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IN VIVO EVALUATION OF GADOLINIUM ORTHOVANADATE GdVO4:Eu3+ NANOPARTICLE TOXICITY

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Biomedical application of nanoparticles has been actively studied for decades. In particular, they can be used as drug delivery systems. In order to be used for such purposes, nanoparticles should be safe. Thus, the study of their safety profile is of huge importance.
The aim of our research was to assess the possible toxic effects of orally administered gadolinium orthovanadate GdVO4:Eu3+ nanoparticles (VNPs).
Material and methods. Twenty female adult WAG rats were randomly divided into two equal groups with ten animals in each. The rats from group A were daily orally exposed to the solution of VNPs at a dose of 20 μg / kg of weight during two weeks against the background of standard diet. The rats from group B were used as controls. They obtained the same volume of drinking water. To obtain VNPs, 10 mL of aqueous solution of rare-earth chlorides (0.01 mol / L) was mixed with 8 mL of sodium ethylenediaminetetraacetate solution (0.01 mol / L). Eight mL of Na3VO4 (0.01 mol / L) was added dropwise to the obtained solution (pH=13). The mixture was intensively stirred using a magnetic stirrer until yellowish transparent solution was formed. After cooling and dialyzing, spindle-like nanoparticles – Gd(0,9) Eu(0,1)VO4 – with average size of 8x25 nm were formed.
When the animals were sacrificed, blood was collected to prepare serum and determine circulating concentrations of IL-1β (by ELISA), middle molecules, C-reactive protein and seromucoid (spectrophotometrically). Samples of small intestine were collected to assess morphology (hematoxylin and eosin staining, PAS reaction, and hallocyanine-chrome alum Einarsson's staining) and heat shock protein 90α (HSP90α) expression (immunohistochemically).
Numerical data were statistically analyzed using the Graph Pad Prism 5.0 application.
Results and discussion. Levels of circulating IL-1β, middle molecules, C-reactive protein, and seromucoid were found to be statistically insignificantly ($p > 0.05$) higher in the rats from group A compared with the control group. Such findings indicate the absence of intoxication and inflammation, since IL-1β, C-reactive protein, and seromucoid are widely recognized markers of inflammation, while middle molecules are biomarkers of endogenous intoxication. Biochemical data were consistent with the results of morphological and immunohistochemical studies. No signs of inflammation or damage were found in the small intestine collected from rats of group A and stained using routine staining techniques. HSP90α, a chaperone whose overexpression is observed in response to oxidative stress and inflammation, was found to be normally expressed in the small intestine of animals exposed to VNPs.
Conclusion. Our findings suggest that oral exposure to VNPs at a dose of 20 μg / kg of weight during two weeks by rats results in neither systemic nor local intestinal adverse effects.