THE EFFECT OF NICKEL NANOPARTICLES ADMINISTERED ORALLY ON THE CONTENT OF TRACE ELEMENTS IN THE INTERNAL ORGANS OF RATS

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Background

Assessing the risks of nanomaterials exposure to consumer health requires studying their effect on metabolic processes in the body, in particular, on mineral homeostasis and the exchange of essential and toxic chemical elements. Nickel nanoparticles (NiNPs) are used as components of hydrogenation catalysts, as well as pesticides. The aim of the work was to study the homeostasis of essential and toxic trace elements under the influence of NiNPs oral administration to rats.

Methods

We used two types of NiNPs manufactured by Nanostructured & Amorphous Materials Inc. (USA) with product numbers 0282HW and 0283HW, hereinafter referred to as NiNP1 and NiNP2, respectively. The NPs in the preparations were spherical and had average diameters of 53.7 nm and 70.9 nm respectively (see Fig.1). For a detailed characterization of NiNPs see [1].Wistar rats received Ni in the form of a stomach-soluble salt (basic Ni carbonate) or two types of NiNPs in doses of 0.1; 1.0 and 10 mg/kg body weight in terms of nickel for 92 days in the composition of the consumed diet .The content of Ni as well as 28 other essential, toxic elements and elements without an established biological function (Ag, Al, As, B, Ba, Be, Ca, Cd, Ce, Co, Cr, Cs, Cu , Fe, Ga, Gd, K, La, Mg, Mn, Na, Pb, Rb, Se, Sr, Tl, V, Zn) was determined in the liver, kidneys, and spleen by inductively coupled plasma mass spectrometry using Agilent 7700 series device (Agilent, Japan). The limit of quantification (LOQ) of the elements corresponded to 5 μg/kg wet weight of tissue. The experimental data were developed according to Grabbs criterion and Mann-Whitney U-test with the level of significance $p<0.05$.

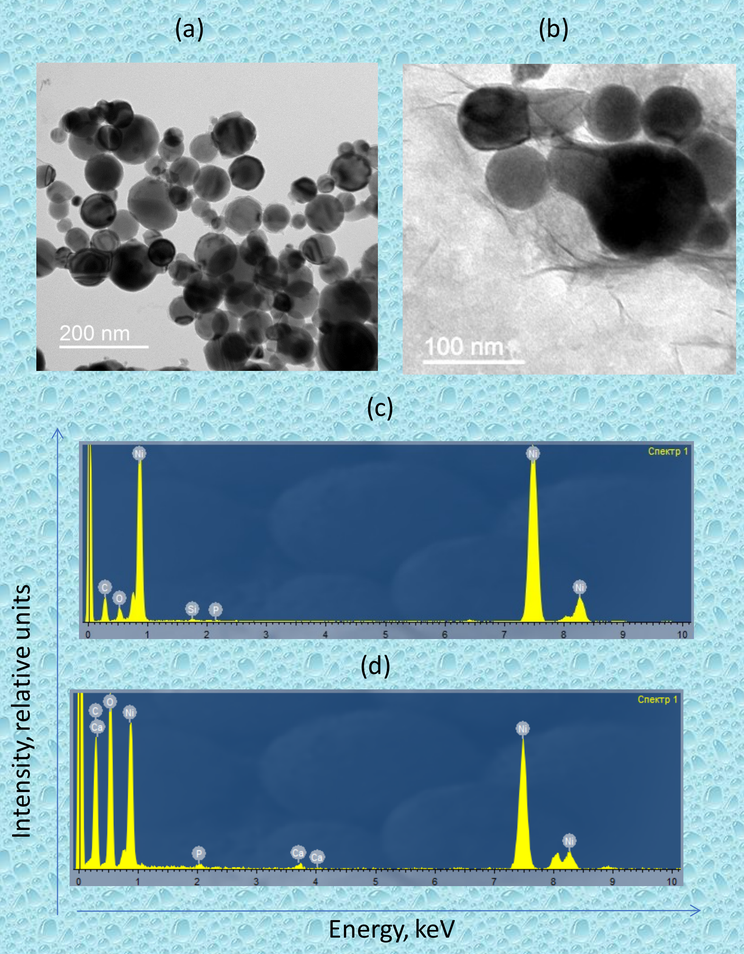

Fig.1 Characterization of NiNPs by transmission electron microscopy: (a, c) NiNP1 (a, c) ; NiNP2 (b, d). Representative micrographs (a, b) and spectra of characteristic electron energy losses (EELS) from particles in the selected region (c, d) (data obtained by Ph.D. A.G. Masyutin).

Results

The content of Ni in the kidneys and brain increased under the influence of both salt and NPs, in the liver and gonads - only after the introduction of the salt form, but not with NPs, in the spleen the level of Ni did not increase with the introduction of all Ni preparations (Fig.2). The levels of Be, Cs, Ce, Gd, La and Tl in all groups of animals and in all their organs were below LOQ, therefore these data were not considered further. The remaining 22 elements (Ag, Al, As, B, Ba, Ca, Cd, Co, Cr, Cu, Fe, Ga, K, Mg, Mn, Na, Pb, Rb, Se, Sr, V, Zn) were present in all or most organ samples above the LOQ. Various changes were observed in indicators of trace elements homeostasis (Tables 1,2), including increased bioaccumulation of Pb in the liver, gonads, and brain (Fig.3), As in the spleen, and Al in the liver and brain. The introduction of NPs was accompanied by inhibition of the accumulation of divalent metal cations: Mg, Mn and Sr in the kidneys; Ba - in the kidneys and spleen; the content of Ca under the influence of NPs increased in the kidneys, but decreased in the gonads **(see supplementary material, Tables S1-S5).** Effects on the bioaccumulation of the trivalent elements Cr and B had different directions depending on the form of Ni in different organs. Many other changes in minerals and trace elements content in the organs tissue were less than 25% in magnitude compared with control although statistically significant. These effects were considered to have no biological significance. A number of effects arising from the administration of Ni in nanoform to animals were absent or had the opposite sign in the case of the salt form administration. NiNPs had little effect on the bioaccumulation of essential elements Cu, Mg, Zn and Fe.

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Table 1. The content of elements in the liver of rats per unit of wet tissue mass

Groups of animals[1]		Groups of animals[1]							
Preparation	Dose of Ni, mg/kg	Ag, μg/kg	Al, mg/kg	B, mg/kg	Ca, мг/kg	Co, μg/kg	Na, g/kg	Pb, μg/kg	V, μg/kg
1.Control	0	7.6±1.3	0.88±0.045	0.43±0.09	336±8	22±1	2.01±0.07	8.5±0.9	50±2
2. Ni-salt	0.1	<LOQ*	1.82±0.26*	0.24±0.01*	310±6*	24±1	1.38±0.26*	14.5±1.4*	46±3
3. Ni-salt	1.0	6.8±4.6	1.49±0.13*	0.24±0.02*	298±5*	32±2*	1.70±0.37*	12.8±1.0*	48±3
4. Ni-salt	10.0	16.7±9.2	1.05±0.08	0.21±0.03*	414±10*	82±4*	1.84±0.07	10.6±2.5	38±2*
5. NiNP1	0.1	18.9±8.3	0.96±0.03	0.52±0.13#	406±9*#	23±1	1.92±0.05#	11.9±0.7*#	60±2*#
6. NiNP1	1.0	8.7±2.0	1.07±0.08*	0.51±0.13#	398±16*#	24±2	2.02±0.10#	15.0±1.3*	65±3*#
7. NiNP1	10.0	14.2±8.5	1.15±0.07*	0.44±0.03	393±12*	28±1*#	1.68±0.06	12.1±0.6*#	50±3
8. NiNP2	0.1	9.7±4.2	1.19±0.07*#	0.20±0.01*#	408±14*#	23±1	1.93±0.07#	15.1±1.2*	59±2*
9. NiNP2	1.0	<LOQ*	0.95±0.04#	0.17±0.01*#	406±8*#	24±1	2.08±0.07#	23.7±2.3*#	53±3
10. NiNP2	10.0	<LOQ*	0.95±0.03	0.17±0.01*	391±3*	22±1	2.05±0.13	25.7±4.1*#	48±2

Notes. * - significant difference with the control group, # - significant difference with the group receiving nickel salt in an equivalent dose, $p<0.05$, Mann-Whitney U-test. Colored cells - the difference with the control is greater than ± 25%. <LOQ - value below the limit of quantification
[1] Number of animals – 6 in each group (Ca, Na), 8 in each group (other elements)

SUPPLEMENTARY MATERIAL:

Table 2. The content of elements in the brain of rats per unit of wet tissue mass

Groups of animals[1]		Elements, measurement units			
Preparation	Dose of Ni, mg/kg	Al, mg/kg	B, μg/kg	Ba, μg/kg	Pb, μg/kg
1.Control	0	0.39±0.02	111±6	19±1	7.1±0.7
2. Ni-salt	0.1	0.70±0.10*	102±5	22±2	10.5±1.1*
3. Ni-salt	1.0	0.60±0.10	92±5*	18±1	5.6±0.3
4. Ni-salt	10.0	0.53±0.11	93±4*	17±1	16.7±0.9*
5. NiNP1	0.1	0.76±0.15*	412±115*#	26±3*#	23.5±2.3*#
6. NiNP1	1.0	0.52±0.08	160±10*#	26±3*	18.2±0.5*#
7. NiNP1	10.0	0.53±0.06*	340±28*#	22±1#	17.6±0.8*
8. NiNP2	0.1	0.54±0.05*	118±3#	17±1#	43.7±1.6*#
9. NiNP2	1.0	0.47±0.06	279±21*#	26±5	46.0±0.9*#
10. NiNP2	10.0	0.97±0.24*	135±16#	31±5#	45.1±2.4*#

Notes. * - significant difference with the control group, # - significant difference with the group receiving nickel salt in an equivalent dose, $p<0.05$, Mann-Whitney U-test. Colored cells - the difference with the control is greater than ± 25%. <LOQ - value below the limit of quantitation
[1] Number of animals – 8 in each group

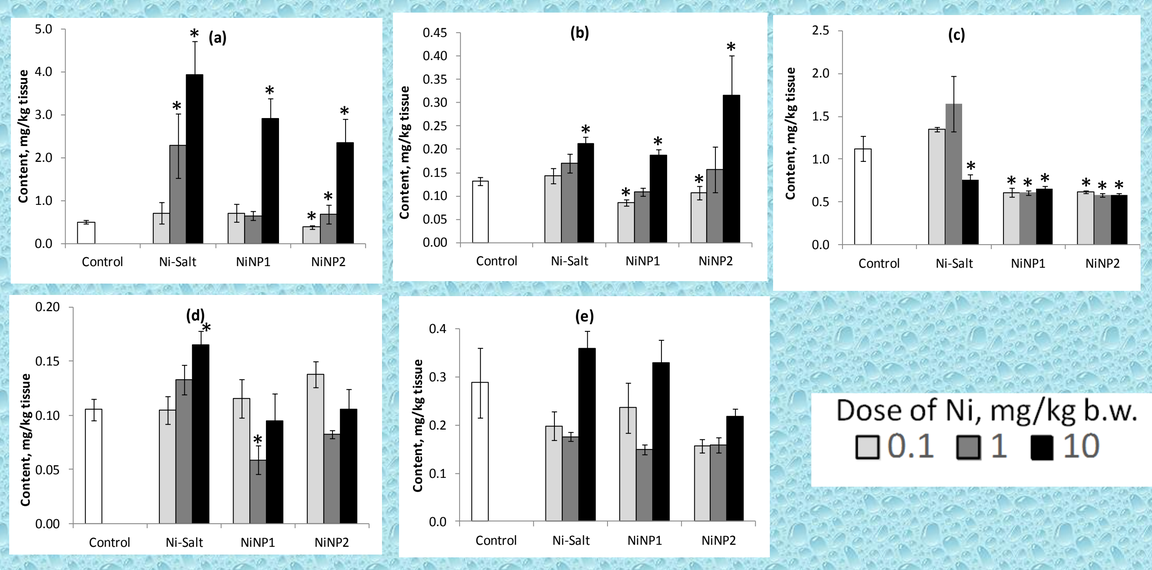

Fig.2 Nickel content (mg/kg of wet tissue mass) in the kidneys (a), brain (b), liver (c), gonads (d), spleen (e) of rats of the control and experimental groups. * - significant difference with the control group, $p<0.05$, Mann-Whitney test. The number of animals - 8 in each group.

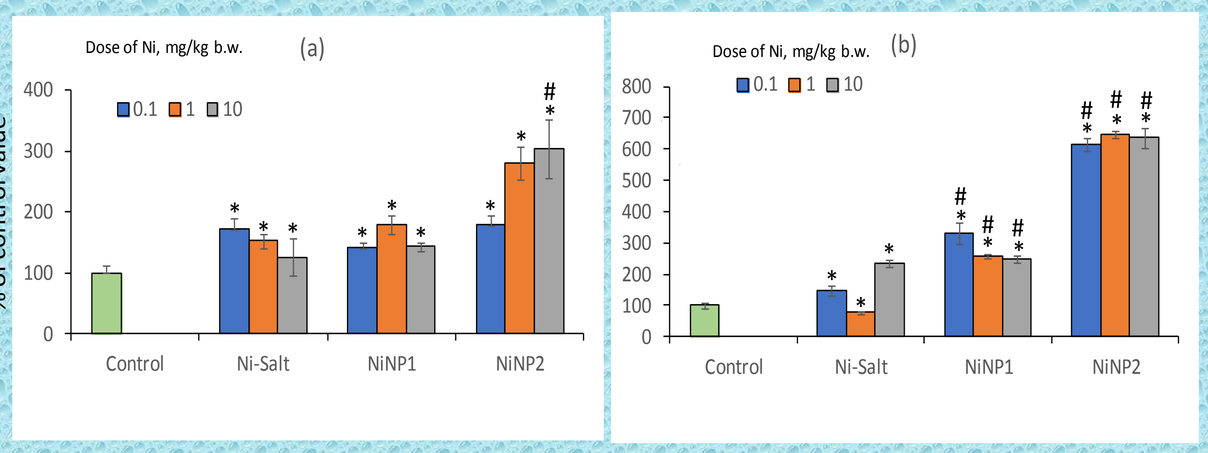

Fig.3 Influence of the Ni salt form and two types of NiNPs consumption on the accumulation of lead (Pb) in the liver (a) and brain (b) of rats. * - significant difference with the control group, # - significant difference with the group receiving Ni salt in an equivalent dose, $p<0.05$, Mann-Whitney test. Number of animals - 8 in each group.

CONCLUSION

Thus, NiNPs administered orally to rats can affect mineral homeostasis. At the same time, the effect of increasing the levels of lead (Pb) in the liver and brain is apparently of greatest practical importance, even though the excess accumulation of Ni itself in the liver with the studied NPs was not detected. A number of effects exerted by NiNPs on the bioaccumulation of metal cations (including Ba++, Sr++, Mn++) were absent when an equivalent dose of soluble Ni salt was administered to animals. The listed NiNP-specific effects can be considered as manifestations of nanometallomic regularities [2,3], i.e., processes mediated by changes in gene expression caused by NPs or products formed from them in the biological environment. The influence exerted by Ni-containing nanomaterials on trace element homeostasis should be taken into account in the toxicological and hygienic assessment of their safety and health risks, especially under conditions of combined contamination with toxic metals, in particular lead and aluminum.

FUNDING

The study was supported by the Program for Fundamental Scientific Research (theme of the Ministry of Education and Science of the Russian Federation No. 0529-2019-0057).

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