A (Q)SAR MODEL FOR GENOTOXICITY PREDICTION OF METAL OXIDE NANOPARTICLES

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Abstract: Within the rapidly increasing nano-industry, the risk assessment of nanoparticles entering into the environment becomes a crucial issue. Nanoscale materials, due to their size (<100 nm), acquiring specific physico-chemical properties that give them unusual characteristics for different applications and in the same way can make them daunting public health concerns. However, their toxicity is still mainly unknown and relatively unexplored. Many metal nanoparticles were found to cause chromosomal aberrations, DNA strand breaks, oxidative DNA damage, and mutations. Computational chemistry can be used for profiling compounds based on both chemical and biological domains as a first step in understanding complex toxicological issues, particularly genotoxicity. This approach then can be used in predictive toxicology to screen and prioritize chemicals in development and safety assessment stages. In the present work, we reviewed and studied a number of metal oxide nanoparticles and acquired the current in vivo and in vitro data on genotoxic effects. We integrated the experimental results found in the literature into a rigorously designed database. Then, we utilized this database for developing the first quantitative structural activity relationship ((Q)SAR) model for prediction of nano metal oxides genotoxicity, by applying quantum-chemical and chem-informatics methods. The quantum-chemical optimization and analysis was performed by Gaussian09 code. Several methods for structure optimization were investigated and suitable were selected and applied. The current model shows a good correlation between selected physico-chemical descriptors and genotoxicity, which can be useful in predicting the genotoxicity of new and untested metal oxide nanoparticles.