

***In vivo* toxicity of Al₂O₃, TiO₂ and SiO₂ nanoparticles acting in different combinations and its alleviation with a complex of bioprotectors**

I.A. Minigalieva¹, S.V. Klinova¹, L.I. Privalova¹, V.G. Panov²,
O.H. Makeyev³, I.E. Valamina³, E.V. Shishkina⁴

¹*The Medical Research Center for Prophylaxis and Health Protection in Industrial Workers, 620014, Ekaterinburg, Russia*

e-mail: klinovasv@ymrc.ru

²*Institute of Industrial Ecology, the Urals Branch of the Russian Academy of Sciences, 620219, Ekaterinburg, Russia*

³*The Central Research Laboratory of the Ural Medical University, 620028, Ekaterinburg, Russia*

⁴*School of Natural Sciences and Mathematics, Ural Federal University, 620002, Ekaterinburg, Russia*

For the animal experiment, stable water suspensions of nanoparticles (NPs) were obtained by laser ablation of 99,99% pure elemental aluminum, titanium or silicon under a layer of deionized water. Male outbred rats with initial body mass 290 g were injected intraperitoneally 3 times a week (up to 18 injections) with suspensions of Al₂O₃-NP, TiO₂-NP or SiO₂-NP in doses 0.25, 0.5 and 0.5 mg per rat, respectively, either separately, or in binary, or in ternary combinations of the same doses, the controls receiving injections of deionized water in the same volume. Toxic effects were estimated with a lot of functional, biochemical and morphometric indices for the organism's status. The results obtained demonstrated that, in many respects, the Al₂O₃-NP was the most toxic as such and the most dangerous component of the studied combinations. Mathematical modeling with the help of the Response Surface Methodology has shown that the organism's response to a simultaneous exposure to any two of the element oxide (EIO) NPs under study is characterized by all possible types of combined toxicity (additivity, subadditivity or superadditivity of unidirectional action and different variants of opposite effects) depending on which outcome this type is estimated for as well as on the levels of the effect and dose. With any third EIO-NP species acting in the background, the type of combined toxicity displayed by the other two EIO-NPs can change significantly. Many adverse effects produced in rats by the combined [Al₂O₃-NP+TiO₂-NP+SiO₂-NP] exposure, including the genotoxic one, were substantially attenuated by per oral administration of a complex of innocuous bioprotective substances during the entire exposure period.