

CHANGES IN THE MAIN INDICATORS OF EMBRYO LETHALITY IN RATS UNDER THE INFLUENCE OF CADMIUM SALTS**Dnipro State Medical University (Dnipro, Ukraine)****irakolosova0405@gmail.com**

Cadmium has a negative impact on health, affecting the kidneys, liver, circulatory and reproductive systems and can lead to the formation of diseases during the intrauterine period. The purpose of our study was to experimentally determine the potential embryotoxic effects of cadmium chloride and cadmium citrate (at a dose of 1.0 mg/kg) in isolation and under conditions of correction with citrates (cerium, zinc, and a nanocomposite based on iodine, sulfur, and selenium citrates). For the study, 180 young female Wistar rats were used, which were divided into 9 groups, depending on the solutions of cadmium salts or saline. The calculation and comparison of standard indicators of embryonic development on the 13th and 20th day of embryogenesis indicate a pronounced embryonic lethal effect of cadmium salts, manifested by an increase in total embryonic mortality due to an increase in preimplantation and postimplantation mortality of rat embryos compared to the control group at both studied periods of embryogenesis and an embryotoxic effect manifested by a decrease in the number of live fetuses per female. In the groups of combined action of cadmium salts with cerium/zinc citrates/nanocomposite (iodine+sulfur+selenium), the use of citrates led to an improvement in the studied parameters compared to the groups of cadmium salts, which indicates a decrease in the negative effect of cadmium on embryonic lethality in rats.

Key words: embryogenesis, embryonic mortality, cadmium chloride, cadmium citrate, experiment.

Connection of the publication with planned research works.

The experimental study was carried out within the framework of the research work of the Department of Medical Biology, Pharmacognosy and Botany of the State Institution "DMA" "Biological basis of morphogenesis of organs and animals under the influence of trace elements and ultramicroelements in the experiment" (state registration number 0118U006635).

Introduction.

Chronic exposure to toxic compounds in the environment, including lead, cadmium, arsenic, mercury and others, are known to cause cancer and other diseases in humans, disrupt cellular processes such as redox balance and various intracellular stress signaling pathways [1-3]. The heavy metal cadmium (Cd) is a widespread environmental pollutant associated with many modern industrial processes, occurring in low concentrations in nature, but it is present in almost all food, water, and cigarette smoke. In European countries, the human body receives 10-30 micrograms of cadmium per day and is very poorly excreted from the body and accumulates for a long time in the blood, kidneys and liver. The half-life of cadmium from the body is 15-30 years [4]. The effects of cadmium on the body depend on the way of intake, dose and duration of exposure [5]. Depending on the dose, Cd either enhances or inhibits progesterone biosynthesis, disrupts intrafollicular processes during oocyte maturation in the ovaries [6], as well as during implantation and further embryo development [7-9]. Cadmium also has a negative effect on the male reproductive system, disrupting the functioning of the testes and causing their dysfunction [10-12].

Due to the fact that cadmium is the most widespread toxicant, a relevant area of research is to de-

termine the morphological changes that occur in the body under the influence of cadmium compounds in the prenatal period of ontogeny, nanoparticles of a substance often have properties that macroscopic samples of these substances do not. The rapid development of the nanotechnology industry has led to a significant increase in the number of various nanomaterials. The search and development of new remedies for the correction and treatment of trace element imbalances requires new knowledge about the peculiarities of trace element metabolism in the human body and the norms of daily requirement for them under conditions of increased man-made load, as well as data on the balance, forms and types of interaction of trace elements and ultramicroelements in case of their simultaneous intake. The question of the interaction of trace elements during pregnancy and their indirect effect on the embryo remains open, as does the search for new bioantagonists to toxicants. Cerium, zinc, selenium are trace elements that increase the efficiency of the immune system and have a wide range of biological activity: they have anti-hypoxic effects, prevent the development of oxygen deficiency at the tissue level, stimulate immunity by suppressing the reproduction of microbial cells, activating macrophages and specific immune cells, and stimulate the production of interferon [13-15].

The aim of the study.

Experimental determination of the embryotoxic effect of cadmium salts (chloride and citrate) in isolation, in combination with cerium/germanium/zinc citrate salts and a nanocomposite based on iodine + sulfur + selenium citrates and evaluation of the potential of citrate compounds to exert a potential bioantagonistic effect on the general course of embryogenesis of cadmium salts.

Object and methods of the study.

Experiments to study the embryotropic effect of intragastric administration of cadmium salts for 13 and 20 days isolated and in combination with metal citrates were performed on 180 white mature female Wistar rats. The rats were kept in the vivarium of Dnipro State Medical University under natural light, on a standard diet and with free access to water and food. The experiment was conducted in a ventilated room at an air temperature of 20-25°C and relative humidity of 50-65%, with animals housed in standard plastic cages with no more than 3-4 animals in each.

Animal maintenance and experiments were carried out in accordance with the provisions of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 2005), the Law of Ukraine "On Protection of Animals from Cruelty" (2006, Article 26), and the "General Ethical Principles for Animal Experiments" adopted by the Fifth National Congress on Bioethics (Kyiv, 2013).

All procedures with animals at all stages of the study were performed in the morning in compliance with generally accepted international requirements. By the method of "blind ranking", the animals were divided into 9 groups, depending on the administration of intragastric solutions: Group 1 (DN№1, female=20, embryos=159) – cadmium chloride in isolation at a dose of 1.0 mg/kg; Group 2 (DN№2, female=20, embryos =188) – cadmium chloride at a dose of 1.0 mg/kg in combination with a solution of cerium citrate at a dose of 1.3 mg/kg; Group 3 (DN№3, female=20, embryos=200) – cadmium chloride at a dose of 1.0 mg/kg in combination with a solution of zinc citrate at a dose of 1.5 mg/kg; Group 4 (DN№4, female=20, embryos=194) – cadmium chloride at a dose of 1.0 mg/kg in combination with a solution of nanocomposite (based on iodine, sulfur and selenium citrates at a dose of 2.0 mg/kg; Group 5 (DN№5, female=20, embryos=166) – cadmium citrate at a dose of 1.0 mg/kg; Group 6 (DN№6, female=20, embryos=185) – cadmium citrate at a dose of 1.0 mg/kg with cerium citrate (1.3 mg/kg); Group 7 (DN№7, female=20, embryos=179) – cadmium citrate at a dose of 1.0 mg/kg with zinc citrate (1.5 mg/kg), group 8 (DN№9, female=20, embryos=180) – cadmium citrate at a dose of 1.0 mg/kg with a nanocomposite at a dose of 2.0 mg/kg, group 9 – control (female=20, embryos=212) – proportional volume of sterile saline solution by the same method.

According to generally accepted experimental procedures, solutions of the test substances were administered to females intragastrically through a gavage tube once a day, at the same time throughout pregnancy. During the administration of the solutions, the condition and behavior of females, body

weight dynamics, rectal temperature, and gestation duration were recorded. In each experimental group, females were divided into 2 subgroups of 10 animals each, depending on the duration of the administration of the test substances. On the 13th and 20th day of pregnancy, the animals were surgically slaughtered and autopsied. After opening the abdominal cavity of females in the uterus, the number of implantation sites and the presence of live and dead fetuses were counted.

The general development of fetuses was assessed by the number of corpus luteum of the ovaries of females, the number of embryos, and the correspondence to the developmental stage according to the generally accepted criteria for embryonic development in rats.

The possible effect of the studied substances on embryo lethality was determined according to generally accepted criteria: preimplantation, postimplantation embryonic mortality, total embryonic mortality, number of fetuses and corpora lutea per female, intrauterine survival rates, morphological (anatomical) malformations, and general fetal retardation, which were calculated using well-known formulas.

To obtain statistical conclusions when comparing samples, the Kruskal-Wallis test and the Mann-Whitney test with the Bonferroni correction were used in the

Table 1 – Number of live fetuses and yellow bodies per female of the control and experimental groups

Groups / Indicators	Day	Live fetuses, units	p criterion Mann-Whitney	Yellow bodies, units	p criterion Mann-Whitney
Control	13	10.00 (10.00; 11.00)	-	11.00 (10.00;11.00)	-
	20	11.00 (10.00; 13.00)	-	11.50 (10.00;13.00)	-
cadmium chloride	13	8.00 (7.00; 8.00)	0.00002 ¹	10.00 (9.00; 11.00)	0.04 ¹
	20	8.00 (8.00; 8.00)	0.002 ¹	10.50 (10.00;11.00)	0.12 ¹
cadmium chloride + cerium citrate	13	9.50 (9.00; 10.00)	0.12 ¹ 0.003 ²	11.00 (10.00; 12.00)	0.91 ¹ 0.14 ²
	20	9.00 (9.00; 10.00)	0.002 ¹ 0.04 ²	11.00 (10.00; 12.00)	0.10 ¹ 0.39 ²
cadmium chloride + zinc citrate	13	9.50 (9.00; 10.00)	0.14 ¹ 0.0007 ²	11.00 (10.00; 12.00)	0.68 ¹ 0.03 ²
	20	9.50 (8.00; 13.00)	0.44 ¹ 0.04 ²	11.50 (10.00; 13.00)	1.00 ¹ 0.17 ²
cadmium chloride + nanocomposite	13	9.50 (9.00; 10.00)	0.06 ¹ 0.03 ²	11.50 (10.00; 13.00)	0.39 ¹ 0.03 ²
	20	9.50 (9.00; 13.00)	0.48 ¹ 0.02 ²	12.00 (11.00; 14.00)	0.43 ¹ 0.01 ²
cadmium citrate	13	8.50 (7.00; 9.00)	0.005 ¹	10.00 (10.00; 11.00)	0.35 ¹
	20	8.50 (7.00; 9.00)	0.003 ¹	10.50 (10.00;11.00)	0.25 ¹
cadmium citrate + cerium citrate	13	10.00 (9.00; 11.00)	0.14 ¹ 0.12 ³	11.00 (10.00; 12.00)	0.97 ¹ 0.39 ³
	20	9.00 (8.00; 11.00)	0.03 ¹ 0.17 ³	10.50 (9.00; 12.00)	0.25 ¹ 0.80 ³
cadmium citrate + zinc citrate	13	9.00 (8.00; 10.00)	0.009 ¹ 0.58 ³	10.00 (9.00; 11.00)	0.08 ¹ 0.35 ³
	20	9.00 (8.00; 10.00)	0.04 ¹ 0.09 ³	11.00 (9.00; 12.00)	0.31 ¹ 1.00 ³
cadmium citrate + nanocomposite	13	9.00 (9.00; 10.00)	0.02 ¹ 0.22 ³	10.00 (10.00; 11.00)	0.22 ¹ 0.85 ³
	20	9.00 (8.00; 10.00)	0.02 ¹ 0.22 ³	10.00 (9.00; 11.00)	0.06 ¹ 0.19 ³

Notes: p¹ – for the control group; p² – for the group of isolated cadmium chloride exposure; p³ – for the group of isolated action of cadmium citrate

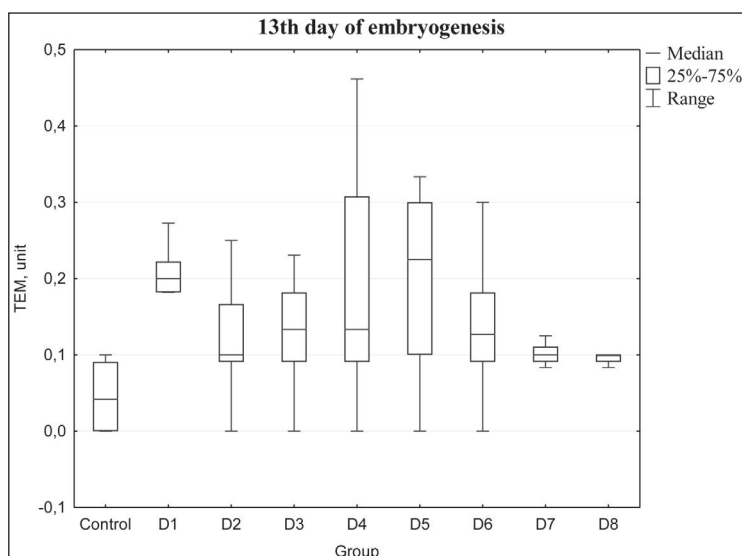


Figure 1 – Indicators of total embryonic mortality in the control and experimental groups on 13th day of embryogenesis.

STATISTICA 10 program (StatSoft Inc., USA) (significance level $p \leq 0.05$).

Research results and their discussion.

The analysis of the results shows that the number of live fetuses on the 13th day of embryogenesis varied in the control group from 9.00 to 12.00 fetuses and averaged 10.00 (10.00; 11.00) embryos (median and 1st, 3rd quartile – Me (25%; 75%)), in the group of isolated action of cadmium chloride – from 7.0 to 9.0 embryos and averaged 8.00 (7.00; 8.00) embryos, in the groups of combined action of chloride with citrates: cerium – from 7.00 to 12.00 embryos and averaged 9.00 (9.00; 10.00), zinc – from 8.00 to 14.0 embryos and averaged 9.50 (9.00; 10.00), iodine + sulfur + selenium (nanocomposite) – from 6.00 to 12.00 embryos and averaged 9.50 (9.00; 10.00), in the group of isolated action of cadmium citrate – from 6.00 to 12.00 embryos and averaged 8.50 (7.00; 9.00) embryos, in the groups of combined action of cadmium citrate with citrates: cerium – from 7.00 to 11.00 embryos and averaged 9.50 (9.00; 10.00), zinc – from 5.00 to 11.00 embryos and averaged 9.00 (8.00; 10.00), iodine + sulfur + selenium (nanocomposite) –

from 5.00 to 11.00 embryos and averaged 9.00 (9.00; 10.00) (**table 1**).

At the same time, on the 20th day, the number of live embryos varied in the control group from 9.00 to 12.00 embryos and averaged 10.00 (10.00; 11.00) embryos, in the group of isolated action of cadmium chloride – from 7.00 to 9.00 embryos and averaged 8.00 (7.00; 8.00) embryos, in the groups of combined action of chloride with citrates: cerium – from 7.00 to 12.00 embryos and averaged 9.00 (9.00; 10.00), zinc – from 8.00 to 14.00 embryos and averaged 9.50 (9.00; 10.00), iodine + sulfur + selenium (nanocomposite) – from 6.00 to 12.00 embryos and averaged 9.50 (9.00; 10.00), in the group of isolated action of cadmium citrate – from 6.00 to 12.00 embryos and averaged 8.50 (7.00; 9.00) embryos, in the groups of combined action of cadmium citrate with citrates cerium – from 7.00 to 11.00 embryos and averaged 9.50 (9.00; 10.00), zinc – from 5.00 to 11.00 embryos and averaged 9.00 (8.00; 10.00), iodine + sulfur + selenium (nanocomposite) – from 5.00 to 11.00 embryos and averaged 9.00 (9.00; 10.00).

Thus, on the 13th day of embryogenesis, the isolated administration of cadmium chloride statistically significantly reduces the number of fetuses by 20.0%, and cadmium citrate by 15%, and on the 20th day of embryogenesis by 27.3% and 22.7% compared to the control group, respectively. At the same time, the analysis of the results obtained in the groups of combined exposure to cadmium salts with metal citrates showed an improvement of this indicator on day 13th of embryogenesis. Thus, under the influence of cadmium chloride with cerium/zinc citrates/nanocomposite, the number of embryos was significantly higher by 18.8% relative to the group of isolated exposure to cadmium chloride, and under the combined effect of cadmium citrate with zinc citrate and nanocomposite, the number of fetuses increased by 5.9%, and with cerium citrate by 17.6% relative to the group of isolated exposure to cadmium citrate. On the 20th day of embryogenesis in the groups of combined action of cadmium salts with metal citrates, the number of fetuses was also higher than in the groups of isolated action of cadmium salts. In the groups of combined exposure to cadmium chloride and cerium citrate, the number of fetuses was 12.5% higher, and with zinc citrate and nanocomposite – 18.8% higher compared to the group of isolated exposure to cadmium chloride. Under the combined effect of cadmium citrate with cerium citrate, zinc citrate and nanocomposite, the fetuses yield was 5.9% higher compared to the isolated effect of cadmium citrate.

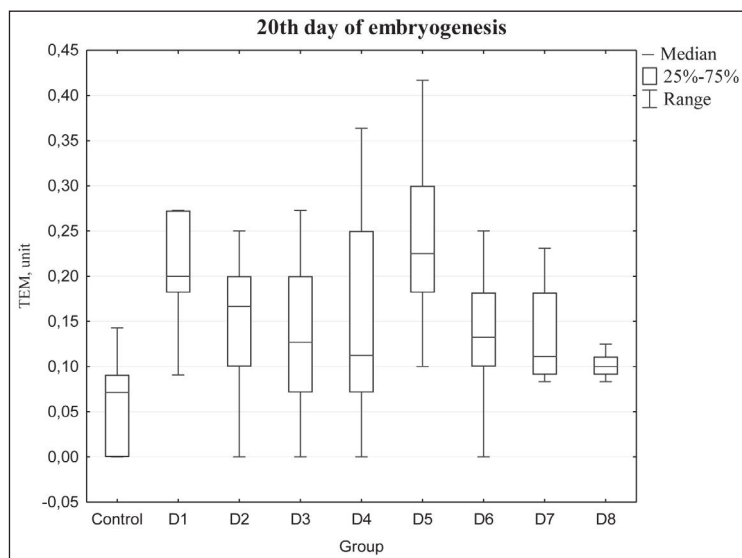


Figure 2 – Indicators of total embryonic mortality in the control and experimental groups on 20th day of embryogenesis.

The number of corpora lutea in the groups of isolated administration of cadmium salts on day 13th of embryogenesis decreased by 9.1%, and on day 20th – by 8.7% compared to the control group. Under the complex action of cadmium chloride with cerium citrate, the number of corpus luteum increased by 10.0% (day 13) and 4.8% (day 20), with zinc citrate

by 10.0% (day 13) and 9.5% (day 20), with nanocomposite by 15.0% (day 13) and 14.3% (day 20).

The analysis of the results of embryolethal effects (**table 2**) shows that the total embryonic mortality (TEM) on the 13th day of embryogenesis varied in the control group from 0.00 to 0.10 units and averaged 0.04 (0.00; 0.09) units (median and 1st, 3rd quartiles – Me (25%; 75%)), in the group of isolated action of cadmium chloride – from 0.11 to 0.30 units and averaged 0.20 (0.18; 0.22) units, in the groups of combined action of chloride with citrates: cerium – from 0.00 to 0.25 units and averaged 0.10 (0.09; 0.17), zinc – from 0.00 to 0.23 units and averaged 0.13 (0.09; 0.18), iodine + sulfur + selenium (nanocomposite) – from 0.00 to 0.46 units and averaged 0.13 (0.09; 0.31), in the group of isolated action of cadmium citrate – from 0.00 to 0.33 units and averaged 0.23 (0.10; 0.30), in the groups of combined action of cadmium citrate with citrates: cerium – from 0.00 to 0.30 units and averaged 0.13 (0.09; 0.18), zinc – from 0.08 to 0.17 units and averaged 0.10 (0.09; 0.11), iodine + sulfur + selenium (nanocomposite) – from 0.08 to 0.17 units and averaged 0.10 (0.09; 0.10) (**table 2, fig. 1**).

At the same time, on the 20th day of embryogenesis, the total embryonic mortality varied in the control group from 0.00 to 0.14 units and averaged 0.07 (0.00; 0.09) units (median and 1st, 3rd quartile – Me (25%; 75%)), in the group of isolated action of cadmium chloride – from 0.09 to 0.44 units and averaged 0.20 (0.18; 0.27) units, in the groups of combined action of chloride with citrates: cerium – from 0.00 to 0.25 units and averaged 0.17 (0.10; 0.20), zinc – from 0.00 to 0.27 units and averaged 0.13 (0.07; 0.20), iodine + sulfur + selenium (nanocomposite) – from 0.00 to 0.36 units and averaged 0.11 (0.07; 0.25), in the group of isolated action of cadmium citrate – from 0.10 to 0.42 units and averaged 0.23 (0.18; 0.30), in the groups of combined action of cadmium citrate with citrates: cerium – from 0.00 to 0.25 units and averaged 0.13 (0.10; 0.18), zinc – from 0.00 to 0.27 units and averaged 0.13 (0.07; 0.20), iodine + sulfur + selenium (nanocomposite) – from 0.00 to 0.36 units and averaged 0.11 (0.07; 0.25) (**fig. 2**).

It should be noted that statistically significantly higher rates of total embryonic mortality were observed with the isolated administration of cadmium salts both on day 13th of embryogenesis: the administration of cadmium chloride increased the TEM by 5.0 times and cadmium citrate by 5.8 times, and on day 20th of embryogenesis: by 2.9 times and cadmium citrate by 3.3

Table 2 – Number of live fetuses and yellow bodies per female of the control and experimental groups

Groups / Indicators	Day	TEM, units	P criterion Mann-Whitney	Pre-implantation mortality, units	P criterion Mann-Whitney	Postimplantation mortality, units	P criterion Mann-Whitney
Control	13	0.04 (0.00; 0.09)	-	0.00 (0.00; 0.00)	-	0.00 (0.00; 0.09)	-
	20	0.07 (0.00; 0.09)	-	0.00 (0.00; 0.00)	-	0.00 (0.00; 0.09)	-
cadmium chloride	13	0.20 (0.18; 0.22)	0.00001 ¹	0.11 (0.09; 0.20)	0.00002 ¹	0.10 (0.00; 0.13)	0.09 ¹
	20	0.20 (0.18; 0.27)	0.00008 ¹	0.10 (0.09; 0.18)	0.00001 ¹	0.11 (0.00; 0.17)	0.06 ¹
cadmium chloride + cerium citrate	13	0.10 (0.09; 0.17)	0.01 ¹ 0.01 ²	0.00 (0.00; 0.11)	0.39 ¹ 0.04 ²	0.09 (0.00; 0.10)	0.14 ¹ 0.44 ²
	20	0.17 (0.10; 0.20)	0.00008 ¹ 0.08 ²	0.13 (0.00; 0.17)	0.00001 ¹ 0.44 ²	0.05 (0.00; 0.10)	0.06 ¹ 0.08 ²
cadmium chloride + zinc citrate	13	0.13 (0.09; 0.18)	0.009 ¹ 0.02 ²	0.09 (0.07; 0.10)	0.01 ¹ 0.01 ²	0.05 (0.00; 0.10)	0.31 ¹ 0.28 ²
	20	0.13 (0.07; 0.20)	0.03 ¹ 0.05 ²	0.05 (0.00; 0.15)	0.14 ¹ 0.25 ²	0.07 (0.00; 0.10)	0.53 ¹ 0.14 ²
cadmium chloride + nano-composite	13	0.13 (0.09; 0.31)	0.03 ¹ 0.44 ²	0.13 (0.09; 0.23)	0.0005 ¹ 0.74 ²	0.00 (0.00; 0.00)	0.74 ¹ 0.06 ²
	20	0.11 (0.07; 0.25)	0.06 ¹ 0.12 ²	0.07 (0.00; 0.23)	0.04 ¹ 0.12 ²	0.04 (0.00; 0.09)	0.91 ¹ 0.04 ²
cadmium citrate	13	0.23 (0.10; 0.30)	0.004 ¹	0.10 (0.08; 0.10)	0.002 ¹	0.11 (0.00; 0.18)	0.03 ¹
	20	0.23 (0.18; 0.30)	0.00008 ¹	0.10 (0.10; 0.18)	0.00001 ¹	0.11 (0.10; 0.14)	0.08 ¹
cadmium citrate + cerium citrate	13	0.13 (0.09; 0.18)	0.01 ¹ 0.17 ³	0.09 (0.00; 0.10)	0.03 ¹ 0.44 ³	0.04 (0.00; 0.09)	0.53 ¹
	20	0.13 (0.10; 0.18)	0.007 ¹ 0.02 ³	0.10 (0.00; 0.15)	0.02 ¹ 0.17 ³	0.00 (0.00; 0.09)	0.97 ¹ 0.02 ³
cadmium citrate + zinc citrate	13	0.10 (0.09; 0.11)	0.003 ¹ 0.06 ³	0.09 (0.00; 0.10)	0.05 ¹ 0.44 ³	0.00 (0.00; 0.09)	0.68 ¹ 0.17 ³
	20	0.11 (0.09; 0.18)	0.005 ¹ 0.01 ³	0.10 (0.00; 0.13)	0.01 ¹ 0.28 ³	0.00 (0.00; 0.09)	0.97 ¹ 0.02 ³
cadmium citrate + nano-composite	13	0.10 (0.09; 0.11)	0.005 ¹ 0.04 ³	0.09 (0.00; 0.10)	0.06 ¹ 0.28 ³	0.00 (0.00; 0.09)	0.74 ¹ 0.12 ³
	20	0.10 (0.09; 0.11)	0.01 ¹ 0.004 ³	0.10 (0.00; 0.10)	0.05 ¹ 0.06 ³	0.04 (0.00; 0.10)	0.68 ¹ 0.004 ³

Notes: p¹ – for the control group; p² – for the group of isolated cadmium chloride exposure; p³ – for the group of isolated action of cadmium citrate

times compared to the control group, respectively. At the same time, this indicator improved in the group of isolated action of cadmium chloride in combination with cadmium chloride and metal citrates: with cerium citrate by 50.0% (day 13) and 15.0% (day 20), with zinc citrate by 35.0% both on the 13th and 20th day, with nanocomposite by 35.0% (day 13) and 45% (day 20), and with the complex effect of cadmium citrate with cerium citrate by 43.5% (13th and 20th days), with zinc citrate by 56.5% (13th day) and 52.2% (20th day), and with nanocomposite by 56.5% (13th and 20th days) in the group of isolated cadmium citrate exposure.

The analysis of preimplantation and postimplantation mortality rates when rats were administered cadmium salts during 13 and 20 days of embryogenesis revealed a tendency to increase these indicators compared to the corresponding values of the control group, and in the groups of combined exposure to cadmium salts with cerium/zinc/iodine citrates + sulfur + selenium (nanocomposite), a decrease in these indicators compared to the isolated administration of cadmium salts.

Conclusions.

In the course of the experimental study, it was found that the result of intragastric administration of cadmium chloride and cadmium citrate to Wistar rats at a dose of 1.0 mg/kg (in terms of metal) was a significant increase in the total embryonic mortality rate 5.0 times (13th day) and 2.9 times (20th day) in the group of isolated exposure to cadmium chloride and 5.8 times and 3.3 times, respectively, in the group of isolated exposure to cadmium citrate; preimplantation mortality: 11.0 and 10.0 times in the group exposed to cadmium chloride, and 10.0 times in the group exposed to cadmium citrate; and postimplantation mortality: 10.0 and 11.0 times and 10.0 times, respectively, compared to the control

group at both studied periods of embryogenesis, indicating the embryolethal effect of these cadmium salts. At the same time, the number of fetuses per female in the cadmium chloride group decreased by 20.0% on day 13th of embryogenesis and by 27.3% on day 20th, and in the cadmium citrate group by 15% and 22.7%, respectively, compared to the control group.

Prospects for further research.

In our opinion, it is promising to identify and compare the level of cadmium accumulation in embryonic organs by polyelement analysis and histological studies, which will help to identify changes at the tissue level and may explain the level of embryonic mortality.

References

1. Arustamian OM, Tkachyshyn VS, Aleksiyshuk OY. The effect of cadmium compounds on the human body. *Emergency medicine.* 2016;7(78):109-14.
2. Genchi G, Sinicropi MS, Lauria G, Carocci A, Catalano A. The Effects of Cadmium Toxicity. *International J of Environmental Research and Public Health.* 2020;17:3782.
3. Zhan S, Huang J. Effects of Cigarette Smoking on Preimplantation Embryo Development. *Adv Exp Med Biol.* 2021;1300:137-150.
4. Grigoryuk IP, Kovbasenko RV, Dmitriev OP, Teslyuk VV, Kovbasenko VM. Biological features of cadmium action on the ecological state of phytocenoses. Kyiv: CP "Komprint"; 2019. 329 s.
5. Rafati Rahimzadeh M, Rafati Rahimzadeh M, Kazemi S, Moghadamnia AA. Cadmium toxicity and treatment: An update. *Caspian J Intern Med.* 2017;8(3):135-45.
6. Lee S, Min J, Min K. Female infertility associated with blood lead and cadmium levels. *International journal of environmental research and public health.* 2020;17(5):1794.
7. Nasiadek M, Danilewicz M, Sitarek, K, Świątkowska E, Daragó A, Stragierowicz J, et al. The effect of repeated cadmium oral exposure on the level of sex hormones, estrous cyclicity, and endometrium morphometry in female rats. *Environ. Sci. Pollut. Res.* 2018;25:28025-38.
8. Geng HX, Wang L. Cadmium: Toxic effects on placental and embryonic development. *Environ Toxicol Pharmacol.* 2019;67:102-7.
9. Gull A, Dar A, Sharma M. Effects of Heavy Metals on the Health of Pregnant Women and Fetus: A Review. *International J of Theoretical, Applied Sciences.* 2018;10(1):1-9.
10. de Angelis C, Galdiero M, Pivonello C, Salzano C, Gianfrilli D, Piscitelli P, et al. The environment and male reproduction: The effect of cadmium exposure on reproductive function and its implication in fertility. *Reprod Toxicol.* 2017;73:105-27.
11. Liu H, Wang R, Ou Yang H, Wang Y, Wu J, Li M, et al. Cadmium induced mouse spermatogonia apoptosis via mitochondrial calcium overload mediated by IP3R-MCU signal pathway. *Toxicology.* 2023;486:153448.
12. Massányi M, Satarug S, Madeddu R, Stawarz R, Massányi P. Evidence for Ovarian and Testicular Toxicities of Cadmium and Detoxification by Natural Substances. *Stresses.* 2022;2(1):1-16.
13. 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;67:2411-8.
14. Skalny AV. Assessment and correction of the elemental status of the population – a promising direction of domestic health care and environmental monitoring. *Trace elements in medicine.* 2018;19(1):5-13.
15. Yildiz A, Kaya Y, Tanriverdi O. Effect of the Interaction Between Selenium and Zinc on DNA Repair in Association With Cancer Prevention. *J Cancer Prev.* 2019;24(3):146-54.

ЗМІНА ОСНОВНИХ ПОКАЗНИКІВ ЕМБРІОЛЕТАЛЬНОСТІ У ЩУРІВ ПІД ДІЄЮ СОЛЕЙ КАДМІЮ

Колосова І. І.

Резюме. У населення сучасного мегаполісу спостерігається накопичення в організмі різних хімічних, у тому числі токсичних, елементів, зокрема кадмію. Кадмій надходить в організм людини через шлунково-кишковий тракт з харчовими продуктами та питною водою і дихальні шляхи, значна кількість кадмію абсорбується з сигаретного диму. Акумуляючись в організмі кадмій негативно впливає на здоров'я, вражаючи нирки, печінку, кровоносні та репродуктивні системи та може призвести до формування захворювань під час внутрішньоутробного періоду. Метою нашого дослідження було експериментальне визначення потенційного ембріотоксичного впливу хлориду кадмію та цитрату кадмію (у дозі 1,0 мг/кг) ізольовано та за умов корекції цитратами (церію, цинку та нанокompозиту на основі цитратів йоду, сульфур у селену) при внутрішньошлунковому введенні з першої до 19-ї доби ембріонального розвитку. Для дослідження використували 180 молодих самиць щурів лінії Wistar, яких було розділено на 9 груп, в залежності від отримуваних розчинів солей кадмію або фізіологічного розчину. Обрахування та порівняння стандартних показників ембріонального розвитку, а саме: середня кількість плодів, загальна ембріональна смертність, доімплантаційна смертність та постімплантаційна смертність на 13-ту та 20-ту добу ембріогенезу свідчать про виражений ембріолетальний ефект солей кадмію, що проявляється підвищенням загальної ембріональної смертності за рахунок зростання доімплантаційної та постімплантаційної смертності ембріонів щурів порівняно з контрольною групою на обох досліджуваних термінах ембріогенезу та ембріотоксичний ефект, що виявляється зниженням кількості живих плодів на одну самицю. В групах комбінованої дії солей кадмію з цитратами церію/цинку/ нанокompозиту (йод+сульфур+селен) використання цитратів призвело до покращення досліджуваних показників порівняно з групами солей кадмію, що свідчить про зменшення негативно-го впливу кадмію на показники ембріональної летальності у щурів.

Ключові слова: ембріогенез, ембріональна смертність, хлорид кадмію, цитрат кадмію, експеримент.

CHANGES IN THE MAIN INDICATORS OF EMBRYO LETHALITY IN RATS UNDER THE INFLUENCE OF CADMIUM SALTS**Kolosova I. I.**

Abstract. The population of a modern metropolis has an accumulation of various chemical, including toxic, elements in their bodies, including cadmium. Cadmium enters the human body through the gastrointestinal tract with food and drinking water and the respiratory tract, and a significant amount of cadmium is absorbed from cigarette smoke. Accumulating in the body, cadmium has a negative impact on health, affecting the kidneys, liver, circulatory and reproductive systems, and can lead to the formation of diseases during the intrauterine period. The aim of our study was to experimentally determine the potential embryotoxic effects of cadmium chloride and cadmium citrate (at a dose of 1.0 mg/kg) in isolation and under conditions of correction with citrates (cerium, zinc and a nanocomposite based on iodine, sulfur and selenium citrates) when administered intragastrically from the 1st to the 20th day of embryonic development. For the study, 180 young female Wistar rats were used, which were divided into 9 groups, depending on the solutions of cadmium salts or saline. Standard indicators of embryonic development, namely: the average number of fetuses, total embryonic mortality, preimplantation mortality and postimplantation mortality on the 13th and 20th day of embryogenesis indicate a pronounced embryonic lethal effect of cadmium salts, manifested by an increase in total embryonic mortality due to an increase in preimplantation and postimplantation mortality of rat embryos compared to the control group at both studied periods of embryogenesis and an embryotoxic effect manifested by a decrease in the number of live fetuses per female. In the groups of combined action of cadmium salts with cerium/zinc citrates/nanocomposite (iodine + sulfur + selenium), the use of citrates led to an improvement in the studied indicators (reduction in the number of fetuses and their weight, intrauterine survival rate, an increase in total, preimplantation and postimplantation embryonic mortality) compared to the groups of cadmium salts, which indicates a decrease in the negative effect of cadmium on embryonic mortality in rats.

Key words: embryogenesis, embryonic mortality, cadmium chloride, cadmium citrate, experiment.

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