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Original Paper

The effect of colloidal silver on clinical, morphological parameters and mineral composition of blood of calves

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The problem of the calf livestock to be preserved under the use restriction conditions of the antibiotics in case of the infectious diseases requires the search for alternative antimicrobial agents, to which the nanocompounds of the noble metals are belonged. The influence of the colloid silver solution on the indicators of the clinical condition, mineral turnover and morphological composition of the blood of the black-pied Holstein calves aged from birth to 30 days had been analyzed. It had been established that the calf rearing with the colloid silver solution composed of colostrum (milk) at a dose of 1.0 and 2.0 mg/l from the 1 to the 10 day every twenty-four hours, from the 11 to the 30 day, which is carried out once a decade, does not influence on the indicators of the clinical condition, but dose-dependently contributes to the increasing silver content in the blood. Nanosilver at a dose of 2.0 mg/l of colostrum causes the increasing iron and zinc accumulation in the blood of the calves on the 3 day after birth. With the increasing calf age up to 30 days as well as with the increasing oral use interval of the colloid silver solution, its influence on the exchange of zinc, iron and copper in the blood is decreased. On the 3 and 10 day after the calf rearing with the colloid silver solution at a dose of 1.0 mg/l, the erythrocyte number reduction in their blood was found by 15.0% and 12.3%, the dose of nanosilver of 2.0 mg/l of colostrum causes a similar influence only on the 10 day. On the 30 day after the increasing interval of the calf rearing the erythrocyte number in the blood of both studied groups had been equal with the control one. The leukocyte number in the blood of the healthy calves practically did not depend on the dose of the colloid silver, as well as on its use period. The dose of the colloid silver equal to 1.0 mg/l of colostrum (milk) influences on the blood leukogram in a lesser extent than the dose equal to 2.0 mg/l, but both drug doses for 30 day increase the lymphocyte percentage in the blood of the healthy calves. The obtained results make it possible to select an effective dose and interval of nanosilver application to the calves, taking into account the indicators of their clinical condition, mineral turnover and morphological composition of the blood, as well as to consider it as a prophylactic agent in case of the infectious diseases.

Keywords: calves, nanosilver, mineral turnover, blood, clinical condition

1 Introduction

Diseases of infectious ethiology in both humans and animals are one of the most important health problems throughout the world, the main reason of which is the development of multi-drug resistant microorganisms to a number of the antibiotics. This problem is especially relevant in the cattle rearing business, where the greatest morbidity and mortality of the calves occurs in the first weeks of life (Zeedan et al., 2018; Olentsova et al., 2020). The main causative agents of the calves include opportunistic and pathogenic microflora, which, with the irrational use of the antibiotics, generates the resistant and multi-drug resistant strains, which in turn influences the effectiveness of the antibiotic therapy in both humans and animals (El-Gohary et al., 2020). Therefore, this problem solution is possible due to the development of new high-effective alternative drugs with bactericidal, bacteriostatic, virulicidal and fungicidal activities on pathogenic and opportunistic microorganisms (Sanches-Lopez et al., 2020). Such agents include the silver drugs obtained with the help of the nanotechnologies, which selectively influence the resident microflora of the body, had a prolonged action, are non- toxic, do not had high cumulative activity and can be implemented into

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a commercial production (Youssef et al., 2019; Estevez et al., 2021; Zheltonozhskaya et al., 2021).

The studies had shown that the nanoparticles of the noble metal had been effective for the disease treatment due to the antibiotic-resistant bacteria in both *in vitro* and *in vivo* studies (George et al., 2019; Thorat et al., 2021). With regard to the nanomaterial-based drugs, today the scientists and practitioners actively discuss the comparison of their benefits and harms for the health of animals, humans and environment. However, it should be taken into account that the nanomaterial-based drugs cannot be completely safe, so their use requires not only the improvement of the synthesis methods, but also the application modes, in particular, the body injection dose and the application interval.

These questions require an urgent solution, since the use of the nanosilver-based drugs in the cattle rearing business is limited due to the insufficient clinical justification of their application as a precaution of the infectious diseases among the young livestock. Therefore, our studies had been aimed at studying the influence of the colloid nanosilver solution on the indicators of the clinical condition, morphological composition of the blood and mineral turnover among the calves.

2 Material and methods

All calf experiments had been carried out in compliance with the requirements of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes dated 1986, as well as the Law of Ukraine "On the Protection of Animals from Cruelty" No. 3447-IV dated 21.02.2006 as amended on 04.08.2017. All procedures, which were experimentally planned in the calves, had been approved by the bioethics commission of the National University of Bioresources and Nature Management of Ukraine.

The study had been carried out under conditions of a private farm in Kremenchuk district, Poltava region (Ukraine), specializing in the milk. The calves had been kept in individual in an exposed site with the proper conditions for feeding and husbandry. 30 new-born calves of the black-pied Holstein breed, which were randomly divided into 3 groups, had been used for the experiment: control and two of 10 each. The calves of the 1 studied group were given the colloid silver with colostrum (milk) at a concentration of 1.0 mg/l, and the calves of the 2 group – 2.0 mg/l from the 1 to the 10 day every twenty-four hours, from the 11 to the 30 day – once a decade, the calves of the control group were not given the drug.

The experiment used nanosilver produced by "NANOMATERIALS AND NANOTECHNOLOGIES" LLC (Kyiv, Ukraine). Among the calves, the body weight had been determined on Axis scales (Poland) with an accuracy of 100 g, the rectal body temperature with the help of the mercury thermometer, the pulse on the submandibular artery, the respiration rate by counting the chest wall vibrations for 1 hour after birth, on the 3^{rd}, 10^{th} and 30^{th} days of life. The blood samples had been taken from the calves of the control and studied groups before morning feeding on the 3^{rd}, 10^{th} and 30^{th} days of life from the jugular vein in compliance with the asepsis and antiseptic rules. EDTA anticoagulant had been used to stabilize the blood. The content of silver, copper, zinc and iron had been determined in the blood. Mineralization was carried out with the help of the closed-type microwave sample digestor Milestone Ethnos Easy (Italy). After carrying out the mineralization and filtration, the samples had been analyzed with the help of spectrometer Plasma Quant PQ 9000 ICP OES (Analytik Jena, Germany). Standard multicomponent solutions for atomic emission spectrometry (Merck, Germany) had been used to calibrate the spectrometer. Analytical signals had been automatically processed with the help of the spectrometer software, using the calibration functions, taking into account the background correction, and if necessary, the mutual influence of the studied elements.

The number of erythrocytes, leukocytes, hemoglobin content and leukogram with the help of Vet Auto Hematology Analyzer BC-2800 Vet (Mindray, China) had been determined in the calf blood.

Statistical processing of the obtained results had been carried out with the help of one-way ANOVA test. The obtained data had been compared between the groups with the help of Tukey test. The data specified in the tables are presented as x ±SD (mean ±standard deviation). The difference between the group values had been considered significant at $p < 0.05$ using Bonferroni correction.

3 Results and discussion

The calf rearing with the colloid silver solution composed of colostrum (milk) at a dose of 1.0 mg/l and 2.0 mg/l during the entire study period had not influence on the indicators of their clinical condition (table 1), in particular, the body weight and temperature, as well as the respiration rate and pulse compared to the control group. This is due to a low dose of the colloid silver in the calf diet, as well as its entry into the digestive system with colostrum or milk, the components of which also influence on the absorption and detoxification intensity

Table 1 Indicators of clinical condition of calves when using colloid silver solution, x ±SD

Indicator	Calf group		
	control	1st studied	2nd studied
1 hour after birth			
Mass of calf (kg)	42.20 ±2.16	42.26 ±1.47	42.36 ±2.07
Body temperature (°C)	40.06 ±0.31	39.30 ±0.38	40.08 ±0.54
Pulse, beats per minute	136.20 ±1.29	134.41 ±2.17	138.41 ±1.61
Respiration rate, breaths per minute	43.80 ±1.19	44.80 ±2.30	44.20 ±1.78
3 days after birth			
Mass of calf (kg)	43.20 ±2.17	43.24 ±1.49	43.41 ±2.18
Body temperature (°C)	39.70 ±0.21	38.81 ±0.16	39.24 ±0.38
Pulse, beats per minute	120.61 ±3.49	127.41 ±1.48	129.42 ±1.89
Respiration rate, breaths per minute	41.00 ±1.27	41.20 ±1.67	42.60 ±1.30
10 days after birth			
Mass of calf (kg)	45.61 ±2.11	47.11 ±1.46	48.21 ±1.98
Body temperature (°C)	39.34 ±0.23	38.94 ±0.22	38.98 ±0.28
Pulse, beats per minute	128.63 ±2.36	124.82 ±3.01	127.00 ±3.24
Respiration rate, breaths per minute	39.10 ±1.51	42.30 ±2.44	42.20 ±2.31
30 days after birth			
Mass of calf (kg)	50.12 ±1.58	52.46 ±1.64	53.01 ±2.26
Body temperature (°C)	39.24 ±0.39	38.28 ±0.35	38.90 ±0.23
Pulse, beats per minute	126.40 ±4.28	123.61 ±1.15	119.00 ±1.70
Respiration rate, breaths per minute	38.20 ±1.85	38.60 ±2.41	39.80 ±1.39

of the chemicals. Furthermore, the increasing application interval of the colloid silver solution after the 10 day of the study had also provided the sufficient time for the clearance of this excessive element from the calf body.

The calf rearing with the colloid silver solution composed of colostrum dose-dependently had increased (p <0.05) the silver content in their blood on the 3 day of life compared to the control group (table 2). It is evidence that the colloid silver can be absorbed into the blood from the digestive system of the calves. The absorption of the silver nanoparticles by the enterocytes due to the coordination of amino acids, short peptides and, possibly, bacterial helcophores, which are synthesized by the symbiotic microflora of the digestive system of the animals, is the basis of this mechanism (McCabe et al., 2017). In this regard, silver first enters the liver, and then enters the peripheral blood as part of the protein fraction, which is transported to other organs (Hanson et al., 2001).

Copper is one of the important microelements for the normal vital activity of the calf body, which is involved in the regulation of a significant number of the metabolic processes in the tissues and has the antibacterial properties. As far as its content in the calf blood is concerned, the drug of the colloid silver solution had not practically influence this indicator on the 3 day of the study. Iron as a microelement plays an important role in the recovery processes of the body, provides the hematopoiesis, as well as the course of almost all metabolic reactions that determine the growth intensity and immune function of the body, which is especially important in the first days of postnatal ontogenesis of the calves. Zinc is also one of the main components of the many enzyme systems, which regulates the processes of cell differentiation, growth and development of the body (Stefanidou et al., 2006). The content of zinc and iron in the calf blood had increased on the 3rd day only at a dose of the colloid silver solution of 2.0 mg/l of colostrum (p <0.05) compared to the control group and in the calves that were given the colloid silver at a dose of 1 mg/l. Such increasing zinc content in the blood may be the consequence of nanosilver on the various tissues cells in the calf body, which is manifested by the release of its significant amount into the extracellular space. This fact had been proven *in vitro* on brain cells of laboratory rats (Afifi & Abdelazim, 2015; Ziemińska & Strużyńska, 2016). With regard to the increasing iron content in the calf blood, our data are consistent with the study results on the application of nanosilver in broiler chickens (Ognik et al., 2016).

The calf rearing with the colloid nanosilver solution composed of colostrum (milk) during the first 10 days of life at doses of 1 mg/l and 2 mg/l had dose-dependently contributed (*p* <0.05) the increasing content and had not influence the content of zinc and iron in their blood compared to the control group (table 2). In this regard, the increase (*p* <0.05) in the copper content in the calf blood was found only for the doses of nanosilver of 2 mg/l compared to similar indicators among the calves that received this drug at a dose of 1 mg/l of colostrum (milk). The data, which had been obtained by us, are consistent with the hypothesis based on the ability of silver to influence on copper transport, as well as the level and activity of ceruloplasmin in the animal tissues (Puchkova et al., 2019).

The increasing interval between the application of the colloid nanosilver solution to the calves on the 30 day of life continued to contribute to the increased (*p* <0.05) accumulation of silver in the animal blood of both studied groups compared to the control group (table 3). At the same time, the concentration of copper was significantly higher (*p* <0.05) in the blood of the calves that were given the colloid silver solution at a dose of 1 mg/l with colostrum (milk) compared to the control group. The calf rearing with different doses of the colloid silver solution did not practically change the content of zinc and iron in the blood compared to the control group. It shows the absence of a significant influence of nanosilver on the content of macro- and microelements in the animal blood serum as well as it is consistent with similar studies conducted on poultry (Ognik et al., 2016).

It is known that all substances absorbed into the blood make contact with the formed elements, in particular, with erythrocytes. As you can see in table 3, on the 3 and 10 days after the calf rearing with the colloid silver solution composed of colostrum at a dose of 1.0 mg/l, the erythrocyte number in the calf blood had decreased by 15% and 12.3% (*p* <0.05), respectively, compared to the control group. The introduction of nanosilver into the calf body at a dose of 2.0 mg/l caused a similar influence only on the 10 day, but the erythrocyte number in the blood had been equal with the control group already on the 30 day after the increasing interval of the calf rearing with the nanosilver drug in the blood of both studied groups. This decrease in the erythrocyte number in the calf blood during the application of the colloid silver solution may be related to the phenomenon of hemolysis, however, as indicated in the study by Huang et al. (2016), hemolysis of erythrocytes occurs if the concentration of the nanosilver drug in the blood is at the level of 40 µg/ml, while such concentration had not been reached in our experiment (Table 2).

The hemoglobin content in the calf blood of the second studied group on the 3rd and 30th days, although was within

Table 2 Microelement content in calf blood when using colloid silver solution, µg/l, x ±SD

Indicator	Calf group		
	control	1st studied	2nd studied
3 days after birth			
Silver	0.004 ±0.001	0.031 ±0.001*	0.059 ±0.002*,**
Copper	0.716 ±0.055	0.716 ±0.055	0.836 ±0.043
Zinc	1.946 ±0.155	1.726 ±0.061	2.954 ±0.217*,**
Iron	227.126 ±9.481	208.364 ±5.828	259.042 ±7.773*,**
10 days after birth			
Silver	0.008 ±0.003	0.027 ±0.004*	0.050 ±0.008*,**
Copper	0.796 ±0.047	0.734 ±0.042	0.892 ±0.025**
Zinc	2.616 ±0.407	1.998 ±0.292	3.932 ±1.446
Iron	229.482 ±5.425	221.946 ±10.008	246.356 ±4.931
30 days after birth			
Silver	0.018 ±0.003	0.037 ±0.005*	0.044 ±0.009*
Copper	0.834 ±0.046	1.298 ±0.180*	0.940 ±0.020
Zinc	1.922 ±0.275	3.054 ±0.657	2.732 ±0.331
Iron	227.682 ±5.517	249.204 ±36.463	244.686 ±4.028

* *p* <0.05 compared to the control group, ** *p* <0.05 compared to the 1 studied group

the control group, was lower than that of the calves of the first studied group, which may be related to the increased dose of the nanosilver drug. Similar changes in the influence of the nanosilver drug on the number of erythrocytes and the hemoglobin content in the blood had been found in the study of laboratory rats, which Al-Baker et al. (2020) relate to the development of anaemia. The decreased erythrocyte number in the animal blood means that their destruction has increased, which may be the consequence of the iron deficiency. In our case, no iron deficiency in the calf blood was discover, but on the contrary, its increasing content in the blood on the 3rd day of the experiment, which excludes the iron deficiency anaemia (Table 2).

Table 3 Hematological indicators of calves when using colloid silver solution, x ±SD

Indicator		Calf group		
		control	1 studied	2 studied
3 days after birth				
Erythrocytes (10^{12}/l)		5.81±0.60	4.94±0.49*	5.10±0.43
Hemoglobin (g/l)		127.72±6.61	128.66±12.38	117.94±5.79**
Leukocytes (10^{9}/l)		4.65±0.89	5.24±1.37	5.02±0.47
Neutrophils	immature (%)	8.20±1.30	6.40±1.67	5.20±0.84*
	stab (%)	12.20±3.56	9.40±1.67	7.60±2.07*
	segmented (%)	34.20±6.83	40.80±3.83	39.60±14.26
Basophiles (%)		0	0	0
Eosinophils (%)		0	0	0
Monocytes (%)		1.00±0.19	1.60±0.45	1.40±0.57
Lymphocytes (%)		44.40±9.13	41.60±3.65	46.20±13.61
10 days after birth				
Erythrocytes (10^{12}/l)		7.14±0.40	6.26±0.47*	5.89±0.38*
Hemoglobin (g/l)		138.56±18.97	129.98±16.70	124.20±8.53
Leukocytes (10^{9}/l)		6.14±0.48	6.18±0.20	5.98±0.28
Neutrophils	immature (%)	3.00±1.00	2.80±1.10	2.20±0.42
	stab (%)	6.60±1.14	6.40±1.52	4.80±0.84
	segmented (%)	35.40±4.16	39.20±7.05	32.80±8.56
Basophiles (%)		0	0	0
Eosinophils (%)		0.20±0.45	0	0.20±0.45
Monocytes (%)		2.00±0.50	2.00±0.50	2.40±0.57
Lymphocytes (%)		52.80±4.87	49.60±7.64	57.60±9.61
30 days after birth				
Erythrocytes (10^{12}/l)		10.99±0.28	10.46±0.40	11.49±0.68
Hemoglobin (g/l)		141.92±14.06	142.56±8.76	125.46±7.81**
Leukocytes (10^{9}/l)		9.58±1.87	10.19±0.79	8.24±1.29
Neutrophils	immature (%)	0	0	0
	stab (%)	4.60±0.55	3.60±0.89	2.60±0.89*,**
	segmented (%)	29.20±7.40	20.60±7.54	17.80±2.39*
Basophiles (%)		0.40±0.27	0.20±0.22	0.60±0.27
Eosinophils (%)		0.80±0.42	0.20±0.22	0.60±0.27
Monocytes (%)		2.80±0.55	2.00±0.50	2.60±0.57
Lymphocytes (%)		62.20±6.46	73.40±8.08*	75.80±3.42*

* $p < 0.05$ compared to the control group, ** $p < 0.05$ compared to the 1 studied group

The leukocyte number in the calf blood did not practically depend on the dose of colloid silver, as well as on the term of its application, which shows that there is no toxic influence of this drug on the leukopoiesis processes among the healthy calves.

With regard to the leukogram of the calf blood, a dose of the colloid silver of 1.0 mg/l colostrum (milk) did not influence on the ratio of the blood leukocyte sub-populations on 3 and 10 days, and only on 30 day the lymphocyte proportion had been increased by 11.2% (p <0.05) compared to the control group. The calf rearing with the colloid silver solution at a dose of 2.0 mg/l showed a more pronounced influence, which was manifested in the decreased proportion of immature forms of neutrophils – immature (p <0.05), as well as stab (p <0.05) in the calf blood already on the 3 day compared to the control group. On the 30 day of the application of the colloid silver solution in the calves of the second group, the decreased proportion of segmented neutrophils (p <0.05) in the blood was also found against the background of the increasing proportion of lymphocytes (p <0.05).

Influence of nanosilver at doses of 1.0 and 2.0 mg/l colostrum (milk) on the ratio of basophils, eosinophils and monocytes in the calf blood was not found during the entire experiment period.

Thus, the colloid silver in both tested doses contributes to the redistribution of the leukocyte sub-populations, which is aimed at the increasing proportion of lymphocytes, which provides a specific immunity. Al-Baker et al. (2020), who entered AgNPs orally to rats at doses of 0.2 and 0.4 g/kg of the body weight during 3 days, and then – again after 20 and 30 days at doses of 0.08 and 0.008 g/kg, also found a similar influence, however, they consider it toxic at such large doses. Our data are also consistent with the study results by Malysheva, et al. (2021), obtained using the human lymphocytes, which show the ability of silver nanoparticles to induce the lymphocyte proliferation.

At the same time, today in scientific publications, a significant number of the study results are aimed at determining the nanosilver toxicity *in vitro* and *in vivo*, and the obtained data are quite contradictory, which is related to various sources of obtaining nanosilver, their size, carriers, synthesis methods as well as administration routes and doses to the animals (Ferdous & Nemmar, 2020). Furthermore, the data obtained when comparing the toxicity of the nanosilver drugs with similar indicators of intact animals are mainly discussed by the scientists. In our opinion, the toxicity of the nanosilver drugs should be compared with the toxicity of the antibiotics which are applied in order to treat the infectious diseases among the calves. This assumption is based on the data obtained by Olentsova et al. (2020), which showed that the influence of nanosilver and antibiotic group of third-generation fluoroquinolones on the hematological and biochemical indicators of the calves with diarrhea does not practically differ. In this regard, it should be noted that the cumulative action of silver in the calf body gives the reason to consider the possibility of the increasing interval of its application, which cannot be applied to antibiotics. The data obtained by us give the reason to note the decreased influence of silver when the calf rearing with the colloid solution composed of colostrum, and then with milk with the increasing interval of its application on the morphological composition of the blood, as well as on the indicators of the mineral turnover against the background of providing its stably increased level in the blood.

As for the use of higher doses of nanosilver in calves, it is necessary to take into account its negative effect, which can be manifested in a decrease in mobility, viability and violation of the integrity of the membrane of spermatozoa, as well as cause histopathological changes in the epithelia of the testicles, inflammatory processes of the epididymis and hyperplasia of the prostate gland in males nanosilver in high, close to toxic, doses also accumulates in the ovaries and uterus of females, causing polycystic ovarian changes, follicular atresia, inflammation, apoptosis and necrosis (Dianová etal., 2022), and also disrupts the synthesis of steroid hormones and the function of the reproductive system (Tabandeh et al., 2022).

The research results obtained by us require further verification of the effectiveness of the use of nanosilver on calves for infectious diseases, the causative agents of which are resistant to antibiotics and cause economic losses to farms.

4 Conclusions

Oral administration of the nanosilver drugs to the calves does not influence the clinical condition, contributes to its absorption into the blood and exchange of copper, zinc and iron, depending on the application mode and dose. The content of silver in the blood of calves for doses of nanosilver of 2.0 mg/l of colostrum (milk) increased during continuous use on the third and tenth days within the range of 1.9–1.8 times compared to the dose of 1.0 mg/l, which reflects the possibility of using its nanopreparations for preventive and therapeutic purposes in the case of infectious diseases of animals. During the same periods, it should be taken into account that drinking colloidal silver solution to calves at a dose of 1.0 mg/l can cause a decrease in the number of erythrocytes in the blood by 15.0% and 12.3%, and at a dose of 2.0 mg/l by 21.2% 10 days.The content of silver in the calf blood shows the possibility of using its nanodrugs for preventive and therapeutic purposes in case of the infectious diseases among the animals. The calf rearing with the nanosilver solution at a dose of 1.0 mg/l with colostrum (milk) has a less pronounced influence on the morphological composition of the blood (erythrocytes, leukocytes, and leukogram) than at a dose of 2.0 mg/l, but both doses contribute to the increasing number of lymphocytes in the blood of the healthy calves at reaching the age of 30 days. The obtained study results can be the development basis for the preventive and therapeutic measures with the use of the nanosilver drugs as an alternative to the antibiotics in case of the infectious diseases among the calves.

References

Afifi, M., & Abdelazim, A. M. (2015). Ameliorative effect of zinc oxide and silver nanoparticles on antioxidant system in the brain of diabetic rats. *Asian Pacific Journal of Tropical Biomedicine*, 5(10), 874–877. https://doi.org/10.1016/j.apjtb.2015.06.010

Al-Baker, A.A., Al-Kshab, A.A., & Ismail, H.Kh. (2020). Effect of silver nanoparticles on some blood parameters in rats. *Iraqi Journal of Veterinary Sciences*, 34, 2, 2020, 389–395. https://doi.org/10.33899/ijvs.2020.165812

Dianová, L. et al. (2022). Effects of Selected Metal Nanoparticles (Ag, ZnO, TiO_2) on the Structure and Function of Reproductive Organs. *Toxics*, 10(8), 459. https://doi.org/10.3390/toxics10080459

El-Gohary, F.A. et al. (2020). Enhanced antibacterial activity of silver nanoparticles combined with hydrogen peroxide against multidrug-resistant pathogens isolated from dairy farms and beef slaughterhouses in Egypt. *Infection and Drug Resistance*, 13, 3485–3499. https://doi.org/10.2147/IDR.S271261

Estevez, M.B. et al. (2021). Biogenic silver nanoparticles as a strategy in the fight against multi-resistant *Salmonella enterica* isolated from dairy calves. *Frontiers in Bioengineering and Biotechnology*, 9, 644014. https://doi.org/10.3389/fbioe.2021.644014

Ferdous, Z., & Nemmar, A. (2020). Health Impact of Silver Nanoparticles: A Review of the Biodistribution and Toxicity Following Various Routes of Exposure. *International Journal of Molecular Sciences*, 21(7), 2375. https://doi.org/10.3390/ijms21072375

George, S. et al. (2019). Enhancing the bioavailability of silver through nanotechnology approaches could overcome efflux pump mediated silver resistance in methicillin resistant *Staphylococcus aureus*. *Journal of Biomedical Nanotechnology*, 15, 2216–2228. https://doi.org/10.1166/jbn.2019.2858

Hanson, S. R., Donley, S. A., & Linder, M. C. (2001). Transport of silver in virgin and lactating rats and relation to copper. *Journal of trace elements in medicine and biology: organ of the Society for Minerals and Trace Elements* (GMS), 15(4), 243–253. https://doi.org/10.1016/S0946-672X(01)80040-7

Huang, H. et al. (2016). An Evaluation of Blood Compatibility of Silver Nanoparticles. *Scientific reports*, 6, 25518. https://doi.org/10.1038/srep25518

Malysheva, A. et al. (2021). Cellular binding, uptake and biotransformation of silver nanoparticles in human T lymphocytes. *Nature Nanotechnology*, 16, 926–932. https://doi.org/10.1038/s41565-021-00914-3

McCabe. J. W., Vangala. R., & Angel, L. A. (2017). Binding selectivity of Methanobactin from *Methylosinus trichosporium* OB3b for copper (i), silver (i), zinc (ii), nickel (ii), cobalt (ii), manganese (ii), lead (ii), and iron (II). *Journal of the American Society for Mass Spectrometry*, 28(12), 2588–2601. https://doi.org/10.1007/s13361-017-1778-9

Ognik, K. et al. (2016). Effect of silver nanoparticles on the immune, redox, and lipid status of chicken blood. *Czech Journal of Animal Science*, 61, 450–461. https://doi.org/10.17221/80/2015-CJAS

Olentsova, E. et al. (2020). Silver-based drug effect on the body of calves with diarrhea. *E3S Web Conf.*, 203, 01026. https://doi.org/10.1051/e3sconf/202020301026

Puchkova, L.V. et al. (2019). Silver Ions as a tool for understanding different aspects of copper metabolism. *Nutrients*, 11(6), 1364. https://doi.org/10.3390/nu11061364

Sánchez-López, E. et al. (2020). Metal-based nanoparticles as antimicrobial agents: an overview. *Nanomaterials*, 10, 292. https://doi.org/10.3390/nano10020292

Stefanidou, M. et al. (2006) Zinc: a multipurpose trace element. *Archives of Toxicology*, 80(1), 1. https://doi.org/10.1007/s00204-005-0009-5

Tabandeh, M. R. et al. (2022). Silver nanoparticles induce oxidative stress, apoptosis and impaired steroidogenesis in ovarian granulosa cells of cattle. *Animal reproduction science*, 236, 106908. https://doi.org/10.1016/j.anireprosci.2021.106908

Thorat, N. D. et al. (2021). Photo-responsive functional gold nanocapsules for inactivation of community-acquired, highly virulent, multidrug-resistant MRSA. *Journal of Materials Chemistry B*, 9, 846–856. https://doi.org/10.1039/D0TB02047H

Youssef, F. S. et al. (2019). Application of some nanoparticles in the field of veterinary medicine. *International Journal of Veterinary Science*, 7, 78–93. https://doi.org/10.1080/23144599.2019.1691379

Zeedan, G. S. G. et al. (2018). Antibacterial efficacy of green silver nanoparticles against bacteriaisolated from calf diarrhoea. *Asian Journal of Epidemiology*, 11, 65–73. https://doi.org/10.3923/aje.2018.65.73

Zheltonozhskaya, T.B. et al. (2021). Polymer/inorganic hybrids containing silver nanoparticles and their activity in the disinfection of fish aquariums/ponds. *Polymer-Plastics Technology and Materials*, 60(4), 369–391. https://doi.org/10.1080/25740881.2020.1811318

Ziemińska, E., & Strużyńska, L. (2016). Zinc modulates nanosilver-induced toxicity in primary neuronal cultures. *Neurotoxicity Research*, 29, 325–343. https://doi.org/10.1007/s12640-015-9583-3