11. Panda L. Antibacterial activity of ascorbic acid: pH effect, specific action or both?: In abstracts of papers of the American chemical society. 16TH ST, NW, Washington, DC 20036 USA: *Amer Chemical Soc*, 2018. Vol. 255. P. 1155.
DOI: http://dx.doi.org/10.13140/RG.2.2.22321.48482

12. Piqué N., Berlanga M., Miñana-Galbis D. Health Benefits of Heat-Killed (Tyndallized) Probiotics: an Overview. *Int J Mol Sci*. 2019. Vol. 20, No. 10. P. E2534. DOI: http://dx.doi.org/10.3390/ijms20102534

13. Recent advances in combinatorial biosynthesis for drug discovery / E. L. Ang et al. *Drug Des Devel Ther*. 2015. No. 823.
DOI: http://dx.doi.org/10.2147/dddt.s63023

14. Singh A., Vishwakarma V., Singhal B. Metabiotics: The Functional Metabolic Signatures of Probiotics: Current State-of-Art and Future Research Priorities-Metabiotics: Probiotics Effector Molecules. *Advances in Bioscience and Biotechnology.* 2018. Vol. 9, No. 4. P. 147-189. DOI: http://dx.doi.org/10.4236/abb.2018.94012

15. Synthesis of dynamic riboflavin derivatives and the study of their ability to urease photoinactivation / A. V. Martynov et al. *Annals of Mechnikov Institute*. 2019. No. 3. P. 44-49.
DOI: http://doi.org/10.5281/zenodo.3469432.

16. Verghese R. J., Mathew S. K., David A. Antimicrobial activity of Vitamin C demonstrated on uropathogenic Escherichia coli and Klebsiella pneumoniae. *J Curr Res Sci Med.* 2017. No. 3. P. 88-93 DOI: http://dx.doi.org/10.4103/jcrsm.jcrsm_35_17

The article was received
2019.11.19

UDC 616.36-008:546.48:591.3
https://doi.org/10.26641/2307-0404.2020.1.200395

O.O. Nefodov,
D.V. Bilyshko,
K.A. Kushnaryova,
O.S. Shevchenko,
V.F. Shatorna,
O.I. Kefeli-Ianovska,
O.G. Kozlovskaya

DETERMINATION OF THE EFFECT OF CADMIUM ON EMBRYOGENESIS WITH ISOLATED ADMINISTRATION AND IN COMBINATION WITH SELENIUM AND GERMANIUM CITRATES

SE «Dnipropetrovsk medical academy of Health Ministry of Ukraine»
Department of Clinical Anatomy, Anatomy and Operative Surgery
V. Vernadsky str., 9, Dnipro, 49044, Ukraine
ДЗ «Дніпропетровська медична академія МОЗ України»
кафедра клінічної анатомії, анатомії та оперативної хірургії
(зав. – д. мед. н., доц. О.О. Нефьодова)
вул. В. Вернадського, 9, Дніпро, 49044, Україна
e-mail: elenanefedova1803@gmail.com

Цитування: Медичні перспективи. 2020. Т. 25, № 1. С. 24-31
Cited: Medicni perspektivi. 2020;25(1):24-31

Key words: *embryogenesis in rat, cadmium, germanium citrate, selenium citrate, liver*
Ключові слова: *ембріогенез щура, кадмій, цитрат германію, цитрат селену, печінка*
Ключевые слова: *эмбриогенез крысы, кадмий, цитрат германия, цитрат селена, печень*

Abstract. Determination of the effect of cadmium on embryogenesis with isolated administration and in combination with selenium and germanium citrates. Nefodov O.O., Bilyshko D.V., Kushnaryova K.A., Shevchenko O.S., Shatorna V.F., Kefeli-Ianovska O.I., Kozlovskaya O.G. *Cadmium compounds are part of the heavy metals found in biological systems forming the ecological crisis of the planet. An urgent task for researchers is to*

determine the morphological changes that occur in the body under the action of cadmium compounds in both prenatal and postnatal ontogenesis. The article discusses the results of the experimental effect of intragastric administration of cadmium chloride / cadmium citrate to pregnant female rats on the embryogenesis in isolation and in combination with selenium and germanium citrates. The aspect of the accumulation of cadmium salts in the liver of a 20-day-old embryo by polyelement analysis was also studied. The use of multielement analysis showed that the highest level of cadmium accumulation in the liver of embryos was found in the group of isolated administration of cadmium chloride. It has been proven that cadmium citrate accumulates in the liver to a lesser extent than cadmium chloride. The accumulation of cadmium chloride with selenium citrates, germanium in the groups of combined administration showed a decrease in the cadmium content in the liver of embryos. An analysis of the basic indicators of embryonic development of the performed experiment proved the embryotoxic effect of cadmium salts during enteral administration in modeling chronic cadmium intoxication, which is expressed in a decrease in the number of embryos in the litter and an increase in embryonic mortality in relation to the control group at all studied developmental periods. A decrease in embryonic mortality and an increase in the number of embryos at all stages of gestation in the experiment with the combined administration of cadmium salts with germanium citrate and selenium citrate indicates their antagonistic effect on cadmium embryotoxicity.

Реферат. Определение влияния кадмия на показатели эмбриогенеза при изолированном введении и в комбинации с цитратами селена и германия. Нефедов А.А., Билышко Д.В., Кушнарева Е.А., Шевченко Е.С., Шаторная В.Ф., Кефели-Яновская Е.И., Козловская А.Г. *Соединения кадмия, находящиеся в биологических системах, формируют экологический кризис планеты. Актуальной задачей для исследователей является определение морфологических изменений, возникающих в организме под действием соединений кадмия как в пренатальном, так и в постнатальном онтогенезе. В статье рассмотрены результаты влияния внутрижелудочного введения хлорида кадмия/цитрата кадмия на показатели эмбриогенеза беременным самкам крыс изолированно и в комбинации с цитратами селена и германия. Изучался также аспект накопления солей кадмия в печени 20-дневного эмбриона путем полиэлементного анализа. Использование полиэлементного анализа показало, что наивысший уровень накопления кадмия в печени эмбрионов обнаружено в группе изолированного введения хлорида кадмия. Доказано, что цитрат кадмия в меньшей степени накапливается в печени, чем хлорид кадмия. Накопление в группах комбинированного введения хлорида кадмия с цитратами селена, германия продемонстрировали снижение содержания кадмия в печени эмбрионов. Анализ базовых показателей эмбрионального развития проведенного эксперимента доказал эмбриотоксическое действие солей кадмия при энтеральном введении при моделировании хронической кадмиевой интоксикации, что выражается в уменьшении количества эмбрионов в помете и увеличении показателей эмбриональной смертности по отношению к группе контроля на всех исследуемых сроках развития. Снижение показателей эмбриональной смертности и увеличение количества эмбрионов на всех стадиях гестации в эксперименте при комбинированном введении солей кадмия с цитратом германия и цитратом селена свидетельствует об их антагонистическом действии на эмбриотоксичность кадмия.*

The changing state of the environment in industrialized countries encourages intensive study of the impact of environmental factors on biological objects. Among the most dangerous man-made environmental pollutants, heavy metals occupy a priority position, and prolonged contact with toxicants leads to impaired functioning of both the adult organism and the formation of prenatal dysadaptive processes. By affecting the balance of trace elements, cadmium can be accumulated in the human body and lead to acute and late complications [3, 7, 8]. Increasing content of heavy metals in environmental objects has an impact on the balance of trace elements in the human body, causing the so-called microelementoses. The problem of the latter is extremely important in all countries of the world, its solution, by definition of WHO is the main task in ensuring the health of the Earth's population in the XXI century. [11, 13]. Considering that cadmium belongs to the group of the most widespread pollutants, we believe that the urgent task for researchers is to determine the morphological changes that occur in the body under the action of cadmium compounds in both prenatal and postnatal ontogeny [4, 6]. The development of new remedies for the correction and treatment of trace element imbalance is constrained by the lack of knowledge about the features of trace elements exchange in the human body and the norm of daily requirement for them in conditions of high technogenic load, as well as data on the balance, forms and types of interaction of trace elements and ultramicroelements. The question of the interaction of trace elements during pregnancy and their indirect effect on the embryo remains open, as well as the search for new bioantagonists to toxic substances.

Germanium and selenium are trace elements that are essential. They increase the efficiency of the immune system in humans and have a wide range of biological activity: they have antihypoxic action, prevent the development of oxygen deficiency at the tissue level, stimulate immunity, suppress the

processes of reproduction of microbial cells, activating macrophages and specific cells of immunity [2, 4, 12].

All of the above indicates the need to study the morphogenetic changes that occur in embryogenesis of rat embryos and in the early stages after birth under the influence of cadmium compounds both in isolated administration and in combination with germanium and selenium citrates.

The purpose of the study is to experimentally investigate the effect of cadmium salts on the overall course of embryogenesis and accumulation in rat liver in isolated administration and in combination with germanium and selenium citrates.

MATERIALS AND METHODS OF RESEARCH

To simulate chronic toxicity during cadmium exposure throughout pregnancy, female rats of Wistar line were administered cadmium citrate or cadmium chloride isolated (at a dose of 1.0 mg/kg) or in combination with germanium citrate or selenium citrate per os daily. The selected dose of cadmium-containing compounds corresponds to 1/100 LD50 for cadmium [9].

The experimental model used solutions of cadmium citrate, selenium and germanium, obtained by the aquanotechnological method [1]. Given the pronounced antioxidant and antihypoxic properties of germanium and selenium, it was decided to use citrates of these metals as potential biological antagonists and against the background of cadmium intoxication [2, 4, 12].

Solutions of citrate forms of nanometals (cadmium, selenium and germanium) were obtained in accordance with the agreement on scientific cooperation at the Research Institute of Nanobiotechnology and Resource Conservation of Ukraine (Head – Professor V.A. Linnik).

In accordance with the conditions and requirements of embryonic experiments, we provided a complete diet, drinking water and careful care of the animals; the introduction of metal solutions was carried out from the first day of pregnancy daily, at the same time of a day (from 10 to 12 hours) [3, 5, 10].

For embryonic studies female rats with a dated gestation were taken. On the 13th and 20th day of pregnancy, animals were sacrificed operatively. Infant rats were removed from the uterus, live-dead test was done, they were weighed, photographed, and fixed in 10% formalin solution for further histological examination.

All rats were divided into 7 groups in which the animals received the following solutions: group 1 – control (n=145) – 0.5 ml of 0.9% NaCl. Group 2 – cadmium chloride at a dose of 1.0 mg/kg (n=126). Group 3 – cadmium citrate at a dose of 1.0 mg/kg (n=135). Group 4 – cadmium chloride at a dose of 1.0 mg/kg and selenium citrate at a dose of 0.1 mg/kg (n=147). Group 5 – cadmium citrate at a dose of 1.0 mg/kg and selenium citrate at a dose of 0.1 mg/kg (n=129). Group 6 – cadmium chloride at a dose of 1.0 mg/kg and germanium citrate at a dose of 0.1 mg/kg (n=147). Group 7 – cadmium citrate at a dose of 1.0 mg/kg and germanium citrate at a dose of 0.1 mg/kg (n=135).

The general development of the fetus was evaluated by the number of embryos, the number of yellow bodies of the ovaries of females, its compliance with the stage of development according to generally accepted criteria for the embryonic development of rats.

The embryotoxic effect of the test substances was evaluated by the following indicators:

1. Total embryonic mortality =

$$TEM = \frac{C - A}{C}$$

where A – the number of live fetuses
C – number of yellow bodies of pregnancy

2. Pre-implantation mortality =

$$PIM = \frac{C - (A + B)}{C}$$

where A is the number of live fetuses
B – number of dead (resorbed) fetuses
C – number of yellow bodies of pregnancy

3. Postimplantation mortality =

$$PostIM = \frac{B}{A + B}$$

where A is the number of live fetuses
B – number of dead (resorbed) fetuses

4. Number of fetuses per 1 female

Part of the embryos was frozen to measure cadmium content in embryonic samples by polyelement analysis. Polyelement analysis of biological materials by atomic emission method 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) in accordance with the agreement on scientific and creative cooperation (2018). Sampling and measurement of the metal content was carried out in accordance with GOST (AUSS) 30823-2002 The purpose of the analysis was to evaluate the dynamics of cadmium accumulation in the rat liver with isolated administration and in combination with zinc and selenium citrates.

Statistical analysis and analysis of results were performed according to conventional methods using

licensed statistical analysis software Statistica v.6.1 (StatSoft Inc., Serial No. AGAR909E415822FA) and Microsoft Excel. The reliability of statistical studies was performed using the Student's t-test.

Animal studies were performed in the vivarium setting of DMA in accordance with the "General Ethical Principles for Animal Experiments" (Kyiv, 2001), which are consistent with the European Convention for the Protection of Experimental Animals (Strasbourg, 1985).

RESULTS AND DISCUSSION

All the females in the experiment survived. In the control group, all embryos met standard criteria for rat embryonic development. There were no developmental defects in infant rats. The calculation of the average values of embryogenesis showed that in the group of isolated exposure to cadmium salts there was a decrease in the number of embryos during both pregnancy periods and an increase in the total embryonic mortality.

Thus, in the experimental group of the impact of cadmium citrate on the studied pregnancy, the number of living fetuses decreases relative to the control group in the following order: day 13 of pregnancy – by 7.4% ($p<0.05$), day 20 of pregnancy – by 10.2% ($p<0.05$).

In the experimental group of combined administration of cadmium chloride and germanium citrate, as well as cadmium chloride and selenium citrate, the average number of living fetuses per one female did not differ significantly from the control group (Fig. 1).

The analysis of the obtained results showed that on day 13 of embryogenesis the smallest indicator of the average values of the number of live embryos per female was observed in the group of isolated exposure to cadmium chloride and was equal to 8.13±0.31. On day 20, indicator decreased to 7.62±0.34 and was significantly less than the control group ($p<0.01$), this may be explained by the duration of destabilizing factor.

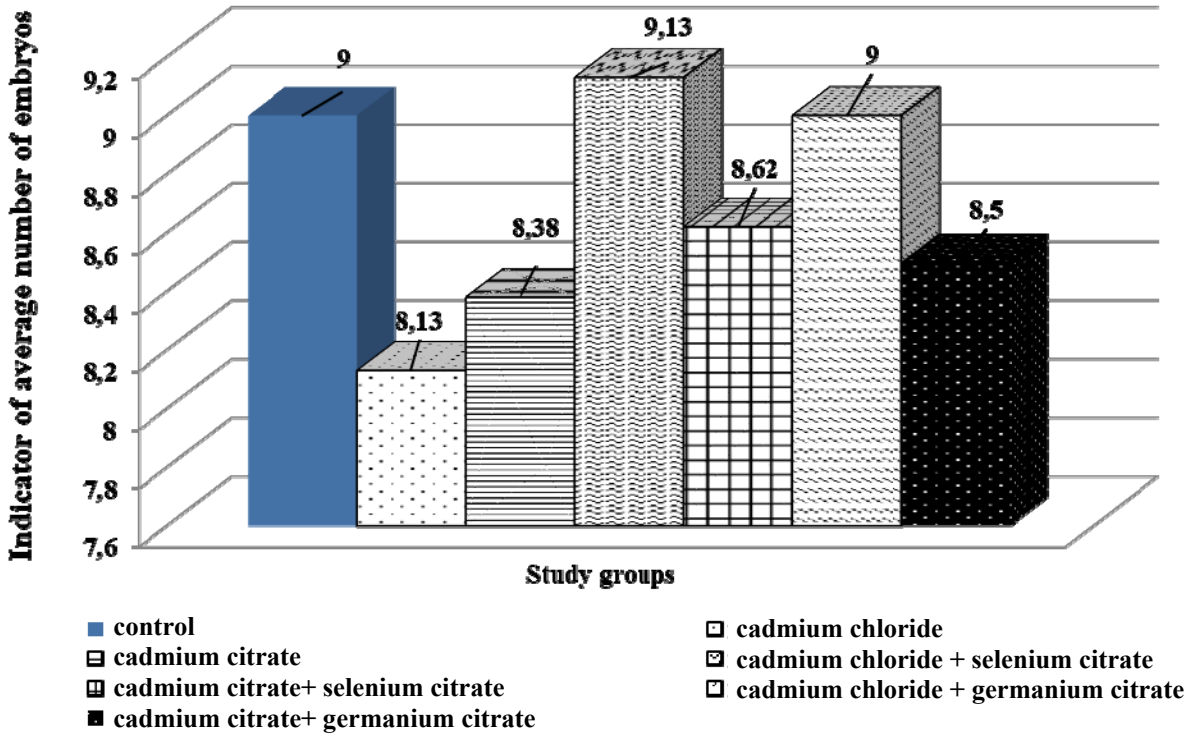

Fig. 1. Number of embryos per 1 female rat (average value) in control and experimental group on day 13 of embryogenesis

In the group of isolated effects of cadmium citrate the number of living fetuses was: day 13 of pregnancy – 8.38±0.19, day 20 – 8.50±0.34. This was significantly lower than in the cadmium chloride group ($p<0.05$).

In the groups of combined administration of cadmium salts with selenium citrate and germanium, the number of embryos in the litter of rats had no significant differences from the control group, indicating the modifying effect of metal citrates on

the embryotoxicity of cadmium compounds in the experiment ($p<0.05$) (Fig. 1, 2).

The next studied indicator of embryogenesis was total embryonic mortality, which directly depends on the pre-implantation and post-implantation mortality of embryos. In the groups of isolated administration of cadmium salts, this indicator was highest both on day 13 and on day 20 of embryonic development (Fig. 3). Thus, in the group of isolated administration of cadmium chloride, the total embryo mortality rate on day 13 was 0.15±0.02 (control 0.05±0.02) and exceeded the control values three times ($p<0.05$), and at the end embryogenesis increased to 0.25±0.02 (control remained 0.05±0.02), i.e. 5-fold increase ($p<0.01$), which is logical because cadmium intoxication continued. In the group of isolated exposure to cadmium citrate, this indicator was 0.15±0.02 on day 13, as well as in the impact of cadmium chloride, and on day 20 it was slightly lower than that of in exposure to cadmium chloride – 0.16±0.03 ($p<0.05$ vs. control).

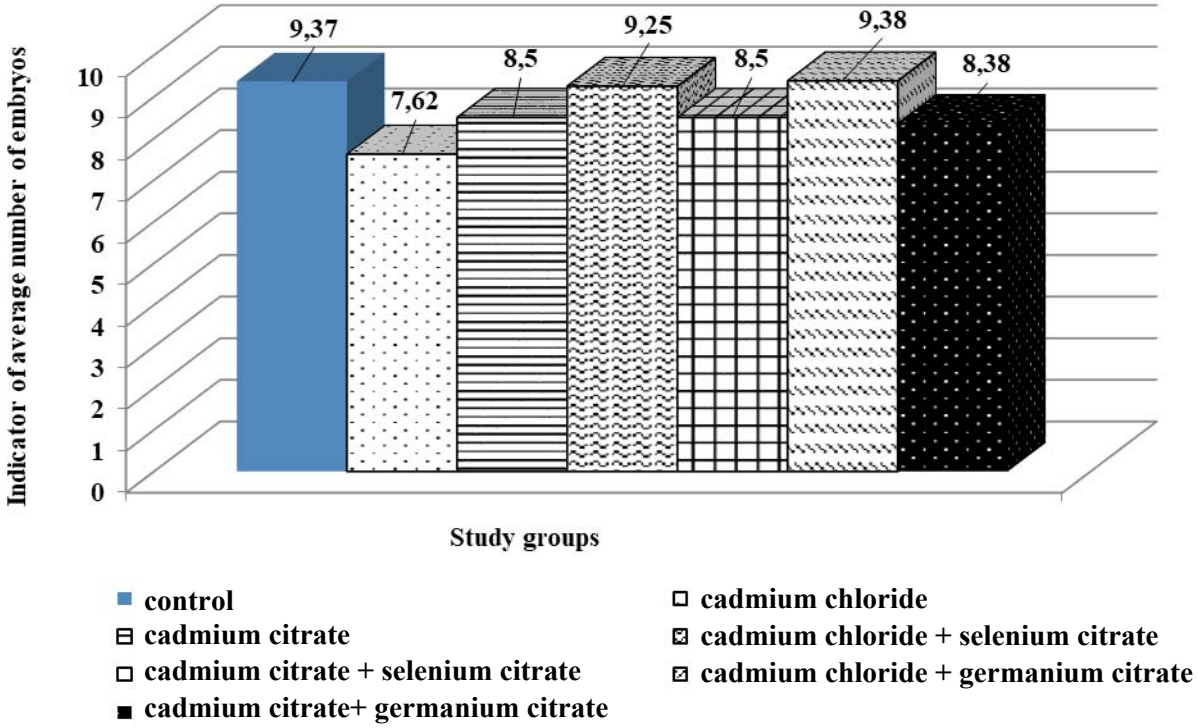

Fig. 2. Average number of embryos per 1 female rat in control and experimental group on day 20 of embryogenesis

Comparison in groups of exposure to isolated and combined administration of cadmium chloride revealed a modifying effect of citrate on cadmium embryotoxicity by this indicator. Both on day 13 of embryo development and at the end of embryogenesis, selenium and germanium citrates reduced total embryonic mortality compared with isolated administration of cadmium salts (Fig. 3). This is explained by the decrease in both pre-implantation and post-implantation mortality in these groups. Postimplantation mortality at exposure to cadmium chloride on day 13 of embryogenesis was 0.07±0.03 (control 0.025±0.02), and on day 20 it increased twice and reached 0.14±0.03 (control 0.025±0.02). In the groups of combined administration of cadmium chloride with metal citrate, this indicator significantly decreased by 2-2.5 times ($p<0.05$) (compared to the group of introduction of cadmium chloride) in both study periods.

When exposed to cadmium citrate, the preimplantation mortality rate was 0.09±0.03 on day 13 and on day 20, and was significantly higher than the control group ($p<0.05$), indicating the embryotoxic effect of citrate cadmium on embryo before implantation, which occurs on day 3-5 of pregnancy in the female rat.

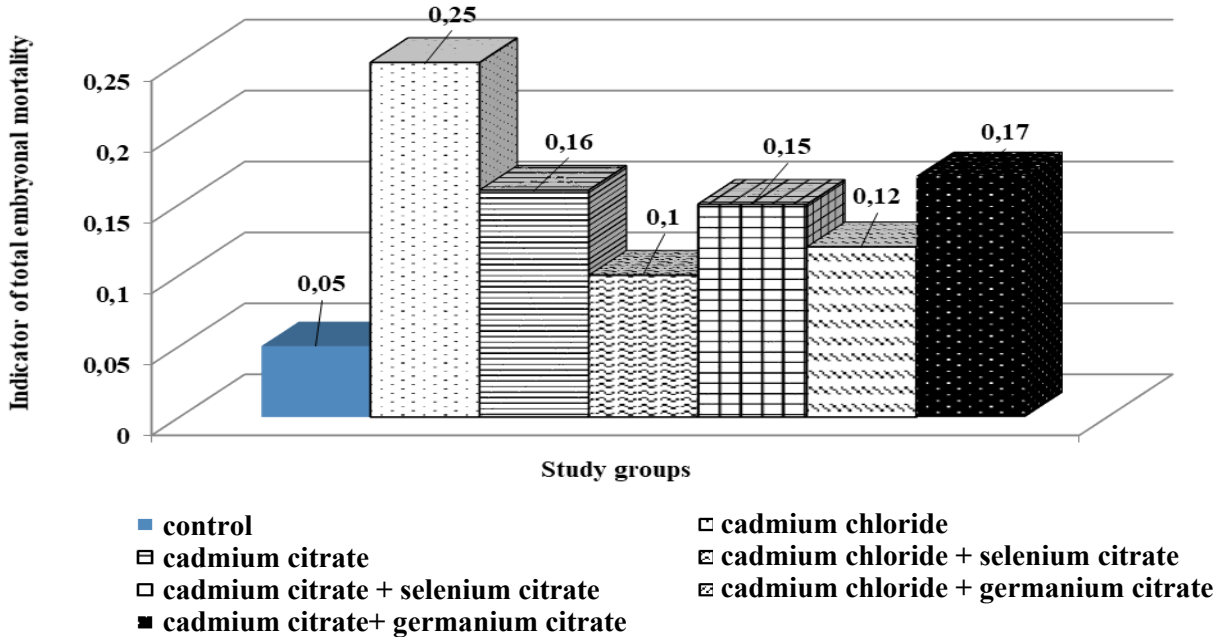

Fig. 3. Total embryonal mortality in control and experimental group on day 20 of embryogenesis

According to the purpose, the determination of cadmium accumulation in the liver of embryos was performed. The use of polyelement analysis showed that the content of cadmium in the liver of embryos on day 20 of the development varied both in the groups of isolated intoxication by cadmium salts and in the groups of combined administration. Thus, in the control group, the level of cadmium accumulation was 0.0065±0.0013 mcg/g, and in the cadmium chloride injection group this indicator was 2.4 times higher than the control values ($p<0.05$) and was equal to 0.0156±0.0023 mcg/g. When exposed to cadmium citrate, the accumulation of this metal in the liver was significantly less than even control and was 0.0007±0.0001 mcg/g ($p<0.001$). In groups of combined administration of cadmium chloride with metal citrate, there was a tendency to decrease of cadmium in the liver compared with the group of cadmium chloride ($p<0.001$) (Fig. 4).

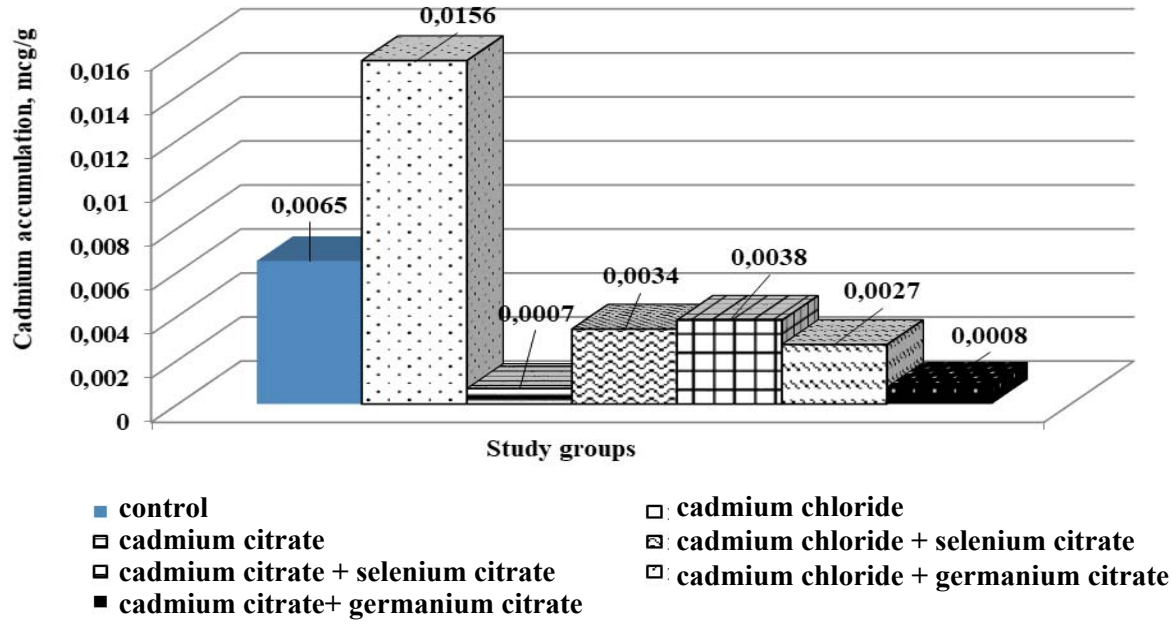

Fig.4. Indicators of cadmium accumulation in liver of rat embryos on day 20 of development by results of polyelement analysis

The data obtained indicate a decrease in the accumulation of cadmium under the influence of germanium and selenium citrates, which allows to consider metal citrates as potential bioantagonists of cadmium salts.

CONCLUSIONS

1. Analysis of baseline indicators of embryonic development of the experiment conducted proved the embryotoxic effect of cadmium salts at a dose of 1.0 mg/kg in enteral administration, which is reflected in a decrease in the number of embryos and an increase in embryonic mortality rates (total mortality in the cadmium chloride group was 3 times higher on day 13 ($p<0.05$) and 5 times higher on day 20 ($p<0.01$) relative to the control group.
2. Decrease in embryonic mortality rates at all stages of gestation in the combined administration of cadmium salts with germanium citrate and selenium citrate by 2-2.5 times compared with the cadmium chloride group ($p<0.05$) indicates their antagonistic effect on embryotoxicity.
3. The accumulation of cadmium in the liver is the highest of all experimental groups with isolated administration of cadmium chloride (2.4 times higher than the control group ($p<0.05$). The introduction of metal citrate against the background of cadmium intoxication leads to a decrease in the level of cadmium accumulation in the liver of rat embryos.

Prospects for further research. In the future, histological studies of the parenchymatous organs of embryos subjected to cadmium compounds and metal citrates are planned, which will help to detect changes at the tissue level and explain the causes of mortality.

REFERENCES

1. Borisevich VB, Kaplunenko VG, Kosinov MV. [Nanomaterials in Biology. Fundamentals of nano-veterinary medicine]. Kyiv: VD Avicenna; 2010. p. 416
2. Tadzhikulova OD, Abdullaeva GT, Ergashev NA, Komilov ED, Asrarov MI, Kulkaraev AK. [The influence of heavy metals on the blood glucose and glycogen content of rat liver]. Universum: chemistry and biology. 2019;3(57):53-58. Russian.
3. Dinerman AA. [The role of environmental pollutants in the violation of embryonic development]. Moskva: Medicine; 1980. p. 191. Russian.
4. Shatornaya VF, Garets VI, Kononova II, Stepanov SV, Dikhno NI [Combining effect of heavy metals on rat embryogenesis in experiment]. World of Medicine and Biology. 2014;4:170-4. Russian.
5. Garets VI, Shatorna VF, Ostrovskaya SS, Kononova II, Krasnov OO. [Methodical approaches to determination of embryotoxicity and teratogenicity of heavy metals in morphological experiments[. Ukrainian Journal of Medicine, Biology and Sports. 2015;1(1):189-94. Ukrainian.
6. Onul NM. [The content of trace elements in the body of the female and the fetus during physiological pregnancy and exposure to heavy metals]. Actual problems of modern medicine. 2014;14(3):235-8. Ukrainian.
7. Skalny AV. [Assessment and correction of the elemental status of the population is a promising area of domestic health care and environmental monitoring]. Microelements in medicine. 2018;19 (1):5-13. Russian.
8. Skalny AV, Zaitseva I P, Tinkov AA. [Microelements and sports. Personalized correction of the elemental status of athletes]. Moskva: Sport; 2018. p. 288. Russian.
9. Fedorenko VI. Substantiation of allowable daily doses of lead and cadmium in diets. Medical perspectives. 2019;24(1):73-80.
doi: https://doi.org/10.26641/2307-0404.2019.1.162310
10. Shafran LM, Pikhtieva OG, Bolshoy DV. [An algorithm for laboratory tests for suspected dyshomeostasis of heavy metals]. Actual problems of transport medicine. 2014;1(4):97-105. Ukrainian.
11. Azad Gull, Ashaq Ahmad Dar, Manoj Sharma. Effects of Heavy Metals on the Health of Pregnant Women and Fetus: A Review. International Journal of Theoretical & Applied Sciences. 2018;10(1):01-09.
12. Lamas GA, Navas-Acien A, et al. Heavy metals, cardiovascular disease, and the unexpected benefits of edetate chelation therapy. J Am Coll. Cardiol. 2016;67:2411-8. doi: https://doi.org/10.1016/j.jacc.2016.02.066
13. Jacobo-Estrada Tania, Santoyo-Sánchez Mitzi, Thévenod Frank, Olivier Barbier. Cadmium Handling, Toxicity and Molecular Targets Involved during Pregnancy: Lessons from Experimental Models. International Journal of Molecular Sciences. 2017;18:136-55. doi: https://doi.org/10.3390/ijms18071590

СПИСОК ЛІТЕРАТУРИ

1. Борисевич В. Б., Каплуненко В. Г., Косінов М. В. Наноматеріали в біології. *Основи нановетеринарії*. Київ: ВД «Авіцена», 2010. 416 с.
2. Влияние тяжелых металлов на содержание глюкозы крови и гликогена печени крыс / О. Д. Таджикулова и др. Universum: химия и биология. 2019. Т. 57, № 3. С. 53-58.
3. Динерман А. А. Роль загрязнителей окружающей среды в нарушении эмбрионального развития. Москва: Медицина, 1980. 191 с.

4. Комбинирующее влияние тяжелых металлов на эмбриогенез крысы в эксперименте / В. Ф. Шаторная и др. *Мир Медицины и Биологии*. 2014. Т. 46, № 4. С. 170-174.

5. Методичні підходи до визначення ембріотоксичності та тератогенності важких металів в морфологічних експериментах / В. І. Гарець та ін. *Укр. журнал медицини, біології та спорту.* 2015. Т.1, № 1. С. 189-194.

6. Онул Н. М. Вміст мікроелементів в організмі самки і плоду при фізіологічній вагітності та впливі важких металів. *Актуальні проблеми сучасної медицини.* 2014. Т. 14. Вип 3. С. 235-238.

7. Скальный А. В. Оценка и коррекция элементного статуса населения – перспективное направление отечественного здравоохранения и экологического мониторинга. *Микроэлементы в медицине*. 2018. Т. 19, № 1. С. 5-13.

8. Скальный А. В., Зайцева И. П., Тиньков А. А. Микроэлементы и спорт. Персонализированная коррекция элементного статуса спортсменов: монография. Москва: Спорт, 2018. 288 с.

9. Федоренко В. І. Обґрунтування допустимих добових доз свинцю і кадмію в добових раціонах харчування. *Медичні перспективи*. 2019. Т. 24, № 1. С. 73-80. DOI: https://doi.org/10.26641/2307-0404.2019.1.162310

10. Шафран Л. М., Пихтєєва О. Г., Большой Д. В. Алгоритм лабораторних досліджень при підозрі на дисгомеостаз важких металів. *Актуальні проблеми транспортної медицини.* 2014. Т.1 (38-1), №4. С. 97-105.

11. Gull Azad, Dar Ashaq Ahmad, Sharma Manoj. Effects of Heavy Metals on the Health of Pregnant Women and Fetus: A Review. *Inter. Journal of Theoretical & Applied Sciences.* 2018. Vol. 10, No. 1. P. 1-9.

12. Lamas G. A., Navas-Acien A, Mark D. B., Lee K. L. Heavy metals, cardiovascular disease, and the unexpected benefits of edetate chelation therapy. *J Am Coll. Cardiol.* 2016. Vol. 67. P. 2411-2418. DOI: https://doi.org/10.1016/j.jacc.2016.02.066

13. Jacobo-Estrada Tania, Santoyo-Sánchez Mitzi, Thévenod Frank, Olivier Barbier. Cadmium Handling, Toxicity and Molecular Targets Involved during Pregnancy: Lessons from Experimental Models. *Inter. Journal of Molecular Sciences.* 2017. No. 18. P. 136-155. DOI: https://doi.org/10.3390/ijms18071590

The article was received
2019.10.16