Chapter 70
Review of Current and Emerging Approaches for Quantitative Nanostructure–Activity Relationship Modeling: The Case of Inorganic Nanoparticles

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ABSTRACT

Quantitative structure-activity/property relationships (QSAR/QSPR) approaches that have been applied with success in a number of studies are currently used as indispensable tools in the computational analysis of nanomaterials. Evolution of nano-QSAR methodology to the ranks of novel field of knowledge has resulted in the development of new so-called "nano-descriptors" and extension of the statistical approaches domain. This brief review focuses on the critical analysis of advantages and disadvantages of existing methods of nanoparticles' representation and their analysis in framework of structure-activity relationships. It summarizes recent QSAR/QSPR studies on inorganic nanomaterials. Here the authors describe practices for the QSAR modeling of inorganic nanoparticles, existing datasets, and discuss applicable descriptors and future perspectives of this field. About 50 different (Q)SAR/SPR models for inorganic nanomaterials have been developed during the past 5 years. An analysis of these peer reviewed publications shows that the most popular property of nanoparticles modeled via QSAR is their toxicity towards different bacteria, cell lines, and microorganisms. It has been clearly shown how nano-QSAR can contribute to the elucidation of toxicity mechanisms and different physical properties of inorganic nanomaterials.

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INTRODUCTION

Despite more than 50 years of history, the nanotechnology still represents the cutting edge of research and industrial endeavors. Enormous amount of money is being spent every year on the creation of new of nanomaterials and investigation of their various characteristics. Usually experimental testing of nanoparticles (NPs) is costly and time-consuming. Thus, promising approach in applications of nanomaterials is development of intelligent testing strategy, which can save time and the cost of products and also reduce number of lengthy and expensive animal tests. Different computational methods have been developed to reach this aim, for example Quantitative Structure-Activity Relationships (QSAR) as the most time-effective technique.

Essentially, the purpose of Quantitative Structure-Activity Relationships (QSAR) studies is to establish a numerical correlation between features of chemical structure and experimental activity using different statistical methods. Over the years more than 5000 different descriptors have been developed; different statistical tools and metrics are adapted to QSAR purposes (Roy, Kar, & Das, 2015). Ideally, developed QSAR model should be able to reproduce the experimental results, explain possible chemical, physical or biological outcomes, and be a source of new information for related, but not studied yet species. It means that it is possible to predict effects induced by unstudied NPs on the basis of structural similarity with NPs for which endpoints were already measured. In this context, the application of the QSAR paradigm to NPs appears as a logical step in NPs investigation (Winkler et al. 2013).

There is a vast potential of QSAR studies in application to nanotechnology. For instance, theoretical characterization based on QSAR models is potentially helpful in optimization and choosing appropriate synthesis stages of NPs. Comprehensive QSAR models are able to predict variety of physicochemical properties of NPs and provide useful information to identification of potential pharmacological leads. Rational design of new nanomaterials can be based on decisions extracted from QSAR models, namely such studies guide selection of parameters of synthesis which can lead to appearing optimal properties of interest. Last, but not least: QSAR is applicable to pre-screening and early identification procedures of hazardous NPs. This is important designing step providing the safe nanomaterials. On this basis, the principle idea of interactions between experimentalist and cheminformatitian is presented on Figure 1.

As one can see in Figure 1, better experimental data helps build better QSAR models, which are helpful to predict better conditions for next series of experiments.

Increasing numbers of nano-QSAR papers is the result of the awareness about the potential of QSAR studies as powerful approach, which allows to make quick and cheap analysis, predictions and obtain far-reaching conclusions.

However, nanomaterials are not structurally homogenous: nanotubes, fullerenes, nanocrystals and clusters are different and they can behave with no common patterns. Therefore, NPs properties should be studied and compared within the most appropriately chosen sub-classes of structural similarity (Puzyn, Leszczynska, & Leszczynski, 2009).

In this review the authors gathered data on inorganic NPs (metals, metal and silica oxides) for which QSAR/QSPR and chemometric studies have been reported in the literature. All papers were analyzed and descriptors and statistical approaches that applied to NPs studies are briefly summarized. At the time of writing near 50 QSAR/QSPR and chemometric studies have been already published. On this basis the latest experimental datasets on various toxic and physicochemical properties of inorganic NPs investigated in framework of nanoinfrormatics have been gathered and discussed.