NanoQSAR models on the toxicity of quantum dots

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QSARs (Quantitative Structure-Activity Relationships) are mathematical models relating the structure of molecules with a biological property or activity, through the use of statistical tools. They are used to predict properties and biological effects of new structures, quickly and at a very low cost in comparison to experimental approaches.

QSAR models for discrete organic molecules are widely used and can be accepted for regulatory purposes [1]. On the contrary, QSAR models on nanomaterials (NMs), commonly known as nanoQSARs, are still at an early stage. One of the challenges in this domain is the identification and description of what a particular NM is. Discrete molecules can be totally identified and characterized by their chemical structure, represented for example by the SMILES code, but this approach is insufficient for NMs, as a key component of their definition is the size and shape or the particles. Another particularity of NMs is the potential complexity of their chemical composition (Figure 1), as they could be formed by different parts: the core, a shell, impurities or dopants and ligands or coating.

As a direct consequence of the structural complexity of NMs, the development of QSAR models requires the codification of nanoform's information that exceeds the classical molecular descriptors. All these particularities should somehow be codified as NM descriptors that are the bases of the development of nanoQSAR models (in a similar way that molecular descriptors are fundamental for QSAR models).

After an extensive analysis of existing calculated and experimental features used to define and describe NMs in the literature, we propose a classification of the descriptors (Figure 2). Our classification differentiates between those descriptors that codify a direct and indirect description of the structure, and those that provide additional experimental knowledge. Direct descriptors provide information from the chemical composition of the core (a), the surface substituents (b) or the physical structure (c). Indirect descriptors codify information of experimental features that depend on the structure (d) or may cause changes in the structure (e). In addition, the classification includes features that do not describe the NM, but the conditions of the endpoint measurement (f).

Quantum dots (QDs) are a particular group of NMs which are characterized by their unique optical and electronic properties. Those nanoparticles present discrete electronic levels that lead to a UV-visible emission patterns which depend on the size of the particle (Figure 3). We have developed preliminary nanoQSAR models for the cytotoxicity of QDs, using a dataset compiled by Bilal et al. [2] and discussed the influence of the descriptors used in the performance of the models.

In this work we present the development of predictive models, as well as a discussion in the effect of different changes in the selected features, including calculated descriptors and experimental measurements.

References

[1] R. Gozalbes, J.V. de Julián, IJQSPR, 3 (2018) 1-24.

[2] M. Bilal, E. Oh, R. Liu, J.C. Breger, I.L. Medintz, Y. Cohen, Small, 15 (2019) 1900510.

Figures

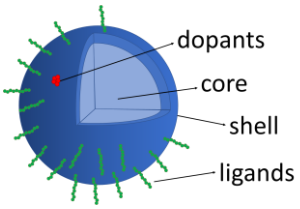

Figure 1. Schematic depiction of the parts of a complex nanoparticle

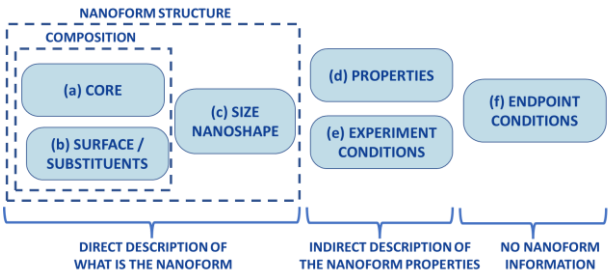

Figure 2. Classification of nanoQSAR descriptors

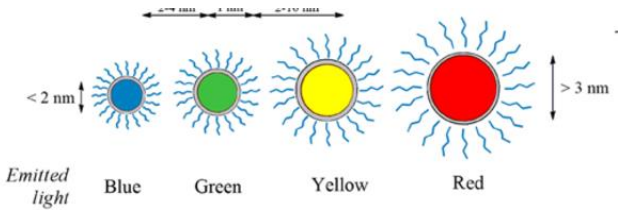

Figure 3. QDs light emission dependence on the size