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EXPERIMENTAL DETERMINATION OF THE ACCUMULATION OF CADMIUM SALTS IN THE HEART OF THE EMBRYO OF RAT AND THEIR EFFECT ON RAT CARDIOGENESIS

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Ключові слова: *ембріон щура, кардіогенез, кадмій, цитрати металів, цитрат сірки, цитрат йоду, серце*
Ключевые слова: *эмбрион крысы, кардиогенез, кадмий, цитраты металлов, цитрат серы, цитрат йода, сердце*

Abstract. Experimental determination of the accumulation of cadmium salts in the heart of the embryo of rat and their effect on rat cardiogenesis. Nefedova E.A., Halperin A.I., Shatornaya V.F., Shevchenko I.V., Demidenko Yu.V., Pridius I.A., Myasoyed Yu.P. *The article discusses the results of an experimental effect of cadmium chloride / cadmium citrate on the cardiogenesis in conditions of intragastric administration to pregnant female rats. The aspect of accumulation of cadmium salts in the heart of the embryo was studied under the condition of daily administration of a salt solution to female rats from the first day of pregnancy to the end of embryogenesis (20 days). In addition to the groups of isolated cadmium administration, there were groups of combined administration of cadmium salts with citrates of germanium, cerium, and the iodine + sulfur composite. The second task was to study the effect of the studied salt solutions on the cardiogenesis of rat's embryos, for which serial histological sections of the heart were made. The thickness of the compact myocardium of the heart chambers was measured as the main indicator of cardiogenesis. The use of multielement analysis*

showed that the highest level of cadmium accumulation was found in the group of isolated cadmium citrate administration against the background of a decrease in the zinc content in the heart tissues of the embryo. It has been proven that cadmium citrate maintains a high level of accumulation in the groups with combined administration of cerium citrate, germanium citrate, iodine + sulfur citrate composites, but in these groups the level of zinc in the myocardium significantly increases, which can be regarded as an element of the compensatory effect of cerium citrate, germanium and composite iodine + sulfur. The effect of the indicated doses of cadmium salts on cardiogenesis in rats was reflected in the thickness of the myocardial layer of all chambers of the heart in different ways: cadmium chloride thickened the walls of the left and right ventricles, both atria with a thickening of the interventricular septum. Cadmium citrate provokes thinning of the myocardium of the wall of both ventricles and local thickening of the interventricular septum. In the groups of combined administration, the indicators of the thickness of the compact myocardium restored, which indicates the modifying effect of citrates of the studied trace elements on the cardiotoxicity of cadmium salts.

Реферат. Экспериментальное определение накопления в сердце эмбрионов солей кадмия и их влияния на кардиогенез крысы. Нефедова Е.А., Гальперин А.И., Шаторная В.Ф., Шевченко И.В., Демиденко Ю.В., Придиус И.А., Мясоед Ю.П. *В статье рассмотрены результаты экспериментального влияния на кардиогенез внутрижелудочного введения кадмия хлорида и цитрата беременным самкам крыс. Изучался аспект накопления солей кадмия в сердце эмбриона при условии ежедневного введения раствора солей самкам с первого дня беременности до конца эмбриогенеза (20 дней). Кроме групп изолированного введения кадмия, были группы комбинированного введения солей кадмия с цитратами германия, церия и композита йод+сера. Второй задачей было изучение влияния исследуемых растворов солей на кардиогенез крысиных эмбрионов, для чего изготавливались серийные гистологические срезы сердца и проводились измерения толщины камер сердца и межжелудочковой перегородки. Измеряли толщину компактного миокарда камер сердца как основного показателя кардиогенеза. Использование полиэлементного анализа подчеркнуло, что наиболее высокий уровень накопления кадмия обнаружен в группе введения цитрата кадмия как монокомпонента на фоне снижения содержания цинка в тканях сердца эмбриона. Доказано, что цитрат кадмия сохраняет высокий уровень накопления и в группах комбинированного введения с цитратом церия, цитратом германия, композитом цитратов йод+сера, но в этих группах достоверно повышается уровень цинка в миокарде, что может расцениваться как элемент компенсаторного действия цитрата церия, германия и композита йод+сера. Влияние указанных доз солей кадмия на кардиогенез у крыс отражался на толщине миокардиального слоя различных камер сердца по-разному: хлорид кадмия приводил к утолщению стенки левого и правого желудочка, обоих предсердий с утолщением межжелудочковой перегородки. Цитрат кадмия провоцирует истончение миокарда стенки обоих желудочков и локальное утолщение межжелудочковой перегородки. В группах комбинаций показатели толщины компактного миокарда восстанавливались, что говорит о модифицирующем влиянии цитратов исследуемых микроэлементов на кардиотоксичность солей кадмия.*

Currently, scientists are attracting considerable attention of fundamental and applied problems in the study of patterns of basic aspects of morpho- and organogenesis under the influence of adverse environmental factors, among which the most harmful are heavy metal compounds [7, 9]. The impact of complex environmental pollution on the human body which occurs due to industrial factors, and many other things contributes to the emergence or exacerbation of chronic diseases, defined in modern science as environmental pathology. The redistribution of microelements caused by human activity, the increase of environmental pollution by toxins have led to the fact that modern medicine pays more and more attention to trace elements and microelements. The stable chemical composition of the human body is a guarantee and a prerequisite for the normal functioning of the human body. Deficiency of trace elements which are of vital importance and increasing concentration of toxins in the environment lead to the fact that adverse effects impact on human life and the course of embryo- and organogenesis [3, 5]. The mechanisms by which cadmium can play a role in dysfunction of the cardiovascular system are actively studied: increase in blood pressure, increase in blood cholesterol levels, increase in mutations in arterial wall cells [1, 10]. Cadmium, like some other metals, directly affects the vascular endothelium, which is accompanied by the release of endothelin to which smooth cells have specific receptors and the mechanism of their action on these cells is associated with the activation of calcium ions through the potential. dependent calcium channels [11]. Long-term exposure of experimental animals to cadmium chloride leads to pronounced morphological changes in the myocardium at all levels of its structural organization. There was a significant increase in the mass of various parts of the heart, dilatation of their chambers, damage to cardiomyocytes, endothelial cells, reduction of ventricular reserve volumes, decreased arterial capacity, dilation of the venous part of the heart, hypoxia, etc. [2, 8], however, the influence of cadmium on the development of the

heart during embryogenesis remains underinvestigated. Therefore, based on the above facts, the leading vector in morphological experimental studies is the establishment of a spectrum of disorders of cardiogenesis in the study of the effect of cadmium salts on female rats during pregnancy and under conditions of compensation.

The aim of the study was to determine in an experiment the degree of increase in cadmium amount in the body of embryos and the effect of cadmium salts administered alone and in combination with metal citrates, iodine and sulfur citrates on cardiogenesis of female rats during pregnancy and under conditions of chronic intoxication.

MATERIALS AND METHODS OF RESEARCH

The experiments were performed on female rats of Wistar line (breeding nursery "Dali", Kyiv). At the beginning of the experiment, all studied animals were examined, weighed, their motor activity and skin condition were taken into account. After external evaluation and culling, experimental studies started simultaneously with the control group. Before and during the experiment, the animals were in the vivarium settings of DMA at a temperature of 20-25^{0}C, humidity of not less than 50%, in ventilated rooms in conditions of temperature, humidity and light in standard plastic cages, no more than 3-4 studt subjects in each, with a standard diet. For the embryological experiment, female rats with the corresponding dated gestational age were obtained by the method of vaginal swabs. In order to model the effects and toxic effects of exposure to cadmium salts, female rats were administered oral solutions of the substances under study during pregnancy daily. In the experimental models, solutions of germanium citrate, cerium, sulfur and iodine composite obtained by aquanan technology were used. Citrates (salts of citric acid) of biometals are safe, moreover, they have antioxidant and radioprotective properties and cause a positive effect on the cardiovascular and immune systems of the body. The experimental animals were divided into the following 9 groups:

1 group – control (n females =8; n embryos =76); group 2 – animals that received a solution of cadmium chloride in a dosage of 1.0 mg/kg (n females =8; n embryos =63); group 3 – animals that received a solution of cadmium citrate in a dosage of 1.0 mg/kg (n females =8; n embryos =70); group 4 – animals that received a solution of cadmium chloride in a dosage of 1.0 mg/kg and a solution of cerium citrate in a dosage of 1.3 mg/kg (n females =8; n embryos =68); group 5 – animals that received a solution of cadmium citrate in a dosage of 1.0 mg/kg and a solution of cerium citrate in a dosage of 1.3 mg/kg (n females =8; n embryos =72); group 6 – animals that received a solution of cadmium chloride in a dosage of 1.0 mg/kg and a solution of germanium citrate in a dosage of 0.1 mg/kg (n females =8; n embryos =68); group 7 – animals that received a solution of cadmium citrate in a dosage of 1.0 mg/kg and a solution of germanium citrate in a dosage of 0.1 mg/kg (n females =8; n embryos =71); group 8 – animals that received a solution of cadmium chloride in a dosage of 1.0 mg/kg and a solution of sulfur and iodine citrate in a dosage of 0.003 mg/kg (n females =8; n embryos =73), group 9 – animals that received a solution of cadmium citrate at a dosage of 1.0 mg/kg and a solution of sulfur and iodine citrate at a dosage of 0.003 mg/kg (n females =8; n embryos =71).

Based on the relevant requirements and compliance with the conditions of the course and implementation of experiments of the embryonic period, diet and drink regimens of full value and observation of female rats were provided; by probing the studied solutions of metals were introduced from the first day of pregnancy at the appropriate time of a day (from 10 to 12 a.m. daily [4, 6]. On day 20 of embryogenesis, the animals were surgically sacrificied, embryos were removed from the uterus, weighed, their length was measured, they were photographed and the heart was removed for further histological examination. Some embryos were subjected to freezing to measure the content of metals (cadmium, zinc) in embryonic samples according to the method of polyelement analysis. Polyelement analysis of materials of biological environment according to the method of atomic emission with electric arc atomization was carried out at the state enterprise "Ukrainian research institute of transport medicine" of the Ministry of Health of Ukraine (Odessa) according to the agreement on scientific and creative cooperation (2018). Preparation of samples and measurement of metal content was carried out in accordance with GOST (AUSS) 30823-2002.

Given the specifics of this goal, in this study a quantitative assessment of a number of indicators of cardiogenesis using histological sections was performed:

- thickness of the compact myocardium of the atrium and ventricle of the embryo in the norm and in the experiment (μm), M±m;
- thickness of the interventricular septum of the embryo heart in the norm and in the experiment (μm), M±m;

Measurements of these heart parameters were performed on a Primo Star trinocular digital microscope (ZEISS) with an AXIOCAM ERc5s video

camera imaging system using licensed programs for linear measurements of microscopic specimens.

The following morphometric parameters were determined as well:

- the average number of embryos per 1 female in the group, M±m;
- weight of the embryo as a whole (wet weight) in the norm and under the influence of cadmium citrate (mg), M±m;
- weights of the isolated heart of the embryo (wet weight) in normal and under the influence of cadmium citrate (mg), M±m;
- cardiofetal index (%), M±m, which we calculated by the formula:

$$- \ CFI = \frac{m}{M} \times 100\%$$

where CFI – cardiofetal index; m - heart mass; M is the mass of the rat embryo.

Statistical evaluation and analysis of results were performed according to generally accepted methods using licensed statistical analysis programs Statistica v.6.1 (StatSoft Inc., serial N AGAR909E415822FA) and Microsoft Excel. The probability of statistical studies was assessed using Student's t-test.

The experiments were performed in accordance with the principles of the Declaration of Helsinki, adopted by the General Assembly of the World Medical Association (2000), the Council of Europe Convention on Human Rights and Biomedicine (1997), the relevant provisions of the WHO, the International Council of medical scientific societies, the International Code of Medical Ethics (1983), "General ethical principles of animal experiments", approved by the First National Congress of Bioethics (Kyiv, 2001), guided by the provisions of the European Convention on protection of vertebrates used in experiments and other educational purposes "(Strasbourg, March 18, 1986).

RESULTS AND DISCUSSION

All experimental females survived. In the introduction of the above doses to embryos, we found no manifestations of teratogenic effects, namely: external injuries, ectopia, hernias and other malformations, using cadmium salts and other substances studied by this method of administration and appropriate doses.

The use of polyelement analysis showed that the cadmium content in the hearts of embryos on day 20 of development varied not only in the groups exposed to cadmium salts, but also in the groups of combined administration. Thus, in the control group (group 1) the level of cadmium accumulation was 0.00042±0.000022 μg/g, and in the group of isolated administration of cadmium chloride (group 2) this indicator more than doubled the control values and was equal to 0.00102±0.000051 μg/g (the difference was significant $p<0.001$), which indicates the penetration of cadmium chloride through the placental barrier and indirect intoxication of rat fetuses in the introduction of study factor to the female at a dosage of 1.0 mg/kg per os daily. According to the literature of recent years, the results obtained do not contradict the ability of cadmium compounds to cross the placenta and accumulate in the internal organs of embryos and fetuses [1]. The change in cadmium content in the heart tissue of the embryo was accompanied by a redistribution of the content of the essential metal – zinc, namely: if the control level of zinc was 6.02±0.143196 μg/g, the effect of cadmium chloride significantly increased ($p<0.001$) this indicator and was equal to 14.22±0.442347 μg/g. At the same time, in the group of isolated administration of cadmium citrate (group 3), the accumulation of cadmium in the heart was 12 times higher than the control values and was 0.00507±0.00029 μg/g due to the nano-size of cadmium citrate and its ability to pass placental barrier and accumulate to a greater extent in the tissues of embryos.

In this group the level of zinc (4.85±0.34 μg/g) also decreased by almost 25% compared to the control, the significance of the difference was $p<0.001$ both in relation to the control and in relation to the group of exposure to cadmium chloride (Table 1).

The obtained results do not contradict the identified trends of recent studies on micronutrient balance shifts in the body, which proved that the toxic properties of cadmium, its absorption and distribution in the body can affect the content of zinc and copper, although these data in the scientific literature are quite contradictory. Copper and zinc inhibit the processes of cadmium absorption and deposition, the study of cadmium accumulation and distribution depends on the dose of zinc in the diet and the antagonistic nature of these elements is quite different for individual organs and depends on age [2].

The combined introduction of cadmium chloride + cerium citrate (group 4) revealed that the cadmium content in the hearts of embryos was 0.00044±0.00002 μg/g (had no significant difference with the control, but had a difference of $p<0.001$ with the group of isolated introduction of cadmium chloride), which indicates the modifying effect of cerium citrate on the ability of cadmium chloride to accumulate in embryonic tissues. The level of zinc

also approached the control values and was 5.49±0.25 μg/g. In the group of cadmium citrate introduction with cerium citrate, the level of cadmium was 0.00086±0.000037 μg/g, which is almost 6 times less than in the group of isolated administration of cadmium citrate. Thus, cerium citrate reduces the accumulation of cadmium in the internal organs of the embryo (namely the heart) when administered in combination with cadmium citrate or chloride in these doses in the experiment on rats (Fig. 1).

Table 1

Comparison of cadmium and zinc content in the hearts of rat embryos on day 20 of embryonic development in all study groups (M±m)

Experimental group	Content of cadmium (μg/g)	Content of zinc (μg/g)
Control	0.00042±0.000022	6.02±0.143196
Cadmium chloride	0.00102±0.000051***	14.22±0.442347***
Cadmium citrate	0.00507±0.00029$^{***, ###}$	4.85±0.34$^{***, ###}$
Cadmium chloride + cerium citrate	0.00044±0.00002$^{###}$	5.49±0.25$^{###}$
Cadmium citrate + cerium citrate	0.00086±0.000037$^{***, @@@}$	7.23±0.25$^{***, @@@}$
Cadmium chloride +germanium citrate	0.00053±0.000039$^{*, ###}$	5.76±0.35$^{###}$
Cadmium citrate + germanium citrate	0.00068±0.000051$^{***,@@@}$	8.76±0.59$^{***,@@@}$
Cadmium chloride + йод, сірка	0.00061±0.000045$^{***, ###}$	7.12±0.24$^{***, ###}$
Cadmium citrate + iodine, sulfur	0.00074±0.000035$^{***,@@@}$	10.85±0.51$^{***,@@@}$

Notes: * – p<0.05; ** – p<0.01; *** – p<0.001; relative to control; # – p<0.05; ## – p<0.01; ### – p<0.001; relative to group of cadmium chloride; @ – p<0.05; @@ – p<0.01; @@@ – p<0.001; relative to group of cadmium citrate.

In the group of introduction of cadmium chloride with germanium citrate (group 6) the cadmium content in the heart of the embryo was 1.3 times higher than the control values and was 0.00053±0.000039 μg/g, while the zinc level was 5.76±0.35 μg/g. When females were administered the combination of cadmium citrate + germanium citrate (group 7), the cadmium content was significantly higher and was equal to 0.00068±0.000051 μg/g, while the zinc content increased to 8.76±0.59 μg/g. The obtained experimental data prove that the compensatory effect of germanium citrate has an impact on the ability of cadmium to accumulate in the internal structures of the embryo in oral administration to rats (Fig. 1). The content of cadmium in the hearts of rat embryos when exposed to a combination of cadmium chloride with iodine and sulfur was 0.00061±0.000045 μg/g, and 1.45 times higher than the control group, while the obtained zinc content values in the tissues of the embryonic heart also exceeded the control values and amounted to 7.12±0.24 μg/g, which had a reliability of p<0.05 both in relation to the control and in relation to the group of single administration of cadmium chloride. In the group of combination of cadmium citrate with iodine and sulfur (group 9) the level of cadmium was 0.00074±0.000035 μg/g, which is 7.7 times less than in the group of administration of cadmium citrate only, but the concentration of zinc has a positive dynamics and increased to 10.85±0.51 μg/g, i.e. nanocomposite of sulfur and iodine reduces the amount of cadmium in the heart of embryos in its experimental combination. The analysis of the literature on our research showed that we were unable to determine or compare scientific data due to the lack of experimental data on the simultaneous effects of cadmium salts with germanium, cerium or iodine composite with sulfur on the part of their microelemental accumulation.

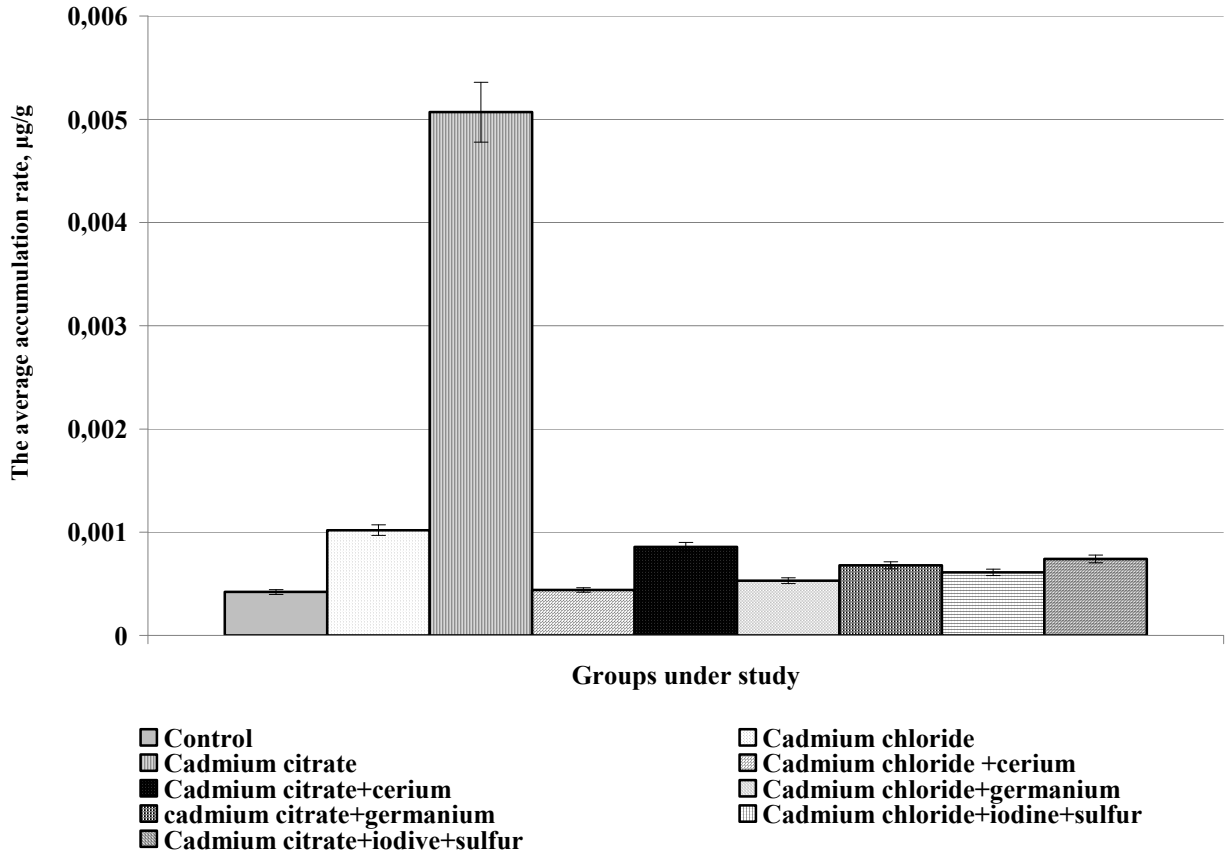

Fig. 1. Values of cadmium accumulation in hearts of rat embryos in control and experimental group on day 20 of pregnancy (µg/g)

Based on the above, the experimental results of multi-element analysis using atomic emission proved a decrease in the cadmium content in the internal organs of embryos in combining cadmium salts with cerium citrate/germanium citrate/iodine citrate with sulfur in per os administration to rats under experimental study. The studied elements are possible bioanthogonists of cadmium salts. It is also proved that the accumulation of cadmium in the tissues of the embryo in citrate form is significantly higher as compared to cadmium chloride.

Disorders of cardiogenesis in the experiment were detected in the study of macroscopic parameters, namely at the level of weighing the heart of rat embryos, i.e: in the group of cadmium intoxication there was a decrease in the mass of the embryos and a significant decrease in heart mass. To exclude errors relatively effect of decreased embryo mass and heart mass on cardiotoxicity, we calculated the cardiofetal index. Taking into account the analysis of the obtained results, under the influence of cadmium chloride on a pregnant female, changes not only in the number of live embryos in the litter but also changes in the massometric parameters of the embryos take place. Thus, in relation to the control group, a significant decrease in the number of live embryos was determined in the group exposed to cadmium salts, although the average fetal weight and heart weight did not have a significant difference (Table 2). At the same time, the quantitative indicators of embryos in the group exposed to cadmium citrate were closer to the control, and the heart weight decreased compared to both groups. An increase in the cardiofetal index in an isolated exposure to cadmium chloride indicates an increase in the weight of the heart in the group with a decrease in the parameters of the body weight of the embryo due to intoxication. In the group exposed to cadmium citrate, the cardiofetal index was almost equal to the control values, although the body weight of the embryos was the lowest of the studied groups.

To determine the morphogenetic changes of the heart chambers under the influence of cadmium salts, we determined the thickness of the compact myocardium of the ventricles, interventricular septum and atria on day 20 of the experiment. The thickness of the ventricle was determined taking into

account the peculiarities of the structure of the heart chamber in 3 zones: the apical part, the middle part and the basal part. In the control group (group 1), the lowest values of the thickness of the compact ventricular myocardium were determined in the apical part of both left and right ventricles, being equal to: 241.38±10.34 μm and 163.38±4.11 μm, respectively. The most pronounced is the compact myocardium of the middle part of the ventricles, the thickness of which in control reached 512.13±3.98 μm in the left and 314.88±5.17 μm in the right, the thickness of the interventricular septum (in the middle part) in this group was equal to 420.75±7.82 μm. The atria had a pronounced heterogeneous thickness, so measurements of the thickest and thinnest sections of the wall were performed for further calculation. The thickness of the myocardium of the right atrium ranged from 40.25±1.33 μm, 133.63±2.79 μm, of the left – 52.13±1.86 and 142.63±3.71 μm. At this stage of development, atria in control have well-formed trabeculae and a pronounced epicardial layer.

Table 2

Indicators of the number and weight of rat embryos and cardiofetal index on day 20 of embryogenesis (M±m)

Indicator	Control	Groups of effect	
		Cadmium chloride	Cadmium citrate
Number of live fetuses per 1 female rat	9.50±0.13	7.88±0.40*	8.75±0.27*
Body mass of 1 fetus. g	2.76±0.07	2.72±0.08	2.64±0.05
Heart mass of embryo. mg	34.08±0.53	34.80±0.58	31.10+1.29*
Cardiofetal index	1.23±0.02	1.33±0.04*	1.22±0.06

Note. * – $p<0.05$; in relation to control.

In the ventricles. the compact myocardium contains developed vessels and the trabecular layer consists of separated formed trabeculae. The epicardium is close to the myocardium, the interventricular septum is fully formed.

Histological studies showed that in the group exposed to cadmium chloride (group 2) changes in the structure of the atria and ventricles were revealed. Atrial endocardial hyperplasia was detected in 12.3% of the studied objects (Fig. 2). while the ventricular endocardium remained normal. The processes of hyperplasia may indicate the formation of compensatory mechanisms from the side of the endothelium in response to the toxic effects of cadmium chloride during embryogenesis. Endothelial hyperplasia was not found in the cadmium citrate group. Also, exposure to cadmium chloride led to local thickening of the atrial wall at this stage of development. The heterogeneity of the thickness of the atrial wall made us measure the thickest and thinnest parts of the atria. If in the control the average thickness of the right atrium was 40.25±1.33 μm in thinned areas, then in exposure to cadmium chloride (group 2) a thickening to 49.88±1.72 μm was observed and in the group affected by cadmium citrate, on the contrary the wall was thinned to 35.50±2.30 μm.

Under the influence of cadmium chloride the thickness of the interventricular septum of the embryo increased from 420.75±7.82 μm in the control to 494.16±6.71 μm, and in the group of cadmium citrate, the thickness of the interventricular septum decreased to 381.50±8.11 μm, although local thickening of the middle part of the septum was observed in 12.4%.

Thus, different chambers of the heart respond to the effects of cadmium salts differently due to different hemodynamic loads of the chambers of the heart. The right half of the heart does not carry a large hemodynamic load in the embryo due to the presence of an arterial duct and the absence of gas exchange in the lungs, the lesser circulation has no functionally high load and the effect on the myocardium of this part of the body is insignificant. The left half is more damaged, which is associated with a greater circulation, it has a bigger hemodynamic load. It should be noted that at the time of birth of a

rat embryo, its heart is not a definitive organ: vessels. valvular apparatus and myocardium are finally formed in the first 2 weeks after birth. However, when exposed to equal doses of different cadmium salts, different processes of heart development were determined, namely: exposure to cadmium chloride led to an increase in the compact layer of myocardium of all chambers of the heart and interventricular septum, and the introduction of cadmium citrate reduced the thickness of chamber walls and septa. In the groups of combinations of cadmium salts with citrates of the investigated microelements, the indicators of compact myocardium were restored, which indicates the antagonistic nature of the effect of the studied substances on the cardiotoxicity of cadmium. In the group exposed to cadmium citrate, the accumulation of cadmium in embryonic tissues is the highest and significantly ($p<0.001$) higher than the accumulation in the group affected by cadmium chloride, despite the identity of the dose of cadmium.

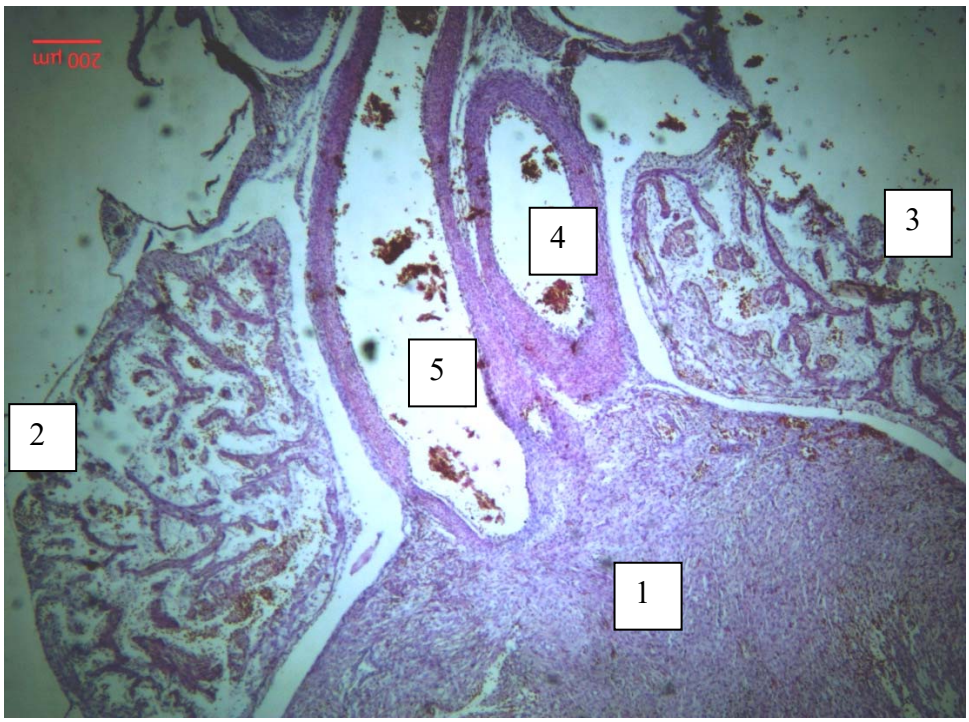

Fig. 2. Photomicrography of heart of rat embryo in control group.
Staining: hematoxylin-eosin. Magnification power: eyep. 10 x lens 4
Indications: 1. Ventricle. 2. Right atrium. 3. Left atrium. 4. Aorta. 5. Pulmonary trunk

CONCLUSIONS

1. The use of polyelement analysis proved that the highest level of cadmium accumulation was found in the group of isolated administration of cadmium citrate ($p<0.001$ compared with group 2) against the background of reduced zinc content in the heart tissue of the embryo. It is proved that cadmium citrate maintains a high level of accumulation in the tissues of rat embryos and in groups of combinations with cerium and germanium citrate, but in these groups the level of zinc in the myocardium significantly increases, which can be regarded as an element of compensatory action of cerium and germanium.
2. The effect of these doses of cadmium salts on cardiogenesis in rats affected the thickness of the myocardial layer of different chambers of the heart in different ways: cadmium chloride led to a thickening of the walls of the ventricles by 1.8 times and the atrial walls by 1.2 times with local thickening of the interventricular septum (from 420.75±7.82 µm in the control to 494.16±6.71 µm in group 2) Cadmium citrate (group 3) provokes thinning of the wall of both myocardial ventricles and the interventricular septum (381.50±8.11 µm), local thickening of the middle part of the septum was observed in 12.4%. In the groups of combined administration of cadmium salts with metal citrates, the recovery of compact myocardial parameters was determined.

Conflict of interest. The authors declare no conflict of interest.

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