ANIMAL SCIENCE AND FOOD TECHNOLOGY

Journal homepage: https://animalscience.com.ua/en
Animal Science and Food Technology, 13(4), 59-68
Received: 07.09.2022 Revised: 10.10.2022 Accepted: 29.10.2022

UDC 636.09:615.356:598.278:591.366
DOI: 10.31548/animal.13(4).2022.59-68

Preclinical study of the effects of vitamin-mineral complex use during normal pregnancy in white rats

Gennadii Tkach*
Doctor of Medical Sciences, Professor.
National University of Life and Environmental Sciences of Ukraine
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine
https://orcid.org/0000-0002-6482-4792

Oleg Shvets
PhD in Medical Sciences, Associate Professor
National University of Life and Environmental Sciences of Ukraine
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine
https://orcid.org/0000-0002-1434-4344

Larysa Bal-Prylypko
Doctor of Technical Sciences, Professor
National University of Life and Environmental Sciences of Ukraine
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine
https://orcid.org/0000-0002-9489-8610

Natalia Slobodyanyuk
PhD in Agricultural Sciences, Associate Professor
National University of Life and Environmental Sciences of Ukraine
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine
https://orcid.org/0000-0002-7724-2919

Svitlana German
Communal Institution of Sumy Regional Council "Shostka Professional Medical College"
41100, 43 Marat Str., Shostka, Sumy region, Ukraine
https://orcid.org/0000-0002-3996-2755

Abstract. Vitamin-mineral deficiency is quite common in the world, which negatively affects the growth and development of children, provokes the development of chronic pathologies, allergic conditions. Children and pregnant women are particularly sensitive to this condition. Considering the vitamin and elemental composition of each of the drugs, it becomes necessary to examine the effect of various complexes on the body. The purpose of the study is to examine the morphological state of organs from the use of a vitamin-mineral complex during normal pregnancy in white rats and their offspring and examine the elemental analysis of target organs and whole blood. The experiment was conducted on pregnant female white laboratory rats and their offspring to achieve this goal. Histological, ultramicroscopic,

Suggested Citation:
Tkach, G., Shvets, O., Bal-Prylypko, L., Slobodyanyuk, N., & German, S. (2022). Preclinical study of the effects of vitamin-mineral complex use during normal pregnancy in white rats. *Animal Science and Food Technology*, 13(4), 59-68.

*Corresponding author

morphometric, atomic-absorptic, functional methods, and statistical analysis are used for the study. A positive effect of the vitamin-mineral complex of the selected composition on both pre- and postnatal development of offspring is identified. The average offspring rate increased by 9.79% (p=0.0443), while the stillbirth rate decreased by 81.82% (p=0.0324). The absence of negative side effects of the complex on the development of basic reflex and behavioural reactions, motor activity, and cognitive activity of offspring is proved. A positive effect on the morphological characteristics of the liver, brain, heart, and kidneys is evident: the number of full hepatocytes in mature animals increased by 8.17% (p=0.0482), and in young animals – by 5.03% (p=0.0137), in the brain tissue of 7-day-old animals, the number of neurons increased by 7.70% (p=0.0438), and the number of functionally defective neurons decreased. Microelement analysis of organs identified a tendency to increase the amount of a number of trace elements, which was reflected in the improvement of the antioxidant systems pf the body. A positive effect of the complex on the processes of hematopoiesis is noted. The results obtained can become morphological evidence for the choice of correction of macro-, microelement, and vitamin balance, prevention of its deficiency in pregnant women, and prevention of the development of deficient conditions in infants

Keywords: animals, offspring, vitamins, morphology, macro- and microelements

Introduction

Vitamin-mineral complexes are widely used all over the world, in particular, in well-developed countries, which is associated with the desire of the population to prevent the development of chronic diseases, hypervitaminosis and avitaminosis, improve health, level the absence of certain nutritional components in the diet, and the impact of adverse environmental factors (Vdovichenko & Ostroglyad, 2017). Vitamin-mineral deficiency is quite common in the world and dangerous for public health, especially for children and pregnant women (Horobets, 2019).

Deviations in macro-, microelement, and vitamin supply lead to changes in metabolism, reduced performance, contribute to the deterioration of physical and mental health, especially in children, and lead to the development of chronic pathology, allergies, and a decrease in reproductive potential (Babaei *et al.*, 2012, Trachtenberg *et al.*, 2013, Sheremeta *et al.*, 2015). The ability of the immune system to counteract pathogenic factors and adverse environmental influences decreases (Horodetska & Blavatska, 2019).

The main causes of vitamin deficiency are alimentary insufficiency, changes in the normal intestine microbiota, impaired assimilation and metabolism, and an increased need for vitamins (Nyssen *et al.*, 2022). The rapid growth of the population leads to a shortage of food, and simultaneously, to a decrease in the supply of elements and vitamins of the body (Nikolaenko & Bal-Prylypko, 2020). The addition of macro-, microelements, and vitamins to the diet has a positive effect on well-being, especially for pregnant women, and as a result, provides high birth rates for healthy offspring (Kotsyubenko, 2012). During pregnancy, there is an additional need for macro-, microelements, and vitamins, which is associated with increased consumption of the latter, increased metabolism, and fetal development (Cetin, *et al.*, 2009).

Researchers around the world now recommend the introduction of dietary supplements. Today, manufacturers offer a huge selection of vitamin-mineral complexes. Having knowledge about the variety and effects of supplements, the doctor can correctly introduce them to the diet to improve metabolic processes and body functions, considering their individual characteristics (Horobets, 2019, WHO technical report..., 2007).

Numerous foreign studies showed that taking vitamin-mineral complexes reduces the risk of cataracts, heart diseases, diabetes, and oncological diseases such as breast, lung, colon, and prostate cancer (Gaziano *et al.*, 2012, Fortmann *et al.*, 2013, Park *et al.*, 2010). In addition, nutraceuticals have a positive effect on the cognitive system, reduce the risk of infectious processes in the elderly (Stephen & Avenell, 2006).

Thus, considering the vitamin, macro-, and microelement composition of each of the additives, and the variety of effects of each component, it becomes necessary to examine the effect of various complexes on the body. The experiment was performed on pregnant rats to ensure the safety of the drug and the absence of side effects, which also identified the effect of taking supplements on the offspring. In addition to the morphofunctional state of organs, it is important to identify the micro- and macronutrient composition, hidden deficiencies or elemental imbalances since the lack, excess, or incorrect ratio of macro- and microelements substantially affects the state of the antioxidant system of the body.

The purpose of the study is to examine the effects of using the vitamin-mineral complex during normal pregnancy in white rats and their offspring, assess the morphofunctional state of organs after a course of taking the vitamin-mineral complex.

The main objectives of the study were:

1. Simulate and perform an experiment during normal pregnancy in white rats.

2. Monitor the overall physical development of the offspring, in particular, examine the rate of occurrence of basic sensory-motor reflexes during feeding, emotional-motor behaviour, the ability to learn, and the memory of animals.

3. Assess the morphofunctional state of target organs (brain, liver, kidneys, heart) using morphometry and light, raster, and transmission electron microscopy.

4. Examine the morphofunctional state of the organs of laboratory animals (brain, heart, kidneys, liver), provided that a vitamin-mineral complex is used as a complementary food.

5. Perform macro- and microelement analysis of target organs and whole blood to assess the functioning of the antioxidant system, and evaluate the main indicators of the general blood test.

Materials and Methods

The experiment was conducted on 10 pregnant female white laboratory rats aged six to twelve months and the offspring obtained from them (20 rats).

Experimental animals were cared for in a vivarium in accordance with the provisions of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), "General Ethical Principles of Animal Experiments", adopted by the First National Congress on Bioethics (Kyiv, 2001), and the Law of Ukraine "On the Protection of Animals from Cruelty" (dated 21.02.2006) (European Convention for..., 1986, Reznikov, 2003).

The animals were divided into the following groups:

- Animals in the control group received dry granulated feed and drinking water as food.
- Animals of the experimental group received dry granular feed and a vitamin-mineral preparation at the appropriate dose, dissolved in drinking water, the composition of which is presented in Table 1.

Calculation of the dose of the additive for animals: the weight of one tablet of the vitamin-mineral complex is 756 mg. According to the instructions, the drug is prescribed 4 tablets a day (2 tablets in the morning and 2 tablets in the evening) for adults, which is 3024 mg. The daily dose per kilogram of adult body weight is 43.2 mg/kg. Formula (1) was used to calculate the amount of vitamin supplement for pregnant rats:

$$\text{Rat dose} = (r \times \text{human dose}) / R \quad (1)$$

where r – the coefficient of species endurance for a rat=3.62; R – the coefficient of species endurance for humans=0.57.

According to the formula, the daily dose for a pregnant animal was 274.4 mg/kg. Considering the average weight of a pregnant rat (200 g), the daily dose is 55 mg. The experimental group consisted of 10 pregnant animals who received 55 mg of vitamin supplements daily for 24 days. The total amount of the supplement per experiment is 1320 mg, which corresponds to 17 tablets of the drug. The content of trace elements and vitamins in the daily dose for the animal is shown in Table 1.

Table 1. *Content of trace elements and vitamins of the complex in the daily dose for the animal*

Trace elements and vitamins	Content in the daily dose (55 mg) for the animal
Zinc	0.08 mg
Iron	0.11 mg
Manganese	0.02 mg
Copper	6.2 μg
Chrome	0.76 μg
Magnesium	1.64 mg
Beta-carotene	0.055 mg
Vitamin B1	0.018 mg
Vitamin B2	0.022 mg
Vitamin B6	0.022 mg
Vitamin B9 (folic acid)	3.64 μg
Vitamin B12	0.018 μg
Vitamin C	1.1 mg
Vitamin D3	0.055 μg
Vitamin E	0.12 mg
Vitamin B3 (PP, nicotinamide)	0.22 mg
Flavanoids	1.46 mg

The weight of pregnant and newborn rats was determined using ACOM JW electronic scales with an accuracy of 0.01 g.

The absolute and relative mass of the liver, heart, brain, and kidneys was determined.

The following organometric parameters were also determined:

- When examining the liver – the greatest length, width, and thickness;
- During the examination of the heart – the total height, width, thickness, and volume of the heart muscle were calculated;
- During the examination of the kidneys – the length, width, thickness, and volume of each of the kidneys;
- During the examination of the brain – width and length.

The above-mentioned linear dimensions were examined using a calliper with an accuracy of 0.1 mm.

For the histological preparations, pieces of the liver, brain, heart, and kidneys were put in a 10% solution of neutral formalin. The samples were then prepared and processed as described earlier in (Rtail *& et al.*, 2020, Dudchenko *& et al.*, 2020). When examining liver preparations, attention was paid to the structure of classic

lobules, perilobular zones, perisinusoid spaces, sinusoids; the number of normal hepatocytes in the visual field was determined; the relative areas occupied by liver beams in the organ of adult and newborn animals were calculated.

During the examination of the brain, the structure of all layers of the organ was visually evaluated, the width of the inner pyramidal layer was determined, its cellular composition was established; the number of normal neurons in the visual field, the glial-neuronal index, and the average diameter of the capillaries of the organ were identified. During the examination of heart preparations, the morphological organisation of the heart muscle at the light-optical level was visually evaluated; attention was paid to the structure of cardiomyocytes.

During the examination of histological preparations of the kidney, its histoarchitectonics were visually examined; morphometrically, the area of the renal body, the diameter of the proximal and distal renal tubules, and the diameter of glomerular capillaries were determined, as the most substantial indicators of the functionality of the organ. Material sampling for electronomicroscopic examination of the structural components of the tissues of the organs under study was performed as described earlier in (Rtail *et al.*, 2020, Dudchenko *et al.*, 2020).

According to the obtained data from transmission electron microscopy of the liver, the morphology of hepatocytes, their main organelles, sinusoids, and bile capillaries was investigated. The diameter of hepatocytes and the hepatocyte nuclei were determined, and the nuclear-cytoplasmic ratio was calculated. During the examination of the brain, the structural organisation of neurons, the brain glia, was investigated using transmission electron microscopy. The area and diameter of neurons in the inner pyramidal layer were determined morphometrically. The nuclear-cytoplasmic ratio was calculated.

During the ultramicroscopy of cardiac preparations, attention was paid to the morphology of cardiomyocytes. The diameter of cardiomyocytes of the left and right ventricles and their relative volume were determined. The three-dimensional organisation of the ventricular myocardium was investigated using raster electric microscopy. During the examination of kidney preparations, the ultamicroscopic organisation of the renal body and its main components were investigated.

For a general blood test, haematological parameters were determined in whole blood: haemoglobin content – by the acetoncyanhydrin method (g/l); haematocrit (%), the number of red blood cells (10^{12}/l), white blood cells (10^{9}/l), and platelets (10^{9}/l), content (%) of lymphocytes, MID (eosinophils, monocytes), reticulocytes, granulocytes. Analysis of elements in blood and organ samples was performed by atomic absorption spectrometry with electrothermal and flame atomisation, as described earlier (Rtail & Tkach, 2020). The content of K, Na, and Ca was determined on an S-115-M1 AT "Selmi" spectrophotometer with flame atomisation in the emission mode (Table 2). The Mg, Fe, Mn, Zn, and Cu content was analysed on a CAS-120.1 atomic absorption machine with an A-5 electrothermal atomiser and a Carl Zeiss Jena graphite furnace in the adsorption mode (Rtail & Tkach, 2020), the characteristics of which are given in Table 3.

Table 2. *Spectral measurement and atomisation conditions for K, Na, Ca*

Element	Wavelength, nm	Spectral gap, nm	Combustible gas	Oxidiser	Temperature flame	Flame type
K	769.9	0.4	C_2H_2	air	2300	oxidising
Na	589.0	0.4	C_2H_2	air	2300	oxidising
Ca	422.7	0.4	C_2H_2	N_2O	2950	stoichiometric

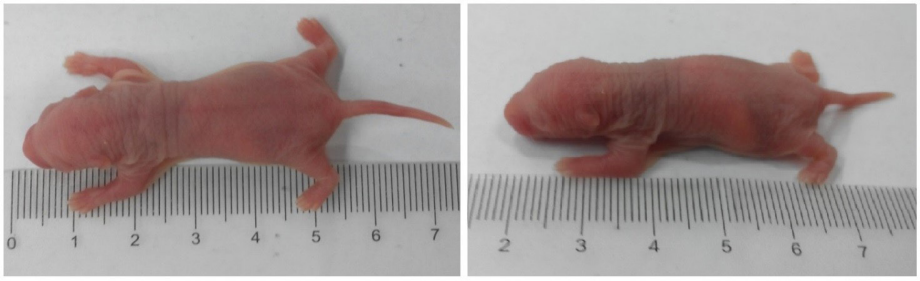
Table 3. *Spectral and temperature-time measurement modes*

Element	Wavelength, nm	Gap width, Nm	Pyrolysis		Atomisation	
			T, ˚C	τ, s	T, ˚C	τ, s
Mg	202.6	0.4	1000	10	2200	5
Fe	372.0	0.4	1000	10	2500	5
Mn	279.5	0.4	1000	10	2500	4
Zn	213.9; 307.4	1.0	600	10	2100	5
Cu	324.7	0.4	1000	10	2500	5

Statistical data processing was performed using a package of applied statistical computer programmes – MS Excel 2016 and SPSS-17. The validity of differences between the two samples was determined using the Student's parametric t-criterion. The difference was considered reliable if the probability of a random difference did not exceed 0.05 ($p \leqslant 0.05$).

Results and Discussion

When using the vitamin-mineral complex as a complementary food for pregnant rats, an increase in the average size of the offspring was identified by 9.79% (p=0.0443), while the stillbirth rate of animals decreased by 81.82% (p=0.0324) relative to the control group of animals. No developmental abnormalities were detected in the comparison groups (Fig. 1 (a, b)).



a) b)

Figure 1 – three-day-old animals whose mothers consumed dry granulated feed as food during pregnancy (a) and dry granulated feed with a vitamin-mineral complex (b)

The weight of newborn animals in the control group increased by 21.11% (p=0.0396) on day 7 of postnatal development, and by 15.69% (p=0.0311) and 5.88% (p=0.0438) on days 14 and 21, respectively. The weight of newborn rats, whose mothers received the vitamin-mineral complex, tended to increase by 28.48% (p=0.0324), 16.56% (p=0.0171), and 5.52% (p=0.0580), respectively, on days 7, 14, and 21 of postnatal development. This allows asserting the positive effect of the complex on the course of pregnancy and postnatal development of the offspring.

The main indicators of the overall development of the offspring in the postnatal period (detachment of the auricle, appearance of primary hair, eruption of incisors, opening of the eyes, omission of testes, and opening of the vagina) were within the physiological norm in both groups. During the examination of the main sensory-motor reflexes of offspring whose mothers consumed a vitamin-mineral complex during pregnancy, it was identified that the timing of their appearance corresponds to the norm and is fully fulfilled. In particular, it was noted that the main reflexes (turning over on a flat surface, avoiding a potential fall, pendulum reflexes) tended to appear earlier, compared to the control group of animals.

When investigating emotional and motor behaviour and fine coordination of movements of newborn rats of the experimental group, no pathological disorders were identified, the animals showed good abilities, not inferior to the animals from the control group. The ability of the offspring of the experimental group to learn was at a high level, which was manifested in such experiments as passive and active avoidance with negative (pain) reinforcement and learning in a maze with positive (food) reinforcement.

Macroscopic examination of internal organs (liver, brain, kidneys, heart) did not identify any congenital developmental abnormalities in 7-day-old animals and pathologies in mature females. Microscopic examination of organ tissues identified a number of positive effects from the use of the vitamin-mineral complex in animals of both age categories. Thus, morphological examination of the liver visually observed a decrease in apoptosis-altered and necrotic cells in mature animals. Therewith, there were almost no functionally defective hepatocytes in 7-day-old animals (Fig. 2). It was identified that when using the drug, the number of full hepatocytes in mature animals increases by 8.17% (p=0.0482), respectively, and in young animals – by 5.03% (p=0.0137), in particular, in the latter cells had signs of high functional activity. Ultramicroscopic examination confirmed the normal architectonics of animal liver tissue (Fig. 3).

Microscopic examination of the liver of rats in the control group of both age categories showed that the classic liver lobules had a polygonal shape. In the corners between the classic hepatic lobules were layers of loose connective tissue that contain interparticle of blood and lymphatic vessels and bile ducts. In 7-day-old animals, interparticle connective tissue septa were not pronounced. Central veins are located in the centre of the classic hepatic lobules. The cytoplasm of most hepatocytes is evenly colored, light. The nuclei are normochromic, located in the centre of the cells. Apoptotically altered or necrotic cells and dilated sinusoid capillaries were detected in the centrilobular zone of classic hepatic lobules in animals of both age categories of the control groups (Figures 4 and 5).

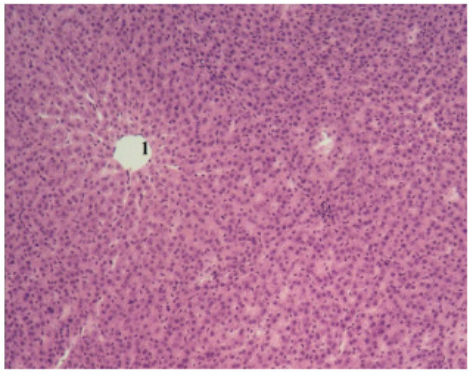


Figure 2 – liver of 7-day-old animals whose mothers received a vitamin-mineral complex during pregnancy: 1 – lumen of the central vein. Magnification x200

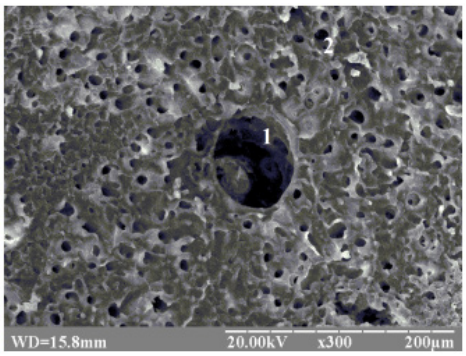


Figure 3 – ultrastructure of the liver of 7-day-old animals whose mothers consumed a vitamin-mineral complex during pregnancy: 1 – lumen of the central vein; 2 – sinusoid capillaries

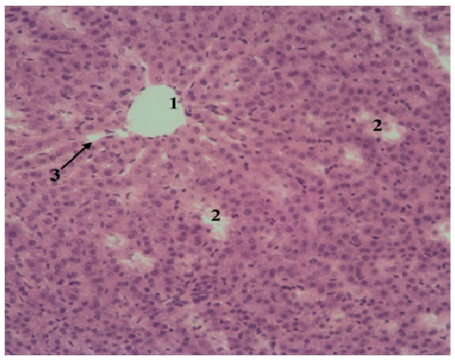


Figure 4 – liver of 7-day-old animals of the control group. Hematoxylin-eosin staining: 1 – central vein lumen; 2 – destroyed hepatocytes; 3 – dilated sinusoid capillaries. Magnification x400

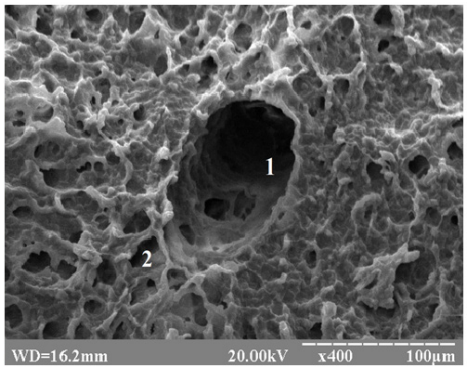


Figure 5 – ultrastructure of the liver of 7-day-old animals of the control group: 1 – lumen of the central vein; 2 – sinusoid capillaries.

In the brain tissue of 7-day-old animals, an increase in the number of neurons was identified by 7.70% (p=0.0438) compared to the control group, and a decrease in the number of functionally defective neurons in the visual field, which was presumably reflected in high learning and memory indicators (Fig. 6). Morphological examination of the heart did not identify any deviations from the norm in both young and mature animals, which indicates the benefit of the vitamin-mineral complex. Microscopic examination of the kidneys identified a decrease in the number of defective glomeruli, tubules, and there was no pathological dilation of capillaries, which was quite often observed in young animals of the control group (Fig. 7).

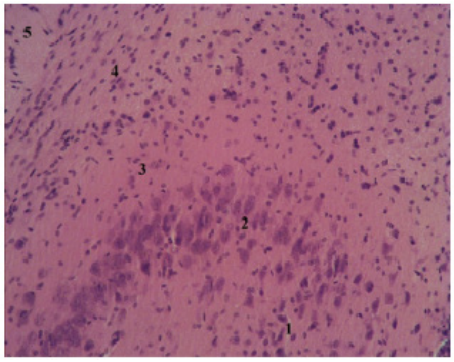


Figure 6 – the brain of 7-day-old rats whose mothers consumed a vitamin-mineral complex during pregnancy. Hematoxylin-eosin staining: 1 – molecular layer; 2 – outer granular layer; 3 – outer pyramidal layer; 4 – inner granular layer; 5 – inner pyramidal layer. Magnification x400

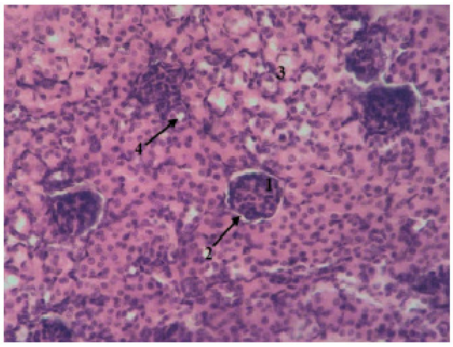


Figure 7 – the cortical substance of the kidneys of 7-day-old animals whose mothers consumed a vitamin-mineral complex during pregnancy. Hematoxylin-eosin staining: 1 – renal glomerulus; 2 – glomerular capsule lumen; 3 – proximal convoluted tubules; 4 – distal convoluted tubules. Magnification x400

In the molecular layer and outer pyramidal layer of the cerebral cortex of 7-day-old rats, a lower density of neurons and microglial cells was observed during the microscopic examination, compared with a group of 7-day-old rats whose mothers consumed a vitamin-mineral complex during pregnancy (Fig. 8). Microscopic examination of the heart of 7-day-old rats in the control group identified a lower expression of connective tissue compared to their mothers. No altered cardiomyocytes in animals of both age categories were observed. During the histological examination of kidney preparations in adult animals of the control group, the capsule, cortical, and medulla substances were clearly detected. In the cortical substance of the kidneys of 7-day-old animals in the control group, morphofunctional glomeruli were identified, the lumen of the capsule of which was not always visualised. Some proximal and distal convoluted tubules tended to narrow. Sometimes dilated blood vessels were observed (Fig. 9).

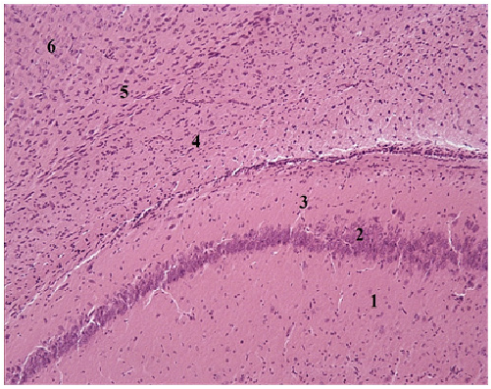


Figure 8 – brain of 7-day-old rats of the control group. Hematoxylin-eosin staining: 1 – molecular layer; 2 – outer granular layer; 3 – outer pyramidal layer; 4 – inner granular layer; 5 – inner pyramidal layer; 6 – polymorphic cell layer. Magnification x200

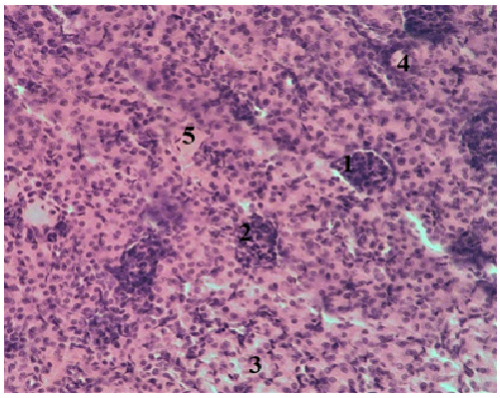


Figure 9 – the cortical substance of the kidney of 7-day-old rats of the control group. Hematoxylin-eosin staining: 1 – renal glomerulus; 2 – morphofunctional glomerulus; 3 – narrowed proximal tubules; 4 – distal renal tubule; 5 – dilated capillary. Magnification x200

Using functional research methods, a tendency to increase the content of zinc, iron, cobalt, magnesium, and copper was identified, to a greater extent in the liver and kidneys. This is presumably reflected in the improvement of the antioxidant systems of the body and the reduction of morphofunctional necrotic cells. Microelement analysis of whole blood showed an increase in iron concentration.

Among the main indicators of the general blood test, the level of haemoglobin and the number of red blood cells experienced the greatest changes. Thus, in animals that consumed a vitamin-mineral complex during pregnancy, the haemoglobin level increased by 3.45% (p=0.0238), and the number of red blood cells – by 11.6% (p=0.0292), respectively, in the control group. In their offspring, the level of haemoglobin increased by 19.05% (p=0.0483), and red blood cells – by 41.75% (p=0.0311) compared to newborn rats whose mothers did not consume the vitamin-mineral complex. Therewith, there was an increase in the color index. In animals that consumed the vitamin-mineral complex during pregnancy, it increased by 14.29% (p=0.0152), and in their offspring – by 11.63% (p=0.0382) according to the control indicators, which allows asserting the positive effect of the complex on the processes of hematopoiesis.

Thus, it was identified that when using a vitamin-mineral complex as a complementary food for pregnant rats, the average size of the offspring increases, while the stillbirth rate of animals decreases. Therewith, no abnormalities in the development of offspring were detected. Bryan *et al.* (2004) also observed an increase in pregnancy cases in cows due to the use of chromium-methionine as a supplement to the main feed. In the studies of Shtapenko (2019), it was shown that organic complexes of manganese, zinc, and chromium in low doses do not have a cytotoxic effect on cultures of cells of reproductive organs. The author notes the high survival rate of cells and an increase in their proliferation rate.

Analysis of the results of the studies by O. Shtapenko (2019) also showed that the use of chromium-methionine in rabbits for 1.5 months before fertilisation contributed to their reproductive function, increased fertilisation and embryo implantation. This allowed getting the maximum number of fetuses and the lowest preimplantation mortality compared to the control. O. Shtapenko (2019) notes that the blood counts of rabbits that consumed chromium-methionine were normal. She highlights an increase in red blood cells and haemoglobin, which indicates the activity of hematopoiesis, increased oxygen uptake by tissues, which indicates a higher favourability of females to scurrility, which positively correlates with reproductive function.

In the study, in the indicators of the general blood test, the level of haemoglobin, the number of red blood cells, and the colour indicator increased both in pregnant females and in their offspring, which allows asserting the positive effect of the vitamin-mineral complex on the processes of hematopoiesis. In addition, an increase in the content of zinc, iron, cobalt, magnesium, and copper, to a greater extent in the liver, kidneys and iron in whole blood was identified, which was identified in improving the antioxidant systems and reducing morphofunctional, necrotic cells.

E. Biletska *et al.* (2014) researched the histomorphological state of the placenta and features of placentogenesis under the influence of zinc chloride and identified a positive effect on placentogenesis and the development of a mature fetoplacental complex. In the study, a decrease in apoptosis-altered and necrotic liver cells in females was observed. In addition, hepatocytes had high functional activity. In 7-day-old animals, there were no functionally defective hepatocytes at all, which confirms the positive effect of adding a vitamin-mineral complex of this composition to the diet of pregnant females.

Conclusions

Thus, after applying the presented vitamin-mineral complex, a positive effect was identified on both pre- and postnatal development of offspring: the average indicators of offspring increased by 9.79% (p=0.0443), while the stillbirth rate decreased by 81.82% (p=0.0324). The absence of

negative side effects of the complex on the investigated target organs (liver, brain, heart, kidneys), and a positive effect on their morphofunctional characteristics is proved: the number of full-fledged hepatocytes increases in mature animals by 8.17% (p=0.0482), and in young animals – by 5.03% (p=0.0137), in the brain tissue of 7-day-old animals, an increase in the number of neurons by 7.70% (p=0.0438), and a decrease in the number of functionally defective neurons, which probably affects the development of basic reflex and behavioural responses, motor activity, and cognitive activity. In addition, the results of functional research methods, in particular, microelement analysis of organs identified a tendency to increase the amount of zinc, iron, cobalt, magnesium, copper, which was reflected in the improvement of the antioxidant systems of the body; there was also a positive effect on the processes of hematopoiesis: the level of haemoglobin increased by 3.45% (p=0.0238), and the number of red blood cells – by 11.6% (p=0.0292).

The results obtained can become morphological evidence for the choice of correction of macro, microelement, and vitamin balance and prevention of their deficiency in pregnant women and prevention of the development of deficient conditions in infants. The prospects for further research are to examine the morphological state of organs from the use of various vitamin-mineral complexes during normal pregnancy in white rats and their offspring, to examine the elemental analysis of target organs and whole blood, and to conduct a comparative-statistical analysis of the influence of vitamin-mineral complexes of different composition.

References

[1] Babaei, H., Roshangar, L., Sakhaee, E., Abshenas, J., Kheirendish, R., & Dehghani, R. (2012). Ultrastructural and morphometrical changes of mice ovaries following experimentally induced copper poisoning. *Iranian Red Crescent Medical Journal,* 14, 558-568.

[2] Biletska, E.M., Onul, N.M., Shatorna, V.F., Kononova, I.I., & Demura, O.V. (2014). Histomorphological status of the placenta and features of placental development under the influence of zinc chloride in experimental animals. *World of Medicine and Biology*, 4(46), 72-74.

[3] Bryan, M.A., Socha, M.T., & Tomlinson, D.J. (2004). Supplementing intensively grazed late-gestation and early-lactation dairy cattle with chromium. *Journal of Dairy Science*, 87(12), 4269-4277. https://doi.org/10.3168/jds.S0022-0302(04)73571-7.

[4] Cetin, I., Berti, C., & Calabrese, S. (2009). Role of micronutrients in the periconceptional period. *Human Reproduction Update*, 16(1), 80-95. https://doi.org/10.1093/humupd/dmp025.

[5] Dudchenko, Y.S., Maksymova, O.S., Pikaliuk, V.S., Muravskyi, D.V., Kyptenko, L.I., & Tkach, G.F. (2020). Morphological characteristics and correction of long tubular bone regeneration under chronic hyperglycemia influence. *Analytical Cellular Pathology*, 1, article number 5472841. doi: 10.1155/2020/5472841.

[6] European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes. (1986, March). Retrieved from https://zakon.rada.gov.ua/laws/show/994_137#Text.

[7] Fortmann, S.P., Burda, B.U., Senger, C.A., Lin, J.S., & Whitlock, E.P. (2013). Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: An updated systematic evidence review for the U.S. preventive services task force. *Annals of Internal Medicine,* 159(12), 824-834. https://doi.org/10.7326/0003-4819-159-12-201312170-00729.

[8] Gaziano, J.M., Sesso, H.D., Christen, W.G., Bubes, V., Smith, J.P., Mac Fadyen, J., Schvartz, M., Manson, J.A.E., Glynn, R.J., & Buring, J.E. (2012). Multivitamins in the prevention of cancer in men: The Physicians' health study II randomized controlled trial. *JAMA*, 308(18), 1871-1880. https://doi.org/10.1001/jama.2012.14641.

[9] Horobets, A.O. (2019). Vitamins and trace elements as specific regulators of physiological and metabolic processes in the body of children and adolescents. *Ukrainian Journal of Perinatology and Pediatrics*, 4(80), 75-92. https://doi.org/10.15574/PP.2019.80.75.

[10] Horodetska, I.Ya., & Blavatska, O.B. (2019). Study of the current state of the market of vitamin products in Ukraine. *Pharmaceutical Journal*, 74(5), 3-11. doi: 10.32352/0367-3057.5.19.01.

[11] Kotsyubenko, G.A. (2012). Reproductive and productive qualities of rabbits under different breeding technologies. *Bulletin of Agrarian Science*, 2, 35-37.

[12] Nikolaenko, M., & Bal-Prylypko, L. (2020). Development of an integrated food quality management system. *Potravinarstvo Slovak Journal of Food Sciences*, 14, 862-873. https://doi.org/10.5219/1434.

[13] Nyssen, O., Vaira, D., Pérez, A., Eder, P., Shvets, O., & Gisbert, J.P. (2022). Empirical second-line therapy in 5000 patients of the European registry on *Helicobacter pylori* management (Hp-EuReg). *Clinical Gastroenterology and Hepatology*, 20(10), 2243-2257. https://doi.org/10.1016/j.cgh.2021.12.025.

[14] Park, Y., Spiegelman, D., Hunter, D.J., & Albanes, D. (2010). Intakes of vitamins A, C, and E and use of multiple vitamin supplements and risk of colon cancer: A pooled analysis of prospective cohort studies. *Cancer Causes Control*, 21, 1745-1757. https://doi.org/10.1007/s10552-010-9549-y.

[15] Reznikov, O.G. (2003). General ethical principles of animal experiments. *Endocrinology*, 8(10), 142-145.

[16] Rtail, R., Maksymova, O., Illiashenko, V., Gortynska, O., Korenkov, O., Moskalenko, P., Nasser, M., & Tkach, G. (2020). Improvement of skeletal muscle regeneration by platelet-rich plasma in rats with experimental chronic hyperglycemia. *BioMed Research International*, article number 6980607. https://doi.org/10.1155/2020/6980607.
[17] Rtail, R.A., & Tkach, G.F. (2020). Chemical-analytical characteristics of different phases of regeneration of striated muscles of rats under conditions of chronic hyperglycemia. *Ukrainian Journal of Occupational Health*, 16(1), 70-76. https://doi.org/10.33573/ujoh2020.01.070.
[18] Sheremeta, V.I., Gruntkovsky, M.S., & Kaplunenko, V.G. (2015). Blood biochemical parameters of female cattle in the use of biological active agents. *Biology of Animals*, 17(2), 164-171.
[19] Shtapenko, O.V. (2019). Biotechnological aspects of regulation of gametogenesis for correction of early embryonic development of animals (Doctoral thesis, National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute", Kyiv, Ukraine).
[20] Stephen, A.I., & Avenell, A. (2006). A systematic review of multivitamin and multimineral supplementation for infection. *Journal of Human Nutrition and Dietetics*, 19(3), 179-190. https://doi.org/10.1111/j.1365-277X.2006.00694.
[21] Trachtenberg, I.M., Chekman, I.S., Linnyk, V.O., Kaplunenko, V.H., Hulich, M.P., Biletska, E.M., Shatorna, V.F., & Onul, N.M. (2013). Interaction of trace elements: Biological, medical and social aspects. *Bulletin of the National Academy of Sciences of Ukraine*, 6, 11-21.
[22] Vdovichenko, V.I., & Ostroglyad, T.V. (2017). Vitamin prophylaxis: Benefit, futility, harm. *Rational Pharmacotherapy*, 4(45), 56-63.
[23] World Health Organization (2007). WHO technical report series No. 935: Protein and amino acid requirements in human nutrition. Retrieved from http://whqlibdoc.who.int/trs/WHO_TRS_935_eng.pdf.

Доклінічне дослідження ефектів від застосування вітамінно-мінерального комплексу під час нормальної вагітності у білих щурів

Геннадій Федорович Ткач
Доктор медичних наук, професор.
Національний університет біоресурсів і природокористування України
03041, вул. Героїв Оборони, 15, м. Київ, Україна
https://orcid.org/0000-0002-6482-4792

Олег Віталійович Швець
Кандидат медичних наук, доцент
Національний університет біоресурсів і природокористування України
03041, вул. Героїв Оборони, 15, м. Київ, Україна
https://orcid.org/0000-0002-1434-4344

Лариса Вацлавівна Баль-Прилипко
Доктор технічних наук, професор
Національний університет біоресурсів і природокористування України
03041, вул. Героїв Оборони, 15, м. Київ, Україна
https://orcid.org/0000-0002-9489-8610

Наталія Михайлівна Слободянюк
Кандидат сільськогосподарських наук, доцент
Національний університет біоресурсів і природокористування України
03041, вул. Героїв Оборони, 15, м. Київ, Україна
https://orcid.org/0000-0002-7724-2919

Світлана Миколаївна Герман
Комунальний заклад Сумської обласної ради «Шосткинський фаховий медичний коледж»
41100, вул. Марата, 43, м. Шостка, Сумська область, Україна
https://orcid.org/0000-0002-3996-2755

Анотація. Вітамінно-мінеральний дефіцит є досить поширеним явищем у світі, що негативно позначається на рості й розвитку дітей, провокує розвиток хронічної патології, алергічних станів. Особливо чутливим до даного стану є дитяче населення та вагітні жінки. Беручи до уваги вітамінний та елементний склад кожного з препаратів, виникає необхідність дослідити ефект різних комплексів на організм. Метою дослідження було вивчити морфологічний стан органів від застосування вітамінно-мінерального комплексу під час нормальної вагітності у білих щурів та їх потомстві та дослідити елементний аналіз органів-мішеней й цільної крові. Для досягнення поставленої мети експеримент був проведений на вагітних самках білих лабораторних щурів та отриманому від них потомстві. Для дослідження використовували гістологічний, ультрамікроскопічний, морфометричний, атомно-абсорбційний, функціональний методи та статистичний аналіз. Було виявлено позитивний вплив вітамінно-мінерального комплексу вибраного складу, як на пре- так і постнатальний розвиток потомства. Середні показники приплоду збільшились на 9,79 % ($p = 0,0443$), водночас зменшився на 81,82 % ($p = 0,0324$) показник мертвонароджуваності. Доведено відсутність негативної побічної дії комплексу на формування основних рефлекторних та поведінкових реакцій, рухову активність, когнітивну діяльність потомства. Показано позитивний вплив на морфологічні характеристики печінки, мозку, серця, нирок: збільшилась кількість повноцінних гепатоцитів у зрілих тварин на 8,17 % ($p = 0,0482$), а у молодих тварин – на 5,03 % ($p = 0,0137$), у тканині головного мозку 7-денних тварин виявлено збільшення кількості нейронів на 7,70 % ($p = 0,0438$), а також зменшення кількості функціонально неповноцінних нейронів. Мікроелементний аналіз органів виявив тенденцію до збільшення кількості низки мікроелементів, що знайшло відбиток у покращенні антиоксидантних систем організму. Відмічено позитивний вплив комплексу на процеси кровотворення. Отримані результати можуть стати морфологічним доказом для вибору корекції макро-, мікроелементного, вітамінного балансу, профілактики його дефіциту у вагітних та попередження розвитку дефіцитних станів у немовлят

Ключові слова: тварини, потомство, вітаміни, морфологія, макро- та мікроелементи