The effect of gadolinium and lanthanum orthovanadate nanoparticles on the content of vitamins (B_2, A, E) and trace elements (Cu, Zn, Se) in the blood serum and liver of broiler chickens

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ABSTRACT

As a result of scientific progress, substances in the nanoscale state are increasingly being introduced into various areas of human activity, including animal husbandry (poultry farming). In particular, nanotechnology is used successfully to enrich food products with minerals, vitamins, antioxidants, that is, they can increase the bioavailability of nutrients by oral administration. In this study, the content of vitamins (A, E, and B_2) and trace elements (Zn, Cu, and Se) in the blood serum and liver of broiler chickens under the influence of gadolinium orthovanadate, lanthanum orthovanadate, and a mixture of all these was investigated. It was established that their administration to broiler chickens for 10 days at a dose of 0.2 mg/l of drinking water (an average of 0.09 mg/kg body weight) increases the bioavailability of vitamins B_2, A, and E and the trace elements selenium, copper and zinc, which was manifested by an increase in their concentrations in the blood serum compared to the control group (from 8.6% to 3.0 times for vitamins, and from 17.8% to 2.5 times for trace elements, $P<0.05$) and liver deposition (from 9.4% to 4.6 times for vitamins and from 6.3 to 56.3% for trace elements, $P<0.05$), with a prolonged effect after administration was stopped. The introduction of nanoparticles (both in mono-solutions and in a mixture), along with a vitamin preparation, indicates the possibility of increasing the content of vitamins and trace elements without their additional introduction, using the dietary resource more fully.

Key words: vitamins; trace elements; broiler chickens; nanoparticles of gadolinium orthovanadates; nanoparticles of lanthanum orthovanadates

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Introduction

Quite recently (in 2011-2012), the Department of Nanostructural Materials named after Yu. V. Malyukin of the Institute of Scintillation Materials of the National Academy of Sciences of Ukraine (Kharkiv, Ukraine), synthesized and standardized, according to stability and size, gadolinium orthovanadate nanoparticles activated with europium (NP $GdVO_4:Eu^{3+}$) (NP Gd) (spindle-shaped geometry, sized 8×25 nm), and lanthanum orthovanadate nanoparticles activated with europium (NP $LaVO_4:Eu^{3+}$) (NP La) (rod-shaped geometry, size 8×80 nm) (KLOCHKOV et al, 2011; KLOCHKOV et al., 2012a). In *in vitro* experiments, NP Gd exhibited enzyme-like properties: in aqueous solutions, inhibition of superoxide anion formation (similar to the action of superoxide dismutase) and acceleration of hydrogen peroxide decomposition (similar to the action of catalase) were observed (MAKSIMCHUK et al., 2021). The antioxidant properties of NP Gd were also observed during X-ray irradiation of aqueous solutions, despite the fact that nanoparticles absorbed the soft X-rays used in the experiment. In aqueous solutions, in the presence of nanoparticles, a decrease in the concentration of hydroxyl radicals, as the main product of water radiolysis, was found, and therefore, it was shown that NP Gd have radioprotective properties (MAKSIMCHUK et al., 2020). Antioxidant properties were also found in NP La (YEFIMOVA et al., 2019).

Due to these properties, these nanoparticles have already been tested in the practice of veterinary obstetrics: complex vitamin and hormonal nano preparations with NP Gd (“Kaplaestrol +OV”, “Kaplaestrol + OV Zn”, “Karafand”, “Karafand +OV, Zn”) have been developed. They ensure normalization of homeostasis indicators, and improvement of the structure of the fetoplacental complex and, as a result, fetal development, by optimizing the state of the prooxidant/antioxidant defense systems and oxygen metabolism, and are used for the treatment of cows and goats with hypogonadism (FEDORENKO et al, 2017). They are also used to increase the viability of newborn lambs (SKLIAROV and KOSHEVOI, 2016), and to prevent gonadal pathology of nutritional deficiency in males (NAUMENKO and KOSHEVOY, 2019). NP La also showed positive effects in reproduction: at a dose of 0.3 mg/kg body weight, the restoration of spermatogenic function and fertility in male rats with chronic prostatitis was recorded, which were not inferior to those under the influence of the comparison drug (CHYSTIAKOVA et al., 2020).

In addition, studies in Wistar rats have shown that prolonged oral intake of gadolinium orthovanadate nanoparticles in the bodies of animals maintained on a standard balanced vivarium diet, both young and aging rats, has a positive effect on the body in terms of a number of physiological and biochemical parameters (NIKITCHENKO et al., 2021a; NIKITCHENKO et al., 2021b).

In our previous studies we have found the membrane-protective effects of both types of nanoparticles in the bodies of white rats, in a dose range of 0.2-1.0 mg/l of drinking water (≈ 0.03-0.15 mg/kg bw) against the background of feeding stress, with an optimal duration of 28-42 days. These were generally manifested in the restoration of reamination processes, slowing down the formation of LOPs (decreased levels of DC and MDA; ($P<0.05$)) within physiological limits, along with a certain increase in total AOA, and adaptive activation of catalase ($P<0.05$) (MASLIUK et al., 2023a; MASLIUK et al., 2023b). The positive effect of NP Gd in the appropriate dose range on the small intestinal wall of white rats was also demonstrated (MASLIUK et al., 2023c).

Thus, on the basis of these studies, the preconditions for the use of these nanoparticles as adaptogenic feed additives have emerged. Broiler chickens were chosen as a model because modern poultry crosses selected for high growth rates are more sensitive to various forms of stress. In particular, feed stress is a fairly common phenomenon in poultry farming, mainly associated with imbalances of nutrients, vitamins, and trace elements in the feed (MASLIUK et al., 2021; MELNYK et al., 2021; OROBCHENKO et al., 2022; BERENDIKA et al., 2023).

It is well known that stress is based on lipid peroxidation (LPO), one of the most important oxidative processes in the body. Currently, LPO is considered one of the major causes of cell damage and death, due to the action of reactive oxygen species (ROS) (SU et al., 2019; JUAN et al., 2021). However, the body has a system of counteracting ROS – the antioxidant defense system (ADS), which includes non-enzymatic and enzymatic components. The enzyme component includes catalase, superoxide dismutase (SOD) and glutathione peroxidase (GP), and the non-enzyme component includes glutathione, and vitamins A and E (JEEVA et al., 2015; IRATO and SANTOVITO, 2021). In turn, the active centers of the SOD enzyme may contain the trace elements zinc and copper, and the GP may contain selenium (NOGALES et al., 2013; ALTOBELLI et al., 2020). From all this, it is logical that the lack or inadequate absorption of one or more elements of ADS can lead to malfunction and further damage to the body›s cells.

In addition to the ADS system, vitamin B_2 (riboflavin) plays an important role in the body of a broiler chicken, and its lack can lead to reduced feed intake, reduced productivity, skin lesions, limb paralysis and improper development (twisted fingers), so today the search for the optimal source of riboflavin in poultry diets or ways to increase its absorption continues (BLUM et al., 2014; LAMBERTZ et al., 2020; LEIBER et al., 2022).

Therefore, the aim of our work was to study the effect of gadolinium and lanthanum orthovanadate nanoparticles on the levels of vitamins (A, E, and B_2) and trace elements (Zn, Cu, and Se) in the blood serum and liver of broiler chickens.

Materials and methods

The location of the experiment. The experiment was conducted in the vivarium of the State Research Institute of Laboratory Diagnostics and Veterinary-Sanitary Expertise in Kyiv, Ukraine. Determination of the content of vitamin E and selenium in blood serum and the liver was carried out in the toxicological monitoring laboratory of the National Scientific Center «Institute of Experimental and Clinical Veterinary Medicine» in Kharkiv, Ukraine.

Experimental birds and rations. Day-old broiler chickens of the Cobb *500* breed (n=150) were used for the research. The birds were kept under optimal conditions: room temperature 28±4°C and relative air humidity 60-70%; the day-night lighting cycle during the experiment was (15-9) hours with provision of changes of the air volume in the vivarium room 18 times per hour according recommendations for Cobb 500 (L-054-01-22 EN, 2022). The research program was reviewed and approved by the Bioethics Commission of the National Scientific Centre «Institute of Experimental and Clinical Veterinary Medicine». Animal experiments were conducted in compliance with the current legislation of EU (Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes, 22 September 2010).

The combined feed «PK 5 1-2 week Start Broiler» was used for feeding the chickens, after the content of nutrients in it had been previously determined according to state standards of Ukraine (SSU): determination of the content of crude protein was carried out following the Kjeldahl method in accordance with SSU ISO 5983:2003, the content of crude fiber – according to SSU ISO 6865:2004, and raw fat – according to SSU ISO 6492:2003; the content of vitamins in accordance with SSU 4687:2006, and trace elements – in accordance with SSU EN 14082:2019 (EN 14082, 2019; SSU 4120, 2002). The results of the research are summarized in Table 1.

Experimental nanoparticles and comparator drug. Experimental samples of nanoparticles of gadolinium orthovanadate (NP $GdVO_4:Eu^{3+}$) (spindle-like geometry, size 8×25 nm) and lanthanum orthovanadate (NP $LaVO_4:Eu^{3+}$) (rod-like geometry, size 8×80 nm) were used in the study, with an initial concentration of 1.0 g/l. Research samples of nanoparticles were synthesized and standardized according to stability and size in the department of nanostructured materials named after Yu.V. Malyukin of the Institute of Scintillation Materials of the National Academy of Sciences of Ukraine (Fig. 1). The veterinary vitamin preparation Devivit Complex (manufacturer LLC «DEVIE», Ukraine) was used as the comparison drug: one milliliter of the preparation contains the active substances: vitamin A – 15000 IU, vitamin

D_3 – 1000 IU, vitamin E – 20 mg, vitamins B_1 – 10 mg, B_2 – 0.5 mg, B_3 – 25 mg, B_5 – 35 mg, B_6 – 3.0 mg, B_{12} – 30 mg.

Table 1. Qualitative composition of the broiler chicken rations (combined feed «PK 5 1-2 week Start Broiler»)

Indicator	Actually defined	Norm (L-054-01-22 EN ,2022; SSU 4120 – 2002; 2002)	± to the norm
Carbohydrates, g/100 g	57.18	Not standardized	–
Energy value, kcal	376.09	290.00	+ 86.09
Mass fraction of fat, %	6.69	Not standardized	–
Mass fraction of crude protein, %	21.79	21.00-22.00	Normal
Mass fraction of crude fiber, %	2.80	Not more than 3.0	Normal
Vitamin B_2, mg/kg	8.28	9.00	– 0.72
Vitamin A, IU/kg	7920.00	10000.00-13000.00	– 2080.00
Vitamin E, mg/kg	212.50	80.00	+ 132.50
Selenium, mg/kg	0.172	0.35	– 0.178
Copper, mg/kg	38.67	15.00	+ 23.67
Zinc, mg/kg	144.99	100.00	+ 44.99

Experimental design. According to the principle of analogues, four experimental and one control group of day-old broiler chickens (n=30) were formed: the chickens in the first experimental group received a solution of NP Gd at a dose of 0.2 mg/l of drinking water for 10 days, the second experimental group received a solution NP La at a dose of 0.2 mg/l of drinking water, the third experimental group – a solution of NP Gd and NP La (NP Gd+NP La) at a dose of 0.2 mg/l of drinking water (on average, chickens received 0.09 (0.13-0.05) mg/kg of body weight NP), and chickens in the fourth experimental group, in order to compare the antioxidant effect, received the veterinary vitamin drug Devivit Complex in a dose of 0.3 ml/l of drinking water, and chickens of the control group received drinking water without additives. After 10 days, NP administration was stopped, and the chickens were observed for another 5 days. The total period of the research was 15 days. During the clinical examination of birds, attention was paid to their behavior, their reaction to external stimuli, the presence of appetite, the condition of their skin and feathers, the color of the mucous membranes, the frequency of breathing and defecation, changes in the color and consistency of feces, etc. (KOTSYUMBAS et al., 2006). Under CO_2 anesthesia, euthanasia of experimental chickens (10 birds from each group) was carried out 5 and 10 days after the start of the administration, and 5 days after the cessation of drug administration to take blood samples by total exsanguination and, after an autopsy, liver samples for further determination of vitamin content (A, E, and B_2) and trace elements (Zn, Cu, Se).

A)

B)

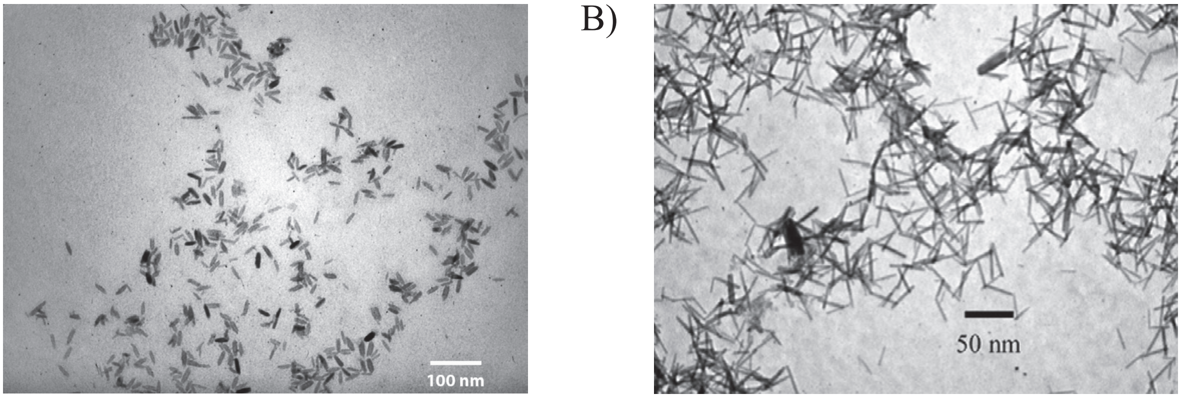

Fig. 1. Photo (transmission electron microscopy, TEM-125K, Selmi, Ukraine) of nanoparticles: A) $GdVO_4:Eu^{3+}$; B) $LaVO_4:Eu^{3+}$ (MALIUKIN, 2017; MALIUKINA et al., 2018)

Research methods. The content of vitamins A and B_2 was determined spectrometrically and fluorometrically (KFK-3-01 photometer, «Zomz», Russian Federation; Fluorophos fluorometer, «Advanced Instruments», USA) (LEVCHENKO et al., 2002; VLIZLO et al., 2012), the content of vitamin E – spectrophotometrically (SHIMADZU UV-1800, Japan) following the methodical recommendations (KUTSAN and OROBCHENKO, 2009). The content of zinc and copper was investigated using the atomic absorption spectrometry method with electrothermal atomization (Spectrometer Varian 240 Z, USA) (EN 14082:2003), selenium – following the method of KUTSAN et al. (2014).

Statistical analysis. The results obtained were processed by variational statistics using the analysis of variance (ANOVA) package StatPlus 7.6.5.0 (AnalystSoft Inc., USA). The probability of the obtained results was assessed by the Tukey test (HSD mean difference) at a probability level of 95.0% ($P<0.05$).

Results

The following changes were found in the vitamin and mineral profiles of both the blood serum and livers of broiler chickens. By determining the concentration of vitamin B_2 in the blood serum of chickens of the first experimental group (NP Gd), it was established that after 5 days of administration, the vitamin content exceeded ($P<0.05$) the control indicator. A similar pattern was observed in the second and fourth experimental groups (NP Laand Devivit complex) but 5 days after stopping administration concentrations of vitamin B_2 decreased ($P<0.05$). In the third experimental group fluctuations in concentration vitamin B_2 were observed as shown in Table 2. If we compare the level of vitamin B_2 in the blood serum of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), in the blood serum of chickens of the second and third experimental groups (NP La and NP Gd+NP La), the concentration of vitamin B_2 was lower ($P<0.05$) throughout the experiment (Table 2).

The concentration of vitamin A exceeded the control at all time periods in all experimental groups ($P<0.05$), with the exception of the third group (Table 2). If we compare the level of vitamin A in the blood serum of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in the first experimental group (NP Gd) there was a decrease in the concentration of vitamin A ($P<0.05$) on the 5th day of administration, and in the second and third research groups (NP La and NP Gd+NP La) the concentration of vitamin A was lower than in the comparison drug group ($P<0.05$) at all periods of the experiment (Table 2).

The concentration of vitamin E in the blood serum of broiler chickens had the following dynamics (Table 2): In the blood serum of chickens of the first and fourth experimental groups (NP Gd) and (Devivit complex), it was established that after 5 and 10 days of administration and 5 days after the cessation of administration, the content of vitamins exceeded the control indicator ($P<0.05$). In the second experimental group (NP La), a significant increase in the concentration of vitamin E was observed only on the 10th day of administration and in the third experimental group (NP Gd+NP La) there were no significant changes in the concentration of vitamin E (Table 2). If we compare the level of vitamin E in the blood serum of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), in the blood serum of chickens of the second and third experimental groups, the concentration of vitamin E was lower ($P<0.05$) in all periods of the experiment, in the first experimental group (NP Gd) - on the 10th day of administration and 5 days after the cessation of administration (Table 2).

Table 2. Dynamics of the concentration of vitamins in the blood serum of broiler chickens that received different doses of antioxidant drugs with drinking water (M±m, n=10)

Period of the experiment, days	Animal groups				
	Control	I experimental (NP $GdVO_4:Eu^{3+}$) 0,2 mg/l	II experimental (NP $LaVO_4:Eu^{3+}$) 0,2 mg/l	III experimental (NP $GdVO_4:Eu^{3+}$ and $LaVO_4:Eu^{3+}$) 0,2 mg/l	IV experimental (drug Devivit complex)
Vitamin B_2, nmol/dm^3					
5 days	68,24±0,77	83,46±0,90[a,b]	76,51±0,86[a,b]	64,00±0,64[a,b]	88,59±1,59[a]
10 days	50,18±1,28	76,55±1,08[a]	65,97±0,80[a,b]	65,15±0,81[a,b]	79,59±1,61[a]
5 days after stopping the introduction	21,29±0,51	20,14±0,48[b]	15,81±0,55[a,b]	14,21±0,41[a,b]	36,75±0,58[a]
Vitamin A, mmol/dm^3					
5 days	5,68±0,07	8,14±0,06[a,b]	7,71±0,07[a,b]	7,14±0,10[a,b]	13,57±0,16[a]
10 days	2,14±0,06	5,71±0,07[a]	3,57±0,06[a,b]	2,14±0,07[b]	5,71±0,05[a]
5 days after stopping the introduction	1,43±0,06	4,14±0,07[a]	3,57±0,07[a,b]	3,57±0,06[a,b]	4,29±0,07[a]
Vitamin E, mmol/dm^3					
5 days	22,50±0,38	24,60±0,46[a,b]	23,90±0,51[b]	22,10±0,36[b]	26,80±0,74[a]
10 days	21,80±0,55	25,10±0,49[a,b]	24,80±0,53[a,b]	22,40±0,57[b]	28,60±0,48[a]
5 days after stopping the introduction	21,00±0,32	22,80±0,44[a]	22,10±0,56[b]	21,70±0,31[b]	23,80±0,43[a]

a=$P<0.05$ - compared with the control group; b=$P<0.05$ - compared with the comparison drug group (Devivit complex)

In the liver of chickens in the first and fourth experimental groups (NP Gd) and (Devivit complex), it was found that after 5, 10 days of administration and 5 days after the end of administration, the content of vitamin B_2 exceeded ($P<0.05$) the control (Table 3). During the introduction of NP La (II experimental group), a decrease in the content of vitamin B_2 was observed after 5 days, then both after 10 days of introduction and 5 days after the end of the introduction, its content in the liver exceeded ($P<0.05$) the control indicators. A somewhat different picture was observed in the third experimental group (NP Gd+ NP La): during the administration period (5 and 10 days), a decrease in the content of vitamin B_2 was recorded, but 5 days after the administration, its content in the liver exceeded ($P<0.05$) control indicators. If we compare the content of vitamin B_2 in the liver of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in all experimental groups the content of vitamin B_2 was lower than in the group of the comparison drug ($P<0.05$) at all periods of the research. (Table 3).

The content of vitamin A in the livers of chickens in all experimental groups at almost all study periods exceeded the control indicator, but was lower than the indicator of the comparison drug. A similar pattern was observed for vitamin E content (Table 3).

Table 3. Dynamics of vitamin concentrations in the liver of broiler chickens that received different doses of antioxidant drugs with drinking water (M±m, n=10)

Period of the experiment, days	Animal groups				
	Control	I experimental (NP $GdVO_4:Eu^{3+}$) 0,2 mg/l	II experimental (NP $LaVO_4:Eu^{3+}$) 0,2 mg/l	III experimental (NP $GdVO_4:Eu^{3+}$ and $LaVO_4:Eu^{3+}$) 0,2 mg/l	IV experimental (drug Devivit complex)
Vitamin B2, mg/kg					
5 days	2,94±0,04	3,32±0,06[a,b]	1,60±0,04[a,b]	1,25±0,03[a,b]	4,44±0,07[a]
10 days	2,69±0,04	4,23±0,05[a,b]	3,36±0,05[a,b]	2,15±0,04[a,b]	5,20±0,06[a]
5 days after stopping the introduction	2,02±0,06	5,31±0,05[a,b]	4,33±0,04[a,b]	2,59±0,04[a,b]	6,48±0,05[a]
Vitamin A, mg/kg					
5 days	24,80±0,27	31,20±0,57[a]	25,80±0,21[b]	22,20±0,34[a,b]	30,00±0,57[a]
10 days	18,60±0,53	24,00±0,66[a,b]	30,00±0,61[a,b]	52,80±0,73[a,b]	85,50±0,92[a]
5 days after stopping the introduction	29,60±0,60	39,00±0,63[a,b]	44,40±0,72[a,b]	37,10±0,64[a,b]	48,00±0,84[a]
Vitamin E, mg/kg					
5 days	12,36±0,19	13,52±0,16[a,b]	13,24±0,18[b]	13,11±0,26[b]	15,81±0,29[a]
10 days	12,12±0,17	13,76±0,38[a,b]	13,51±0,26[a,b]	14,00±0,37[a,b]	18,73±0,25[a]
5 days after stopping the introduction	11,55±0,19	12,89±0,24[a,b]	12,67±0,16[a,b]	12,38±0,23[b]	15,24±0,22[a]

a=P<0.05 - compared with the control group; b=P<0.05 - compared with the comparison drug group (Devivit complex)

Selenium concentration in the blood serum of chickens in the first experimental group (NP Gd) decreased after 10 days (P<0.05), but 5 days after stopping administration, it exceeded the control indicator (P<0.05). In the blood serum of chickens of the second research group (NP La) after 5 days of administration, an increase in the concentration of selenium was observed (P<0.05), and 5 days after the cessation of administration, the concentration of selenium was higher than in the control group (P<0.05). In the blood serum of chickens in the third experimental group (NP Gd+NP La) after 5 days of administration, a decrease (P<0.05) in the concentration of selenium was observed, while after 10 days of administration and 5 days after the administration stopped, there was an increase (P<0.05) in element concentrations relative to the control. During the administration of the vitamin preparation Devivit complex, the concentration of selenium was below the control during the administration period, but 5 days after the cessation of administration probable deviations from the control were not noted (Table 4). If we compare the level of selenium in the blood serum of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in the first and second research groups the concentration of selenium was higher (P<0.05) at all periods of the research. In the blood serum of chickens of the third research group (NP Gd+NP La) on the 10th day of administration and 5 days after the cessation of administration, an increase in the concentration of selenium was observed (P<0.05) (Table 4).

Copper concentration in the blood serum of chickens in experimental group I (NP Gd) had no apparent deviations from the control during the entire period of research. In the blood serum of chickens in the second experimental group (NP La) after 5 days of administration, an increase in the concentration of copper was observed (P<0.05), and after 5 days after stopping the administration, the concentration of copper was higher than in the control (P<0.05). In the blood serum of chickens of the third research group (NP Gd+NP La) after 5 days of administration and 5 days after the cessation of administration, an increase in the concentration of copper was observed (p<0.05). With the introduction of the vitamin preparation Devivit complex (IV experimental group), the concentration of copper exceeded the control after 5 days of administration (P<0.05), and after 10 days it decreased (P<0.05) (Table 4). If we compare the level of copper in the blood serum of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), in the first experimental group (NP Gd), the concentration of copper after 5 days of administration was lower than in the control (P<0.05), but after 10 days of administration it increased (P<0.05). In the blood serum of chickens in the second research group after administration (NP La), the concentration of copper after 10 days of administration and 5 days after the cessation of administration increased relative to the comparison drug group (P<0.05). In the blood serum of chickens in the third experimental group after administration (NP Gd+NP La), the concentration of copper exceeded the indicators of the comparison drug at all times during the research (P<0.05) (Table 4).

The concentration of zinc in the blood serum of chickens in the first experimental group (NP Gd) was lower than in the control during the entire period of the research. In the blood serum of chickens of the second and third research groups (NP La and NP Gd+NP La), the concentration of zinc decreased after 5 days of administration (P<0.05) relative to the control, but after 5 days after the cessation of administration it exceeded (P<0.05) the control indicators. During the introduction of the vitamin preparation Devivit complex (IV research group), the concentration of zinc decreased after 10 days, and after 5 days after the cessation of administration, it exceeded (P<0.05) the control indicator (Table 4). If we compare the level of zinc in the blood serum of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in the first experimental group (NP Gd) the zinc concentration increased after 10 days of administration and 5 days after the cessation of administration (P<0.05) relative to the control. In the blood serum of chickens in the second experimental group after administration (NP La), the concentration of zinc decreased after 5 days of administration relative to the comparison drug, while after 10 days of administration and 5 days after the end of administration it increased (P<0.05). The

Table 4. The dynamics of the concentrations of trace elements in the blood serum of broiler chickens that received different doses of antioxidant drugs with drinking water (M±m, n=10)

Period of the experiment, days	Animal groups				
	Control	I experimental (NP $GdVO_4:Eu^{3+}$) 0,2 mg/l	II experimental (NP $LaVO_4:Eu^{3+}$) 0,2 mg/l	III experimental (NP $GdVO_4:Eu^{3+}$ and $LaVO_4:Eu^{3+}$) 0,2 mg/l	IV experimental (drug Devivit complex)
Selenium, μg/dm^3					
5 days	267,30±5,64	252,90±5,63^b	332,10±7,22^{a,b}	196,10±6,43^a	197,70±6,84^a
10 days	149,10±4,01	124,10±2,94^{a,b}	132,30±2,96^b	279,10±6,37^{a,b}	74,40±6,50^a
5 days after stopping the introduction	178,90±5,10	267,90±4,85^{a,b}	266,30±5,80^{a,b}	443,40±13,61^{a,b}	184,90±6,82
Copper, μg/dm^3					
5 days	99,90±4,22	110,30±3,27^b	159,80±4,31^{a,b}	200,20±4,89^{a,b}	169,80±7,37^a
10 days	169,80±8,10	160,30±8,57^b	159,70±8,53^b	179,60±5,26^b	110,10±4,26^a
5 days after stopping the introduction	260,40±8,56	290,10±9,58	370,20±8,94^{a,b}	649,60±10,93^{a,b}	260,10±7,11
Zinc, mg/dm^3					
5 days	3,19±0,08	2,86±0,09^a	2,46±0,07^{a,b}	2,51±0,06^{a,b}	2,98±0,09
10 days	3,60±0,08	2,81±0,06^{a,b}	3,50±0,06^b	3,58±0,07^b	1,90±0,04^a
5 days after stopping the introduction	3,76±0,06	3,62±0,08^b	4,82±0,06^{a,b}	5,46±0,08^{a,b}	4,43±0,08^a

a=P<0.05 - compared with the control group; b=P<0.05 - compared with the comparison drug group (Devivit complex)

dynamics of zinc in the blood serum of chickens of the third research group were similar (Table 4).

Selenium content in the liver of chickens in the first research group (NP Gd) exceeded (P<0.05) the control indicators throughout the entire period of the research. A slightly different picture was observed in the liver of chickens in the second experimental group (NP La): on the 10th day, there was an evident increase in the content of selenium (P<0.05), while 5 days after the cessation of administration, the content of selenium decreased relative to the control (P <0.05). In the liver of chickens in the third experimental group (NP Gd+NP La) 5 days after the cessation of administration, the selenium content decreased relative to the control (P<0.05). After 10 days of administration of the vitamin preparation Devivit complex, an evident increase was observed in the content of selenium in the liver of chickens (P<0.05) (Table 5). If we compare the content of selenium in the liver of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in the first experimental group (NP Gd), the content of selenium did not show any evident deviations at any timeduring the research. In the liver of chickens of the second experimental group (NP La), the content of selenium increased after 10 days compared to the control group (P<0.05), while after 5 days after the administration was stopped, it decreased (P<0.05). In the liver of chickens in the third experimental group (NP Gd+NP La) 5 days after the cessation of administration, a decrease in selenium content was noted (P<0.05) (Table 5).

The content of copper in the liver of chickens in the first research group (NP Gd) exceeded the control indicators during the entire period of research. In the second (NP La), third (NP Gd+NP La) and fourth (Devivit complex) experimental groups, similar dynamics were recorded regarding the content of copper in the liver: on the 5th day of administration there was a decrease (P<0.05) relative to the control, after 10 days of administration and after 5 days after termination there was an increase (P<0.05) (Table 5). If we compare the content of copper in the liver of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in the first experimental group (NP Gd) the content of copper exceeded the corresponding indicator after 5 days of administration, and after 5 days after stopping administration it decreased (P<0.05). In the liver of chickens in the second (NP La) and third experimental groups (NP Gd+NP La) the content of copper increased after 5 days of administration relative to the comparison drug group (P<0.05) (Table 5).

Table 5. The dynamics of the concentrations of microelements in the liver of broiler chickens that received different doses of antioxidant drugs with drinking water (M±m, n=10)

Period of the experiment, days	Animal group				
	Control	I experimental (NP $GdVO_4:Eu^{3+}$) 0,2 mg/l	II experimental (NP $LaVO_4:Eu^{3+}$) 0,2 mg/l	III experimental (NP $GdVO_4:Eu^{3+}$ and $LaVO_4:Eu^{3+}$) 0,2 mg/l	IV experimental (drug Devivit complex)
Selenium, µg/kg					
5 days	403,10±4,05	451,10±5,31^{a}	424,10±5,66	428,90±8,91	425,20±9,77
10 days	339,70±8,46	374,80±9,08^{a}	400,80±5,35^{a,b}	351,30±5,56	368,20±5,55^{a}
5 days after stopping the introduction	328,10±4,03	370,30±9,01^{a}	285,90±6,67^{a,b}	276,20±6,12^{a,b}	342,10±8,82
Copper, mg/kg					
5 days	5,45±0,06	5,58±0,05^{b}	4,96±0,06^{a,b}	5,19±0,07^{a,b}	4,37±0,07^{a}
10 days	3,96±0,08	5,73±0,06^{a}	5,70±0,08^{a}	5,89±0,07^{a}	5,69±0,08^{a}
5 days after stopping the introduction	3,39±0,06	4,61±0,07^{a,b}	5,25±0,10^{a}	5,30±0,09^{a}	5,05±0,07^{a}
Zinc, mg/kg					
5 days	36,82±0,34	36,30±0,28^{b}	39,15±0,37^{a,b}	30,87±0,43^{a}	31,52±0,54^{a}
10 days	26,82±0,36	31,65±0,60^{a}	33,51±0,42^{a,b}	31,65±0,56^{a}	31,00±0,56^{a}
5 days after stopping the introduction	27,96±0,51	30,71±0,59^{a,b}	31,20±0,53^{a,b}	31,85±0,46^{a,b}	34,05±0,57^{a}

a=P<0.05 - compared with the control group; b=P<0.05 - compared with the comparison drug group (Devivit complex)

Zinc content in the liver of chickens in the first experimental group (NP Gd) increased after 10 days of administration and 5 days after cessation of administration ($P<0.05$). In the liver of chickens in the second research group (NP La) exceeded ($P<0.05$) the control indicators during the entire period of the research. In the third (NP Gd+NP La) and fourth (Devivit complex) research groups, similar dynamics were recorded regarding the content of zinc in the liver: on the 5th day of administration there was a decrease ($P<0.05$) compared to the control, and after 10 days of administration and 5 days after the cessation an increase ($P<0.05$) (Table 5). If we compare the content of zinc in the liver of chickens that received nanoparticles with that in the group of the comparison drug (Devivit complex), then in the first experimental group (NP Gd) the content of zinc exceeded the corresponding indicator after 5 days of administration, and after 5 days after stopping administration it decreased ($P<0.05$). In the liver of chickens in the second experimental group (NP La), the zinc content increased after 5 and 10 days of administration relative to the comparison drug group ($P<0.05$), while after 5 days after the cessation of administration, it decreased ($P<0.05$). In the liver of chickens in the third experimental group (NP Gd+NP La), the zinc content decreased after administration and 5 days after the administration was stopped ($P<0.05$) (Table 5).

Discussion

Breeding of broiler chickens in Ukraine is quite efficient and ensures high-quality meat, early maturity of the birds, low feed costs, a high level of mechanization and automation of production, fast turnover of working capital, return on capital investment, and high profitability (MUNIV and VORONUY, 2017). However, as a result of this, broiler chickens require an increased amount of vitamins and minerals from the first days of life to realize their genetic potential (M'SADEQ et al., 2018; ALAGAWANY et al., 2020). This is not always economically beneficial and pushes scientists to search for substances that increase the absorption of nutrients from the diet.

Today, nanotechnology can play such a role: due to their properties (large surface area compared to volume), nanoparticles can improve the oral administration of biologically active compounds and increase the bioavailability of trace elements. For example, nanotechnology has been used successfully to improve the oral bioavailability of vitamin A by protecting it from physicochemical changes such as temperature, humidity, oxidation, and pH (ARSHAD et al., 2021); and of B vitamins (PENALVA et al., 2015; YAO et al., 2015) and iron - by including it in solid lipid nanoparticles (HOSNEY et al., 2015; KATUWAVILA et al., 2016). A nanosuspension of Ag, Cu, Fe, and MnO_2 colloids had a positive effect on the organism of laboratory animals and poultry (OROBCHENKO et al., 2019; OROBCHENKO et al., 2020; ROMANKO et al., 2023).

We would like to note that this study of gadolinium and lanthanum orthovanadate nanoparticles in broiler chickens is the first of its kind, so we will try to explain the data obtained, taking into account the currently known mechanisms of nutrient absorption and the proven biochemical mechanisms of nanoparticle effects on the cell and the body.

In our studies, the best results in the absorption of vitamin B_2 were obtained by administering NP Gd to broiler chickens (experimental group I), because during the 10-day period of administration, its increase in both blood serum and liver was observed, similar to that of the comparison drug. This effect can be explained by the peculiarities of riboflavin absorption in the digestive tract.

For example, about 75% of riboflavin is absorbed in the small intestine, where flavin adenine dinucleotide (FAD) is cleaved by 5'-nucleotide phosphodiesterase and flavin mononucleotide (FMN) - by alkaline phosphatase in the parietal space, releasing riboflavin, and plant glycosides rich in riboflavin are cleaved by lactase. Inside the enterocytes, riboflavin is reversibly converted to FAD and FMN, after which they are transported into the bloodstream (SUNDARAM, 2000; HALSTED, 2003). FMN is synthesized by phosphorylation of vitamin B_2, and FAD is synthesized by condensation with adenosine diphosphate (SERRANO et al., 2020). FAD and FMN act as electron carriers in a number of redox reactions involved in energy production (MANSOORABADI et al., 2007). Since orthovanadate nanoparticles of rare earth elements can affect mitochondrial potential, respiration and oxidative phosphorylation processes (AVERCHENKO et al., 2016), we can assume the stimulating effect of NP Gd on the synthesis of FAD and FMN and, accordingly, an increase in the concentration of vitamin B_2 in the blood and liver of chickens. The introduction of NP La (experimental group II) and the mixture of NP Gd +NP La (experimental group III) caused a less pronounced effect during the administration period, which is probably due to the different geometry of NP La (rod-shaped), and as a result, a different (longer-lasting) mechanism of influence on the above processes and the lower potential for lanthanum orthovanadate to affect cellular processes (AVERCHENKO et al., 2016), since an increase in riboflavin content in the chicken livers was observed 5 days after the administration of the nanoparticles was stopped.

Almost equal concentrations of vitamins A and E were observed in the blood serum of chickens treated with NP Gd (experimental group I) and NP La (experimental group II) compared to the control, indicating an increase in vitamin absorption in the digestive tract. This effect of orthovanadate nanoparticles can be explained by their positive effect on the small intestinal wall, which is manifested by the stimulation of enterocytes (TKACHENKO et al., 2021; MASLIUK et al., 2023c). However, the best deposition of both vitamins in the liver occurred after 10 days of administration of a mixture of nanoparticles (NP Gd+NP La) (experimental group III).

After absorption, vitamins A and E are involved in lipid peroxidation reactions: Free-radical scavenging reactions of α-tocopherol take place via the a-tocopheroxyl radical as an intermediate. If a suitable free radical is present, a non-radical product can be formed from the coupling of the free radical with the α -tocopheroxyl radical. The reaction products of α -tocopherol with lipid-peroxyl radicals are 8 α -(lipid-dioxy)-α-tocopherones, which are hydrolyzed to α -tocopherylquinone. If the supply of oxygen is insufficient, α -tocopherol can trap the carbon-centered radicals of lipids to form 6-0-(lipid alkyl)-α-tocopherols. On the other hand, the dimer and trimer of α tocopherol is formed by the bimolecular self-reaction of the α-tocopheroxyl radical in a reaction mixture containing a large amount of α-tocopherol (YAMAUCHI, 1997). In our opinion, gadolinium and lanthanum orthovanadate nanoparticles participate in ROS neutralization reactions, thus protecting parts of vitamin E from free radicals, allowing it to be transported from enterocytes and accumulate in the body, thus protecting vitamin A from oxidation. It is believed that for $ReVO_4:Eu^{3+}$ (Re = Gd, Y, La) nanoparticles, the antiradical mechanism of action is possible due to the $Eu^{3+} \leftrightarrow Eu^{2+}$ transition (KLOCHKOV et al., 2012b).

Typically, oxidative stress depletes non-enzymatic antioxidants such as vitamin C, vitamin E, and glutathione (JONES, 2006; SONG et al., 2016), but it also inhibits antioxidant enzymes such as catalase, superoxide dismutase, and glutathione peroxidase, which contain essential trace elements (Cu, Zn, Se) in their active sites.

Our research confirms the ability of gadolinium and lanthanum orthovanadate nanoparticles to increase the digestibility of trace elements, which can be explained by the similarity of the ionic radii and coordination numbers of lanthanides to those of some metal ions important for oxidative homeostasis (Ca, Fe, Mg, Mn, Zn), and by the influence of lanthanide cations on the possibility of electron transfer in the ligands of lanthanide complexes (LIU et al., 2010; ZHAO et al., 2011), which can improve the absorption of the trace elements studied in the digestive tract and their deposition.

In addition, our findings are consistent with those of other types of nanoparticles that increase the bioavailability of nutrients to animals due to their nanoscale size (BUNGLAVAN et al. 2014; VIJAYAKUMAR and BALAKRISHNAN 2014; HILL and LI 2017; YOUSSEF et al. 2019; AMLAN and LALHRIATPUII, 2020).

On the basis of the studies conducted, it was concluded that the stimulation of vitamin and trace element metabolism in chickens by nanoparticles of rare earth orthovanadates can be recommended as promising candidates for inclusion in feed additives and veterinary drugs with adaptogenic effect after completion of further preclinical studies.

Conclusions

The introduction of nanoparticles of orthovanadates of rare earth elements (gadolinium and lanthanum) to broiler chickens for 10 days at a dose of 0.2 mg/l of drinking water (on average 0.09 mg/kg of body weight) leads to stimulation of vitamin and trace element metabolism, which is manifested by an increase in serum concentration and deposition of vitamins (A, E and B_2) and trace elements (Zn, Cu and Se) in the liver.

The increase in blood serum concentrations compared to the control group ranged from 8.6 to 3.0 times for vitamins and from 17.8 to 2.5 times for trace elements ($P<0.05$), and in the liver from 9.4 to 4.6 times for vitamins and from 6.3 to 56.3% for trace elements ($P<0.05$), with gadolinium orthovanadate nanoparticles showing the best results in this regard.

The introduction of REE nanoparticles (both in mono-solutions and in a mixture) together with a vitamin preparation indicates the possibility of increasing the content of vitamins and trace elements without additional administration, using the nutritional resource more fully, and indicates a prolonged effect (the above trends continued for 5 days after stopping the administration). Taking this into account, our next scientific study will be devoted to the indicators of lipid peroxidation in the blood serum of broiler chickens under the influence of nanoparticles of the rare earth element orthovanadates.

Ethics approval

Animal experiments were conducted in compliance with the current legislation of EU (Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes, 22 September 2010).

Declaration of Competing Interest

The authors declare no conflict of interest.

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MASLIUK, A., O. OROBCHENKO, V. USHKALOV, V. KLOCHKOV, S. YEFIMOVA, N. KAVOK, R. SACHUK, O. KURBATSKA: Učinak nanočestica gadolinija i lantan-ortovanadata na sadržaj vitamina (B2, A, E) i elemenata u tragovima (Cu, Zn, Se) u serumu i jetri tovnih pilića. Vet. arhiv 94, 219-236, 2024.

SAŽETAK

Razvojem znanosti i tehnologije sve se više tvari u obliku nanočestica uvode u različita područja ljudske aktivnosti, pa tako i u stočarstvo (peradarstvo). Nanotehnologija se osobito uspješno primjenjuje u obogaćivanju prehrambenih proizvoda mineralima, vitaminima i antioksidansima, čime se može povećati bioraspoloživost tih nutrijenata oralnom primjenom. U ovom je radu istraživan sadržaj vitamina (A, E i B_2) i elemenata u tragovima (Zn, Cu i Se) u serumu i jetri tovnih pilića pod utjecajem gadolinij-ortovanadata, lantan-ortovanadata i mješavine navedenih supstancija. Ustanovljeno je da primjena ovih tvari u tovnih pilića tijekom 10 dana u dozi od 0,2 mg/l u vodi za piće (prosječno 0,09 mg/kg tjelesne mase) povećava bioraspoloživost vitamina B_2, A i E i elemenata u tragovima selena, bakra i cinka, što se očitovalo porastom njihove koncentracije u serumu u usporedbi s kontrolnom skupinom (od 8,6% do 3,0 puta za vitamine i od 17,8% do 2,5 puta za elemente u tragovima, $P<0,05$) i zalihama u jetri (od 9,4% do 4,6 puta za vitamine i od 6,3 do 56,3% za elemente u tragovima, $P<0,05$). Opažen je i produljeni učinak navedenih tvari, nakon što je njihova primjena završila. Uvođenje nanočestica (i kao monootopine i u mješavini), s pripravkom vitamina, moglo bi povećati sadržaj vitamina i elemenata u tragovima bez njihova dodatnog unosa, čime bi se bolje iskoristila nutritivna svojstva hrane.

Ključne riječi: vitamini; elementi u tragovima; tovni pilići; nanočestice gadolinija; ortovanadati; nanočestice lantan-ortovanadata