Integrated computational methods for the development of Safe and Sustainable-by-Design Innovative Advanced Materials: the case of surface modified nanophotocatalyst

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1. Introduction

The rapid development of Innovative Advanced Nanomaterials (IAMs) inevitably exposes organisms to multiple types and combinations of nanoparticles (NPs) at varying levels. Understanding the combined impacts of IAMs and their individual components, as well as predicting the toxicity of IAMs mixtures, is crucial.

The innovative design of IAMs, which considers environmental health and safety concerns alongside functionality, has become an integral part of the Safe and Sustainable by Design (SSbD) approach that has gained prominence in recent EU Commission policies. Accelerating the implementation of SSbD can be achieved through the application of artificial intelligence (AI) and digital tools, including Molecular Modeling (MM), Machine Learning (ML) algorithms, and Quantitative NanoStructure–Activity Relationship (Nano-QSAR) models, enabling early consideration of safety aspects in product design in a cost-effective and policy-compliant manner. However, due to the complex structure of Innovative Advanced Materials computational methods such as predictive ML-based models or Nano-QSAR methods to forecast specific properties and risk of more complex systems, remain limited. In our work, we propose for the first time an approach to support the characterization of IAMs at the theoretical level by developing additive descriptors of nanostructure. The development concept of additive nanostructure descriptors is motivated by the increased need for answering the question: How the structure and the structure modifications influence the functionality and activity of more complex systems such as IAMs? The proposed computational approaches that integrate additive descriptors for IAMs and Nano-QSAR models are the first step for the development of safe and sustainable by designing innovative advanced chemicals and materials.

2. Case study

The case study was developed for photocatalytic properties and *in vitro* cytotoxicity of 29 TiO_2-based IAMs (i.e., hybrids of more than two composition types of nanoparticles). They were evaluated using a combination of the experimental testing and supervised machine learning modeling. TiO_2-based nanoparticles combined with metal clusters of

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silver, and their mixtures with gold, palladium, and platinum were successfully synthesized. Two types of the activity, photocatalytic activity and cytotoxicity, were studied. A novel cheminformatic approach was developed and applied for the computational representation of the photocatalytic activity and cytotoxicity effect. In this approach, features of investigated TiO_2-based hybrid nanomaterials were reflected by a series of novel additive descriptors for IAMs (denoted as “additive descriptors for IAMs”) based on quantum chemical calculations. The obtained experimental data and calculated nanostructure descriptors were used to develop novel predictive Quantitative Structure-Activity Relationship computational models. The proposed modeling approach is an initial step in understanding the relationships between the physicochemical properties of IAMs, their toxicity, and photochemical activity under UV-vis irradiation.

3. Conclusions

We believe that knowledge based on theoretical evidence is critical for developing efficient SSbD strategies and Innovative Advanced Materials to assess hazards induced by combined exposure to multiple components of IAMs and to facilitate their modification with non-animal alternative methods at the earliest possible stage. Moreover, it helps considering properties of much more theoretically possible structures (virtual twins) at the virtual screening stage to select the most optimal ones to be synthesized and then experimentally tested.

4. References

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