinate was performed using polyelement analysis of biological materials by the atomic emission method with electric arc atomization. Preparation and measurement of metal content in samples was carried out in accordance with DSTU 30823-2002. A standard spectral buffering mixture according to DSTU 30823-2002 was used as a solvent. Quantitative measurement of metal content in samples was carried out on an Emas-200 CCD atomic emission spectrometer. Quantitative determination of

metals in the analyzed objects was carried out at the following wavelengths: cadmium – 228.802 nm, zinc – 213.856 nm.

Statistical processing and analysis of the results were performed according to generally accepted methods using licensed statistical analysis programs Statistica v.6.1 (StatSoft Inc., serial number AGAR909E415822FA) and the AtteStat for Microsoft Excel. Differences between groups were considered significant at $p<0.05$.

Results of the study and their discussion. The data obtained as a result of the study demonstrate a complex, dose-dependent nature of the interaction of cadmium chloride with the essential trace element zinc succinate. Isolated chronic administration of cadmium chloride led to a significant increase in the level of cadmium accumulation in the heart tissues of adult females on both the 13th and 20th days of the experiment (Fig. 1).

Analysis and comparison of the level of zinc accumulation in embryos showed that isolated administration of cadmium chloride led to a significant increase in the level of zinc accumulation in embryos on the 13th day, which is probably an initial compensatory reaction, but on the 20th day zinc in the group of isolated administration of cadmium significantly decreased, which reflects a chronic violation of zinc homeostasis caused by a probable blockage of its transfer and sequestration in the placenta. In the group of isolated administration, the level of cadmium increased 10 times (0.1206±0.0045 μg/g) compared to the control (0.0119±0.0013 μg/g), and in the group of a combination of cadmium with zinc succinate it significantly decreased compared to the group of isolated exposure (0.0831±0.0065 μg/g). Therefore, combined simultaneous administration of zinc succinate with cadmium chloride to pregnant females reduces the level of cadmium accumulation by embryos, which indicates the bioantagonistic characteristics of zinc in relation to cadmium in an experiment on rats.

Analyzing the effect of cadmium on the course of embryogenesis, we observed trends that correlated with the level of cadmium accumulation. Isolated administration of cadmium chloride at a dose of 2 mg/kg to female rats reduced the average number of live embryos in the litter, which confirms the negative effect of cadmium on prenatal fetal development. Combined administration of cadmium with zinc succinate reduced the embryotoxicity of cadmium and the number of live embryos in the litter increased both on the 13th and 20th days of the experiment, although not to the control values (Fig. 2).

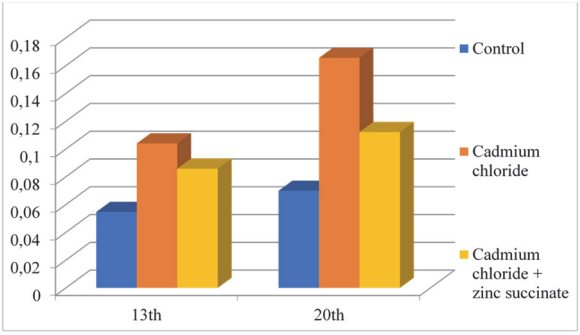

Fig. 1. Dynamics of the level of cadmium accumulation (μg/g) in the hearts of pregnant female rats in the experimental groups at both studied periods of the experiment.

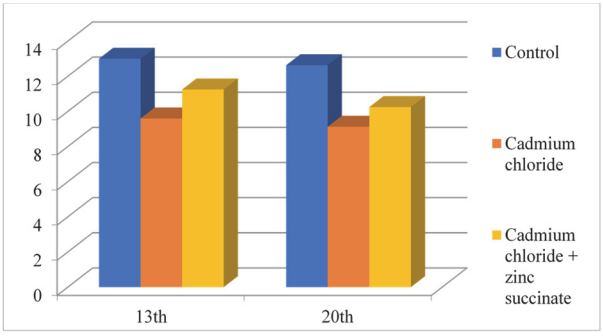

Fig. 2. Average number of live fetuses per female of all experimental groups on the 13th and 20th experiment.

The average number of live embryos in the control group on the 13th day was 13.00±0.46, while in the group of isolated exposure to cadmium chloride this figure significantly decreased to 9.63±0.32, at the same time in the group of combined exposure to cadmium chloride in combination with zinc succinate there was an increase in the number of live embryos to an average value of 11.25±0.62. Analysis of the dynamics of changes in embryo weight indicators in the experimental groups showed that in the control group the weight of embryos at this stage of embryogenesis was 0.066±0.003 g. The effect of cadmium chloride not only led to a decrease in the quantitative indicator of embryos, but also provoked a decrease in the average values of weight data – 0.052±0.003 g. We considered this indicator as one of the criteria proving the high level of embryotoxicity of cadmium chloride during chronic isolated administration in an experiment on rats. The average weight indicators of embryos in the combined administration group demonstrated the compensatory effect of zinc succinate on the embryotoxic effect of cadmium chloride when simultaneously administered to the body of a pregnant female (0.064±0.003 g). These data are also confirmed by calculating the total embryonic mortality in all experimental groups on the 13th and 20th days of the experiment (Fig. 3).

The obtained results confirm the bioantagonistic properties of zinc succinate to embryotoxicity of cadmium when they are simultaneously administered to the body in the studied doses in an experiment on rats.

Investigating the effect of solutions on cardiogenesis we obtained the average value of the thickness of the ventricular myocardium on the 13th day of embryonic development in the group of isolated administration of cadmium chloride was

13.46±0.40 μm, which was statistically significantly different from the same indicator in the control group, the average thickness of the myocardium in which was 21.49±1.03 μm, i.e. a significant decrease in the thickness of the ventricular myocardium of the embryonic heart was observed. At the same time in the group of combined administration of cadmium chloride in combination with zinc succinate, the formation of a layer of ventricular myocardium with an average thickness of 22.10±1.09 μm was noted. These indicators had statistically significant differences in comparison with the group of isolated administration of cadmium chloride. On the 13th day of the experiment the isolated effect of cadmium chloride led to thinning of the thickness of the myocardium of the ventricular heart of the embryos, a delay in cardiogenesis, which indicates the toxic effect of cadmium. And the combined administration of zinc succinate with cadmium restored the studied heart parameters. Also on the 13th day of cardiogenesis, we determined different degrees of formation and development of trabeculae in the ventricles of the heart of rat embryos and almost no formation of them in the atria. The different number of cardiomyocyte layers in the structure of trabeculae and the density of their placement led to sufficient variability in their thickness and length. In the cadmium intoxication group the preservation of cardiac jelly was clearly determined, which is characteristic of an earlier stage of heart development, and the delay in the formation of ventricular trabeculae. At the time of birth of rat fetuses their hearts do not have a definitive state, because the structures of the valve apparatus and the septum of the chambers are not completely formed. As the analysis of the obtained results showed in the final stages of embryogenesis cadmium chloride increases the thickness of the myocardium of all heart chambers and has a hypoxic effect on the walls and vessels of the embryonic heart. According to the results of histological studies we determined the expansion of the diameter of subepicardial vessels with a high level of blood filling, which is a kind of marker of the hypoxic state of the organ. Since the laying and development of these vessels occurs in parallel with the compaction of the compact myocardium, the degree of their blood supply is a certain criterion for assessing the functional state of the ventricles and indicates an increased level of blood circulation in the embryonic heart. In the group of combined exposure to zinc succinate with cadmium chloride on the 20th day of embryogenesis, a high level of blood filling of the vessels and chambers of the heart was also observed, an increase in the diameter of the subepicardial vessels was determined, which indicates that the myocardium suffered from hypoxia. We explain this condition of the walls and vessels of the heart by the continuation of the negative effect of cadmium chloride with combined administration in a chronic experiment on rats.

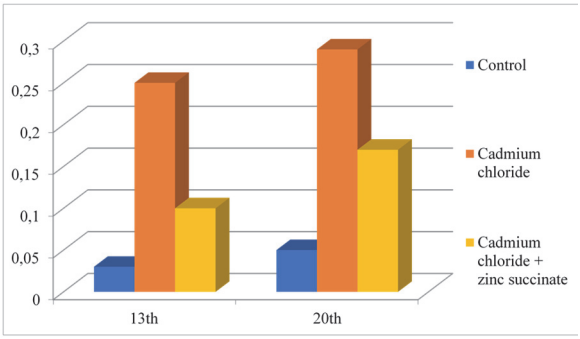

Fig. 3. Dynamics of total embryonic mortality in all experimental groups on the 13th and 20th day of the experiment.

At the same time the combined administration of cadmium chloride and zinc succinate showed a tendency to reduce the negative effect of cadmium chloride on cardiogenesis, since the thickness of the ventricular myocardium approached the control values and was higher than in the group of isolated administration. The thickness of the trabecular myocardium was lower than the control values, but higher than in the group of isolated exposure, the thickness of the atrial myocardium, on the contrary, statistically exceeded the control values. On the 20th day of cardiogenesis we observed a modifying effect of zinc succinate on the formation of the myocardium of all chambers of the rat heart, since the wall thickness indicators were statistically significantly different from the indicators of the group of isolated exposure and approached the control values.

Analyzing the modifying effect of zinc succinate on the cardiotoxic effect of cadmium chloride, it can be noted that zinc succinate has bioantagonistic properties to cadmium and a compensatory corrective effect on rat cardiogenesis both in early and late embryogenesis when they are simultaneously administered to the body of experimental animals.

This result is consistent with the generally recognized cardiotropic and cardiotoxic properties of cadmium, which are associated with the subsequent induction of oxidative damage and possible inflammation. In the group of combined administration of cadmium chloride with zinc succinate, we observed a significant decrease in the level of cadmium accumulation in the hearts of pregnant female rats, which indicates a possible corrective effect of zinc succinate.

The mechanism of this protection is explained by competitive blocking of transport cellular systems, since cadmium and zinc ions use common sarcolemmal and cellular transporters. A high concentration of bioavailable zinc, provided by succinate, saturates these transport proteins, physically preventing the entry of toxic cadmium into cardiomyocytes. At the same time analyzing

the level of zinc in the hearts of experimental animals, it was noted that in the group of isolated administration its reserves on the 13th day were comparable to the level of zinc in the group of combined administration of cadmium+zinc. This phenomenon is probably explained by the induction of metallothionein by cadmium. The initial increase in zinc on the 13th day reflects its sequestration in the tissue, associated with Cd-induced metallothionein as a protective reaction of myocardial tissues. However, long-term steady accumulation of cadmium leads to depletion of systemic zinc reserves and already on the 20th day the zinc level in the group of isolated administration of cadmium chloride decreased. This change from early compensation to late depletion is a typical example of a violation of microelement homeostasis caused by chronic intoxication.

Cadmium is known for its ability to cross the placental barrier at all terms of gestation, which creates a significant risk for cardiogenesis and general fetal development. In our studies we observed the highest level of cadmium accumulation by embryos in the group of isolated administration of cadmium chloride. It is important that the combined administration of cadmium chloride with zinc succinate reduced the level of cadmium accumulation by embryos compared to isolated administration, although it did not form a pronounced tendency to decrease to control values.

The data we obtained on a significant increase in the level of cadmium accumulation in the heart tissues of adult females at both studied experimental periods are consistent with the generally recognized cardiotoxicity of cadmium, which is associated with the induction of oxidative damage and inflammation [5, 10, 11]. We did not find data on the formation of studies aimed at the combined effect of cadmium with zinc succinate on cardiogenesis, therefore, a comparison is not possible. In the heart tissues of adult females and in rat embryos, the results obtained can supplement the already known distribution patterns and mechanisms of their interaction, the effects of embryo- and cardiotoxicity of cadmium and the potential of zinc for the correction of microelement imbalance.

Limitations. Several limitations of this study should be noted. Primarily, this study focused on a single dose of cadmium and zinc succinate. Investigating a wider range of concentrations would provide a more comprehensive understanding of the dose-dependent protective effects of zinc against cadmium-induced cardiotoxicity. The dose of cadmium chloride was higher than the daily chronic environmental intake, but adequate for conducting a model experiment. Additionally, as with all animal models, the findings regarding cadmium-induced embryotoxicity in rats should be extrapolated to human pregnancy with caution, given interspecies differences in placental transfer and metabolism.

Conclusions

1. The results obtained confirm the negative effect of cadmium chloride on embryonic mortality rates in rats, on the course of embryogenesis in general and cardiogenesis in particular, as well as on the heart condition of pregnant female rats with chronic administration at a dose of 2 mg/kg. Combined administration of cadmium chloride with zinc succinate reduces the embryo- and cardiotoxic effect of cadmium chloride, which indicates the bioantagonistic nature of the interaction.

2. Zinc succinate, when simultaneously administered to the body with cadmium salts, reduces the level of cadmium accumulation in the rat heart, which is the basis for the development of mass preventive measures in cadmium-laden regions.

References

1. Rudenko KM, Kosse VA, Trushenko O, Lyulko IV, Topka EH, Filippov YuO, et al. Vplyv kadmiyu ta kuprumu na pokaznyky smertnosti v embriohenezi shchuriv pry vnutrishnoshlunkovomu vvedenni. Visnyk problem biolohiyi ta medytsyny. 2021;3(161):101–5. doi: 10.29254/2077-4214-2021-3-161-101-105. [in Ukrainian].

2. Tsvyetkova NM, Hunko SO. Korelyatyvna kharakterystyka kadmiyu u gruntakh stepovoho Prydniprovya. Biosyst Divers. 2015;23(2):190–6. https://doi.org/10.15421/011527. [in Ukrainian].

3. Chorna VI, Voroshylova NV, Syrovatko VO. Rozpodil kadmiyu v hruntakh Dnipropetrovskoyi oblasti ta yoho akumulyatsiya v produktsiyi roslynnytstva. Ukr J Ecol. 2018;8(1):910–7. doi:10.15421/2018_293. [in Ukrainian].

4. Carroll RE. The relationship of cadmium in the air to cardiovascular disease rate. JAMA. 1966;198:267–9.

5. Chen H, Jin C, Xie L, Wu J. Succinate as a signaling molecule in the mediation of liver diseases. Biochimica et biophysica acta. Molecular basis of disease. 2024;1870(2):166935. doi: 10.1016/j.bbadis.2023.166935.

6. Fitch ML, Kabir R, Ebenebe OV, Taube N, Garbus H, Sinha P, et al. Cadmium exposure induces a sex-dependent decline in left ventricular cardiac function. Life Sci. 2023;324:121712. doi: 10.1016/j.lfs.2023.121712.

7. Kolosova II, Rudenko KM, Lyulko IV, Topka EG. Comparative analysis of the effects of the influence of cadmium chloride on rat embryogenesis at different terms of pregnancy. Visn Probl Biol Med. 2021;3(161):258–62. https://doi.org/10.29254/2077-4214-2021-3-161-258-262.

8. Kulas J, Ninkov M, Tucovic D, Popov AA, Ukropina M, Cakic Milosevic M, et al. Subchronic oral cadmium exposure exerts both stimulatory and suppressive effects on pulmonary inflammation/immune reactivity in rats. Biomed Environ Sci. 2019;32(7):508–19. doi: 10.3967/bes2019.068.

9. Lamas GA, Navas-Acien A, Mark DB, Lee KL. Heavy metals, cardiovascular disease, and the unexpected benefits of edetate chelation therapy. J Am Coll Cardiol. 2016;67(20):2411–8. doi: 10.1016/j.jacc.2016.02.066.

10. Lin H-C, Hao W-M, Chu P-H. Cadmium and cardiovascular disease: an overview of pathophysiology, epidemiology, therapy, and predictive value. Rev Port Cardiol. 2021;40(8):611–7. doi: 10.1016/j.repc.2021.01.009.
11. Lundin KK, Qadeer YK, Wang Z, Virani S, Leischik R, Lavie CJ, et al. Contaminant metals and cardiovascular health. J Cardiovasc Dev Dis. 2023;10(11):450. doi: 10.3390/jcdd10110450.
12. Nasiadek M, Stragierowicz J, Kilanowicz A. An assessment of metallothionein–cadmium binding in rat uterus after subchronic exposure using a long–term observation model. Int J Mol Sci. 2022;23(23):15154. doi: 10.3390/ijms232315154.
13. Shevchenko O, Kozina A, Kosse V. Influence of cadmium salts on the development of the skeletal system and in the correction with succinates of metals (literature review). Mod Sci. 2021;3:129–35.
14. Tymchuk KM, Abramov SV, Kryzhanovsky DG, Fedchenko MP, Filipenko VV, Chernenko GP, et al. Embryotoxic effect of cadmium chloride and cuprum during the entire pregnancy period in white rats. Bull Probl Biol Med. 2022;3(166):115–9. doi: 10.29254/2077-4214-2022-3-166-115-119.
15. Vallée A, Gabet A, Grave C, Blacher J, Olié V. Associations between urinary cadmium levels, blood pressure, and hypertension: the ESTEBAN survey. Environ Sci Pollut Res. 2020;27:10748–56. doi: 10.1007/s11356-019-07249-6.

Conflict of interest. The authors have no conflicts of interest to declare.

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Article received: 19.02.2025.