SUMMARY

Computational methods can significantly support the process of designing functional and safe nanomaterials in accordance with the *safer-by-design* paradigm by applying a quantitative modelling approach of the relationship between the chemical structure and properties of nanomaterials and their biological activity (Quantitative Structure-Property / Activity Relationship, QSPR/QSAR). However, in the case of nanoforms of substances, the challenge is to define the actual structure that determines the observed physicochemical property or biological activity. In the case of metal oxide nanoparticles, this difficulty is due to the labile nature of the structure, which changes depending on the nanoparticle environment and the properties of the dispersion medium. Therefore, the research question of the presented dissertation is: Can the idea of QSPR/QSAR modeling be used to reliably predict the physicochemical properties/biological activity of metal oxide nanoparticles in the face of their structural changes under the influence of interactions with the dispersion medium? My research hypothesis assumes that in the case of metal oxide nanoparticles, it is possible to extend the QSPR/QSAR modeling paradigm by the employment of factors determining or describing the changes in the structure of the nanoparticles influenced by the dispersion medium in relation to their pristine nanoform (i.e. before placing it in the target dispersion medium). This dissertation was aimed at verifying the above hypothesis by: i) including the influence of the dispersion medium in the QSPR model predicting the change of hydrodynamic diameter of selected metal oxide nanoparticles in simplified dispersion systems; ii) including the influence of the dispersion medium in the QSPR model predicting the change in the hydrodynamic diameter of a series of metal oxide nanoparticles in a complex biological medium and the identification of factors determining the composition of protein coronas on the surface of metal oxide nanoparticles; and iii) including the effect of the protein coronas resulting from the interaction of nanoparticle surface with the components of the biological medium in the QSAR model predicting the cytotoxicity of metal oxide nanoparticles towards selected cell lines.

Within the framework of research, I proved the correctness of the hypothesis by achieving the assumed research goals. I developed the QSPR model presenting the relationship between the hydrodynamic diameter of titanium dioxide nanoparticles in

simplified dispersion systems, i.e. aqueous solutions of acids, salts and bases, and the physicochemical characteristics of the analyzed dispersion media. Subsequently, I developed a QSPR model presenting the factors influencing the hydrodynamic diameter of 14 metal oxide nanoparticles in a complex dispersion system, i.e. a biological medium, and I identified the features of nanoforms influencing the composition of the protein coronas formed on them. Finally, I developed a QSAR model including the effect of protein corona on the cytotoxicity of metal oxide nanoparticles towards the human keratinocyte (HaCaT) cell line and adenocarcinoma human alveolar basal epithelial cells (A549). The obtained results, i.e. QSPR and QSAR models with high reliability, confirmed by statistical parameters related to, inter alia, their predictive abilities, constitute an answer to the research question, confirming the possibility of using QSPR/QSAR modeling in a reliable prediction of physicochemical properties/biological activity of metal oxide nanoparticles despite their labile structure in dispersion systems. The inclusion in the QSAR/QSPR models of factors determining changes in the structure of nanoparticles (e.g. pH) or parameters reflecting them (e.g. a change in the concentration of ions in a given dispersion medium) is an opportunity to develop more reliable predictive models that can be used both to predict properties related to the application potential of nanoparticles, as well as their variable toxicity potential depending on the nature of the biological medium. The presented results are the first step towards extending the QSAR/QSPR modeling paradigm for nanomaterials due to the departure from the assumption of an unchanged structure of the analyzed nanoform of a substance by taking into account its lability and presenting its actual nanoform in the analyzed dispersion medium.