

# GONADOTOXICITY OF NANOPARTICLES FROM RARE EARTH METAL

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**Introduction.** The growth of occurrence of male hypofertility, the prevalence of reproductive diseases in people of reproductive and working age well as related processes of depopulation in many countries is one of the pressing problems of today. Existing therapeutic agents for the treatment of hypofunction are often ineffective and modern assisted reproductive technologies are used in single pairs and are too high price. This is the basis for the search of new directions the creation of drugs for the correction of disorders of the reproductive function of men. Vanadium-containing compounds are increasingly attracting attention due to the variety of biological effects, including the impact on the functioning of the reproductive system, and their use in nanoform may alter the bioavailability and provide new properties of nanomaterials, what makes them promising for development of new drugs and requires studies of their harmlessness.

**Aim.** Determination of gonadotoxicity of gadolinium orthovanadate nanoparticles (NPs GdVO<sub>4</sub>) in the intact male rats under chronic intake of compound.

**Materials and methods.** The experiments were were conducted according to international principles of the “European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes” (Strasbourg, 1986) and “General ethical principles of animal research” (Ukraine, 2001). Animals were kept under standard vivarium conditions with diet recommended for this type of animal and the principle of free access to drinking water. The distribution by the groups was done using a table of random numbers. Sexually mature male rats from 6 months of age for 70 days orally received the solution of NPs GdVO<sub>4</sub>, that was synthesized in Institute for Scintillation Materials of the NAS of Ukraine, at doses of 0.03; 0.33 and 3 mg / kg b. w. or reference product tribestan at a dose 68 mg / kg b. w. Individual dose was adjusted by according to body weight, which was controlled once a week. As control were used animals of the corresponding age, which under similar conditions received the solvent of NPs without additional components. The animals were taken out of the experiment by rapid decapitation, the condition of internal organs, their weight and the state of spermatogenesis in rats were studied after 30 and 70 days. The total gonadotropic activity of nanoparticle suspensions also was

determined by biological testing rat pituitary. Statistical evaluation of differences of obtained data with the results of the control group was performed using the t-Student's test and U- criteria Wilcoxon-Mann-Whitney by using Statistica 6.0 and Exel 2003. The difference was considered statistically significant at  $P < 0.05$ .

**Results and discussion.** As a result conducted research it was found that the intake of nanoparticles GdVO<sub>4</sub> in all doses for 30 days was not lead to changes neither in absolute mass, nor in the mass indexes of organs, except spleen weight, which increased in group NPs GdVO<sub>4</sub> (0.03) compared with the control. Long-term admission of NPs was not affected on absolute weight of majority organs, was discovered only increase in weight of the ventral prostate in rats that were received the highest dose of NPs (3.0 mg / kg). In analyzing the mass ratios were not found differences between experimental groups other than the relative weight of the pituitary gland, which was higher in animals that received NPs at a dose of 0.3 mg / kg than benchmarks of animals treated solvent and tribestan. Therefore, long-term use of NPs GdVO<sub>4</sub> in intact sexually mature animals basically not found gonadotoxic impact on the organs mass.

In healthy male rats NPs GdVO<sub>4</sub> irrespective of dose influence on the processes of differentiation and morphogenesis of cells of the spermatogenic epithelium. 30-day receiving of NPs affected on the percentage of pathological forms of spermatozoa. At the longer term admission of NPs appeared dose-dependent effect, which consisted in the emergence of negative differences in the group that was received potentially therapeutic dose (0.3 mg / kg).

According to the results gonadotrophic activity NPs revealed an increase of uterus and ovaries of mice by which explored the suspension of rat pituitary of group NPs GdVO<sub>4</sub> (0.3), in the other groups the difference was not observed. That is the existing gonadotropic activity NPs GdVO<sub>4</sub>, which is manifested in a therapeutic dose (0.3 mg / kg), indicates on increased production of gonadotrophins hormones, that can directly affect on the testes than may be conditioned the decline of parameters of semen in these rats.

**Conclusions.** Thus, NPs GdVO<sub>4</sub> do not demonstrate the gonadotoxic influence on the mass of organs of intact male rats, however, affect on spermatogenesis. The application of NPs for 30 days affected the percentage of pathological forms of gametes. At the longer term admission of NPs appeared dose-dependent effect, which consisted in the more expressive changes in semen quality, and correlated with increased weight of pituitary and the manifestation of gonadotropic activity NPs at a dose of 0.3 mg / kg b. w