concentrates with or without supplemental roughage. *Journal of Animal Science*, *70*(3), 894-903.

30. Perdomo, M. C., Marsola, R. S., Favoreto, M. G., Adesogan, A., Staples, C. R., & Santos, J. E. P. (2020). Effects of feeding live yeast at 2 dosages on performance and feeding behavior of dairy cows under heat stress. *Journal of dairy science*, *103*(1), 325-339.
31. Suarez-Mena, F. X., Zanton, G. I., & Heinrichs, A. J. (2013). Effect of forage particle length on rumen fermentation, sorting and chewing activity of late-lactation and non-lactating dairy cows. *animal*, *7*(2), 272-278.
32. Maulfair, D. D., Zanton, G. I., Fustini, M., & Heinrichs, A. J. (2010). Effect of feed sorting on chewing behavior, production, and rumen fermentation in lactating dairy cows. *Journal of dairy science*, *93*(10), 4791-4803.
33. Kaltenegger, A., Humer, E., Stauder, A., & Zebeli, Q. (2020). Feeding of bakery by-products in the replacement of grains enhanced milk performance, modulated blood metabolic profile, and lowered the risk of rumen acidosis in dairy cows. *Journal of dairy science*, *103*(11), 10122-10135.
34. Komatsu, T., Higashiyama, Y., Fukasawa, M., Katoh, K., & Oshibe, A. (2014). Physiological changes during feeding and rumination in cows. *Animal science journal*, *85*(3), 271-276.
35. Goulart, R. S., Vieira, R. A., Daniel, J. L., Amaral, R. C., Santos, V. P., Toledo Filho, S. G., ... & Nussio, L. G. (2020). Effects of source and concentration of neutral detergent fiber from roughage in beef cattle diets: Comparison of methods to measure the effectiveness of fiber. *Journal of Animal Science*, *98*(5), skaa108.
36. Ran, T., Saleem, A. M., Beauchemin, K. A., Penner, G. B., & Yang, W. (2021). Processing index of barley grain and dietary undigested neutral detergent fiber concentration affected chewing behavior, ruminal pH, and total tract nutrient digestibility of heifers fed a high-grain diet. *Journal of animal science*, *99*(1), skab011.
37. Coons, E. M., Fredin, S. M., Cotanch, K. W., Dann, H. M., Ballard, C. S., Brouillette, J. P., & Grant, R. J. (2019). Influence of a novel bm3 corn silage hybrid with floury kernel genetics on lactational performance and feed efficiency of Holstein cows. *Journal of dairy science*, *102*(11), 9814-9826.

UDC 636.09:577.773.42:661.847-022.532]:001.891.53

COMPARATIVE ASSESSMENT OF TOXICOLOGICAL PROPERTIES OF ZINC NANOPARTICLES DEPENDING ON DOSAGE AND CHEMICAL STRUCTURE

Koshevoy V.I., PhD (Vet. Med.), State Biotechnological University, Kharkiv, Ukraine
ORCID: https://orcid.org/0000-0003-2938-2762

Introduction. Nanoparticles (NPs) of metals, including zinc, can be successfully used to meet the mineral sources of animals and poultry, they are able to increase the rate of growth and their use of feed [1]. It is known that zinc oxide nanoparticles (ZnO-NPs) are superior to conventional sources of zinc in terms of pharmacological activity and bioavailability, have a positive effect on productivity and antioxidant defense, increase reproductive potential, but require detailed clarification of toxicological parameters [2]. It has been proven that the release of Zn^{2+} from ZnO-NPs triggers the synthesis of an excessive amount of intracellular reactive oxygen species, which leads to the autophagic death of immune cells and confirms their potential impact on animal immunity. In addition, the results indicate that ZnO-NPs can be used as an effective fungicide [3, 4].

Recently, the use of metal NPs for the correction of trace element diseases in animals and poultry has become widespread, the main condition of which was a comprehensive assessment of their toxicological properties in order to prevent negative effects on the body and its functions [5].

The vast majority of data on the toxicity of zinc-based NPs to white mice as a biogenic element that is important in the animal and human body concerns ZnO-NPs, among which the main toxicity parameters of ZnO-NPs were determined using *in vitro* systems that lack complex interactions cell-cell, cell-matrix and hormonal effects, which can be determined *in vivo* [6, 7]. Various toxic effects due to dosage, size of NPs are noted for different methods of administration. Thus, **the aim of the study** was a comparative assessment of the toxicity of zinc-based NPs by different methods of administration on mice model.

Results. Oral administration of ZnO-NPs causes a decrease in the body weight of animals, but leads to an increase in its concentration in the blood serum, liver and kidneys, increases the activity of transaminases, but does not affect the intestinal microbiota and the content of Iron, Copper and Manganese in the kidneys, liver, etc [8]. After oral administration, ZnO-NPs were absorbed into the blood stream, after which their biodistribution occurred in the liver, spleen, and kidney, while after intraperitoneal administration, they remained in serum for 72 hours and accumulated in heart, lung, and testis tissues. Clearance of ZnO-NPs in blood serum began 6 hours after oral administration, and compared to zinc oxide microparticles, the nanoform showed a much higher absorption capacity and biodistribution in tissues after intragastric administration [9].

Significant accumulation of nanoparticles in the liver can lead to cell damage after oral exposure to ZnO-NPs (300 mg/kg). ZnO-NPs were also found to induce oxidative stress, as evidenced by increased lipid peroxidation [10]. In a dose of 500 mg/kg body weight noted the development of oxidative stress and a significant increase in the level of dopamine and norepinephrine in the cerebral cortex, which indicates the neurotoxic potential of these nanoparticles. These changes were also confirmed by inhibition of zinc- and copper-dependent superoxide dismutase, which are considered important biomarkers of oxidative stress [11].

During acute intratracheal administration, the loss of body weight of mice, the development of the inflammatory process and hyperplastic changes in the lungs, the accumulation of nitrogen oxide and malondialdehyde in lung homogenates, etc., were observed [12]. The use of a much smaller dose contributed to similar changes – an increase in the level of malondialdehyde in the lungs and a decrease in the total antioxidant capacity were noted after 6 hours, as well as an increase in the activity of lactate dehydrogenase in the bronchoalveolar lavage fluid 1 day after administration. The manifestation of the inflammatory process was observed after 3 and 7 days, which was evidenced by an increase in the number of leukocytes and the concentration of total protein in the bronchoalveolar lavage liquid, as well as histological abnormalities of the lungs [13]. In general, high dose-dependent inhalation toxicity should be noted (toxic events after administration of ≥ 6 μg (≥ 0.3 mg/kg), cases of death – 25-100 μg (≥ 1.4 mg/kg) [14].

At subtoxic doses, ZnO-NPs can stimulate a strong inflammatory and antioxidant response in lung epithelial cells. Cytotoxicity mediated by ZnO-NPs may be a consequence of the failure of the cellular redox mechanism to restrain the excessive formation of reactive oxygen species. In addition, exposure to a single but relatively high dose of ZnO-NPs by intranasal administration can induce acute pulmonary inflammatory reactions in mice [15].

Intraperitoneal administration of ZnO-NPs caused significant changes in hematological and biochemical parameters with higher toxicity after 10 days, while histopathological lesions were observed in the liver, kidney, spleen, heart and brain of mice [16]. Also of concern is the presence of a negative effect of ZnO-NPs on sex hormones, which increased apoptosis and caused a steroidogenic effect in Leydig cells and increased the formation of an autophagic vacuole, possibly due to a change in the activity of an antioxidant enzyme in mouse testicular cells [17].

Conclusions. Having analyzed a significant number of scientific sources, it is possible to conclude that the basis of the toxic effect of zinc-based NPs is dosage. In addition, an important factor is the chemical structure, physical parameters – structure, form-factor and size. Therefore, an important stage in the development of drugs based on ZnO-NPs should be detailed toxicological studies, primarily of hemato-, hepato-, cardio- and nephrotoxicity.

References:
1. Mahmoud, M., Yahia, D., Abdel-Magiud, D. S., Darwish, M., Abd-Elkareem, M., &

Mahmoud, U. T. (2021). Broiler welfare is preserved by long-term low-dose oral exposure to zinc oxide nanoparticles: preliminary study. *Nanotoxicology, 15*(5), 605–620. https://doi.org/10.1080/17435390.2021.1905099

2. Khodaei-Motlagh, M., Masoudi, R., Karimi-Sabet, M. J., & Hatefi, A. (2022). Supplementation of sperm cooling medium with Zinc and Zinc oxide nanoparticles preserves rooster sperm quality and fertility potential. *Theriogenology, 183*, 36–40. https://doi.org/10.1016/j.theriogenology.2022.02.015

3. Patra, P., Mitra, S., Debnath, N., & Goswami, A. (2012). Biochemical-, biophysical-, and microarray-based antifungal evaluation of the buffer-mediated synthesized nano zinc oxide: an in vivo and in vitro toxicity study. *Langmuir: the ACS journal of surfaces and colloids, 28*(49), 16966–16978. https://doi.org/10.1021/la304120k

4. Johnson, B. M., Fraietta, J. A., Gracias, D. T., Hope, J. L., Stairiker, C. J., Patel, P. R., Mueller, Y. M., McHugh, M. D., Jablonowski, L. J., Wheatley, M. A., & Katsikis, P. D. (2015). Acute exposure to ZnO nanoparticles induces autophagic immune cell death. *Nanotoxicology, 9*(6), 737–748. https://doi.org/10.3109/17435390.2014.974709

5. Naumenko, S., Koshevoy, V., Matsenko, O., Miroshnikova, O., Zhukova, I., & Bespalova, I. (2023). Antioxidant properties and toxic risks of using metal nanoparticles on health and productivity in poultry. *Journal of World`s Poultry Research, 13*(3), 292-306. https://doi.org/10.36380/jwpr.2023.32

6. Haberl, N., Hirn, S., Holzer, M., Zuchtriegel, G., Rehberg, M., & Krombach, F. (2015). Effects of acute systemic administration of TiO2, ZnO, SiO2, and Ag nanoparticles on hemodynamics, hemostasis and leukocyte recruitment. *Nanotoxicology, 9*(8), 963–971. https://doi.org/10.3109/17435390.2014.992815

7. Hadrup, N., Rahmani, F., Jacobsen, N. R., Saber, A. T., Jackson, P., Bengtson, S., Williams, A., Wallin, H., Halappanavar, S., & Vogel, U. (2019). Acute phase response and inflammation following pulmonary exposure to low doses of zinc oxide nanoparticles in mice. *Nanotoxicology, 13*(9), 1275–1292. https://doi.org/10.1080/17435390.2019.1654004

8. Wang, C., Cheng, K., Zhou, L., He, J., Zheng, X., Zhang, L., Zhong, X., & Wang, T. (2017). Evaluation of Long-Term Toxicity of Oral Zinc Oxide Nanoparticles and Zinc Sulfate in Mice. *Biological trace element research, 178*(2), 276–282. https://doi.org/10.1007/s12011-017-0934-1

9. Li, C. H., Shen, C. C., Cheng, Y. W., Huang, S. H., Wu, C. C., Kao, C. C., Liao, J. W., & Kang, J. J. (2012). Organ biodistribution, clearance, and genotoxicity of orally administered zinc oxide nanoparticles in mice. *Nanotoxicology, 6*(7), 746–756. https://doi.org/10.3109/17435390.2011.620717

10. Sharma, V., Singh, P., Pandey, A. K., & Dhawan, A. (2012). Induction of oxidative stress, DNA damage and apoptosis in mouse liver after sub-acute oral exposure to zinc oxide nanoparticles. *Mutation research, 745*(1-2), 84–91. https://doi.org/10.1016/j.mrgentox.2011.12.009

11. Shrivastava, R., Raza, S., Yadav, A., Kushwaha, P., & Flora, S. J. (2014). Effects of sub-acute exposure to TiO2, ZnO and Al2O3 nanoparticles on oxidative stress and histological changes in mouse liver and brain. *Drug and chemical toxicology, 37*(3), 336–347. https://doi.org/10.3109/01480545.2013.866134

12. Wang, D., Li, H., Liu, Z., Zhou, J., & Zhang, T. (2017). Acute toxicological effects of zinc oxide nanoparticles in mice after intratracheal instillation. *International journal of occupational and environmental health, 23*(1), 11–19. https://doi.org/10.1080/10773525.2016.1278510

13. Guo, T., Fang, X., Liu, Y., Ruan, Y., Hu, Y., Wang, X., Hu, Y., Wang, G., & Xu, Y. (2022). Acute lung inflammation induced by zinc oxide nanoparticles: Evolution and intervention via NRF2 activator. *Food and chemical toxicology, 162*, article number 112898. https://doi.org/10.1016/j.fct.2022.112898

14. Jacobsen, N. R., Stoeger, T., van den Brule, S., Saber, A. T., Beyerle, A., Vietti, G.,

Mortensen, A., Szarek, J., Budtz, H. C., Kermanizadeh, A., Banerjee, A., Ercal, N., Vogel, U., Wallin, H., & Møller, P. (2015). Acute and subacute pulmonary toxicity and mortality in mice after intratracheal instillation of ZnO nanoparticles in three laboratories. *Food and chemical toxicology, 85*, 84–95. https://doi.org/10.1016/j.fct.2015.08.008

15. Saptarshi, S. R., Feltis, B. N., Wright, P. F., & Lopata, A. L. (2015). Investigating the immunomodulatory nature of zinc oxide nanoparticles at sub-cytotoxic levels in vitro and after intranasal instillation in vivo. *Journal of nanobiotechnology, 13*, article number 6. https://doi.org/10.1186/s12951-015-0067-7

16. Ogunsuyi, O., Ogunsuyi, O., Akanni, O., Alabi, O., Alimba, C., Adaramoye, O., Cambier, S., Eswara, S., Gutleb, A. C., & Bakare, A. (2022). Physiological and histopathological alterations in male Swiss mice after exposure to titanium dioxide (anatase) and zinc oxide nanoparticles and their binary mixture. *Drug and chemical toxicology, 45*(3), 1188–1213. https://doi.org/10.1080/01480545.2020.1811720

17. Bara, N., & Kaul, G. (2018). Enhanced steroidogenic and altered antioxidant response by ZnO nanoparticles in mouse testis Leydig cells. *Toxicology and industrial health, 34*(8), 571–588. https://doi.org/10.1177/0748233718774220

EFFECT OF ETHYLTHIOSULPHANILATE ON THE ENZYMATIC ACTIVITY OF ALKALINE PHOSPHATASE IN RAT BLOOD PLASMA UNDER THE TOXIC EFFECT OF CR(VI)

Kotyk B.I., postgraduate student, Institute of Animal Biology NAAS, Lviv, Ukraine
ORCID: https://orcid.org/0000-0002-3414-1624
Iskra R.Ya., doctor of biology, professor, Ivan Franko National University of Lviv, Lviv, Ukraine
ORCID: https://orcid.org/0000-0001-7248-548X

The active use of Cr(VI) compounds in the industrial sector contributes to its spread in the environment and poisoning of organisms. Cr(VI) is a heavy metal and a powerful pro-oxidant that causes disruption of cellular metabolism by hyperproducing reactive oxygen species (ROS) and impairing the functions of antioxidant defense system (ADS) enzymes [1]. Cr(VI)-induced oxidative stress leads to activation of apoptosis and necrosis in hepatocytes [2]. Alkaline phosphatase (ALP) belongs to a group of enzymes that regulate cellular metabolism by cleaving phosphate residues from protein and nucleotide molecules at alkaline pH [3]. An increase in the activity of ALP under the influence of Cr(VI) is an indicator of hepatotoxicity [4, 5]. Antioxidants inhibit the prooxidant effect of Cr(VI) by supplying their own electrons with subsequent reduction of Cr(VI) to Cr(III) [130]. Ethylthiosulfanylate (ETS) is an organosulfur synthetic compound of the thiosulfonate class. The antioxidant effect of ETS contributes to the normalization of the ADS status in liver tissue under the toxic effects of Cr(VI) [6]. It is also important to investigate whether the antioxidant effect of ETS is sufficient to prevent Cr(VI)-induced hepatotoxicity.

Therefore, the aim of our work was to investigate the features of ETS effect on the enzymatic activity of ALP in the blood of rats under the toxic effect of Cr(VI).

White male *Wistar* laboratory rats were divided into 7 groups with 5 animals each group. The rats in the group I (intact control) were injected daily intraperitoneally (ip) with 150 µl of physiological saline for 14 days. Rats of group II were injected daily intragastrally (ig) with 1000 µl of oil for 14 days and then daily ip injected with physiological saline for 14 days. Animals of group III / IV received $K_2Cr_2O_7$ ip at a dose 2,5 mg Cr(VI)/kg body weight (bw) per day for 7 days / 14 days. Rats of groups V were injected daily ig with an oil solution of ETS at a dose of 100 mg ETS/kg bw for 14 days and then daily ip injected with physiological saline for 14 days. Animals of groups VI and VII were administrated daily ig with an oil solution of ETS at a dose of 100 mg ETS/kg bw for 14 days and then daily ip injected with with $K_2Cr_2O_7$ at a dose 2,5 mg Cr(VI)/kg bw for 7 days (group VI) of 14 days (group VII). We determined the enzymatic activity of ALP in