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TOXICITY ASSESSMENT OF IRON OXIDE NANOCOMPOSITE

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Abstract

Subacute oral administration of a solution containing iron oxide nanoparticles Fe_3O_4 with the addition of a nanostabilizing matrix of natural origin — arabinogalactan — was performed to outbred male rats. The number of neurons per unit area, astroglial cells, degeneratively altered neurons and the number of neuronophagy acts were counted in sections of nervous tissue. The number of Kupffer stellate macrophages and the number of polynuclear hepatocytes were counted in liver sections. The area of the Shumlyansky-Bowman chamber was determined in kidney tissue. As a result, changes characterized as compensatory-adaptive reactions were observed in liver and brain tissues, and signs of organ dysfunction were observed in kidney tissue.

Introduction

It is known that the use of metal oxide nanoparticles is limited by their potential toxicity [1]. The toxicity of oxide nanoparticles can be reduced by using high-molecular compounds, such as arabinogalactan (AG) of Siberian larch [2]. The use of iron oxide nanoparticles encapsulated in an arabinogalactan matrix increases the bioavailability of nanoparticles and reduces the potential toxicity of drugs, but a comprehensive study of their safety is necessary.

Materials and Methods

The investigation was carried out on 30 outbred white male rats weighing 200–220 g. The animals were divided into 2 groups: experimental (EXP, n = 15), which were intragastrically administered 1 ml of an aqueous solution of Fe_3O_4AG at a dose of 500 µg/kg using an atraumatic probe for 10 days, and control (CONT, n = 15). In prepared and stained histological sections of the brain, kidneys and liver, morphometric parameters specific to each organ were calculated.

Results and Discussion

The results of the nervous tissue study showed a marked decrease in the total number of normal neurons per unit area compared to the control. The number of astroglial cells in the experimental group was also reduced compared to the control group (at the trend level, p = 0.05). At the same time, the number of degeneratively altered neurons (darkly colored neurons without a clearly separable nucleus and cytoplasm were considered degeneratively altered) did not have a statistically significant difference from the control. The number of acts of neuronophagy also did not differ from the control group (Table 1).

Table 1

Morphometric indices of the sensorimotor cortex tissue of the brain of white rats under subacute influence of Fe_3O_4AG (Me (Q25–Q75))

Indicators	EXP	CONT	p
Number of normal neurons per unit area (0,2 mm^2)	171,0 (170,0–177,0)*	201,0 (199,0–207,0)	0,001
Number of astroglial cells per unit area (0,2 mm^2)	163,5 (151,0–183,0)	184,0 (178,0–197,0)	0,050
The number of degeneratively altered neurons per unit area (0,2 mm^2)	3,5 (1,0–6,0)	1,0 (1,0–2,0)	0,193
Number of neuronophagy facts	1,5 (0,0–3,0)	0,0 (0,0–0,0)	0,073

* Differences are statistically significant compared to CONT according to the Mann — Whitney test, p < 0,05.

The number of Kupffer stellate macrophages in the liver sinusoidal capillaries did not differ compared to the control group. The number of polynuclear hepatocytes also did not differ statistically significantly from the control group (Table 2).

Table 2

Morphometric indices of liver tissue of white rats under subacute influence of Fe_3O_4AG (Me (Q25–Q75))

Indicators	EXP	CONT	p
Kupffer stellate macrophage count	115,0 (101,0–134,0)	106,0 (103,0–110,0)	0,58
Number of polynuclear hepatocytes	12,5 (11,0–17,0)	13,0 (8,0–15,0)	0,67

In the renal cortex, a statistically significant increase in the area of the Shumlyansky-Bowman capsule was observed compared to the control group (Table 3).

Table 3

Morphometric indices of changes in the area of the Shumlyansky-Bowman capsule in the renal cortex of white rats under subacute exposure to Fe_3O_4AG (Me (Q25–Q75))

Indicator	EXP	CONT	p
Shumlyansky-Bowman capsule area	24676,9 (23657,4–29280,0)*	20741,8 (16801,9–29346,3)	0,018

Thus, the effect of Fe3O4AG on the body of white rats is characterized by the development of morphofunctional changes in various body systems. The nature and intensity of changes in the liver and brain tissue suggest the development of compensatory-adaptive reactions in the body in response to the effect of the iron nanocomposite. However, the effect of the studied nanocomposite on the kidneys led to an increase in the area of the Shumlyansky-Bowman capsule, which may result in a violation of the normal filtration coefficient of the renal glomeruli and, as a consequence, a violation of the normal functioning of the organ, which is a more serious violation. Further studies of this nanocomposite in different doses and routes of administration are needed.

References

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