Beyond the Microscopic: Advancing NanoToxicology through Cutting-Edge In Vitro, In Vivo, and In Silico Models

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Increased use of nanoparticles in medicine and industry, in addition to the positive aspects, certainly represents a threat to the organisms that populate our Planet. Since they are part of the products we use, we must also consider the effects they have on human beings. Regarding ethical issues, we cannot use for research studies human beings or their cellular organelles, hence we study organisms and the cells as prescribed in the "Guide for Use and Care of Laboratory Animals". In this paper we have integrated *in vivo* and *in silico* experiments to comprehend how nanoparticles, specifically CuO-NP, can be involved within the organisms under study. To elucidate this, we used *Danio rerio* and *Carassius carassius* as model organisms. These organisms were exposed to environmentally realistic CuO-NPs doses (*D.rerio* to 1; 5; 10; 25; 50 mg/L while *C.carassius* to 0.5 and 1.0 mg/dL). The *in silico* methodology, molecular docking, presented for the first time in Albania, has aided to reinforce the results obtained from *in vivo* experiments, based on the binding energy. The results show that CuO-NP interacts with the enzymes that affect the degradation of the egg coat in *D. rerio*, He1a (favorable binding energy -2.30 kcal/mol), blocking their activity and thus delaying the hatching time of the embryos. Copper nanoparticles also interact with erythrocyte band 3 (favorable binding energy -2.07 kcal/mol) inhibiting the activity of this protein and causing erythrocyte cytotoxicity, based on the abnormalities in erythrocyte morphology. Molecular binding analysis showed that CuO-NPs, despite having low molecular mass, bind to the minor groove of DNA in an energetically favorable manner (-2.13 kcal/mol), suggesting a direct interaction with the genetic material, instead of secondary events caused by ROS.

References

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[2] Aliko, V.; Qirjo, M.; Sula, E.; Morina, V.; Faggio, C. Antioxidant defense system immune response and erythron profile modulation in goldfish, Carassius auratus, after acute manganese treatment. *Fish and Shellfish Immunology* **2018,** *76*:101-109.

Figures

Figure 1: A best-ranked conformation of the intermolecular interaction between CuO NP and crystallographic DNA