Toxicity assessment of metal-ions binary mixtures: new computational approach for calculation toxicity indexes

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1. Introduction

Assessing the toxicity of mixtures is crucial these days, as large amounts of innovative Advanced Nanomaterials (AdvNMs) and Multicomponent Nanomaterials (MCNMs) are being produced and released into the natural environment. While laboratory mixtures consist of known ingredients and concentrations, environmental mixtures are complex and mainly multi-component, often with unknown proportions. This fact creates an additional issue: the exact concentrations of the mixture components are unknown. To resolve this problem, we propose a new combined approach to calculate the concentrations of mixture components in a theoretical mixture that causes an EC_{50} effect. Based on this approach and a dataset containing nanomaterials-ions mixtures, we calculate several types of mixture toxicity indices: Sum of Toxic Units (STU), Additivity Index (AI), Mixture Toxicity Index (MTI), and Model Deviation Ratio (MDR).

2. New approach for calculate toxicity indexes

In our work, we propose a computational approach to support the prediction of the joint effects of AdvNMs and MCNMs at the early design phase, prior to synthesis. To address the lack of knowledge about the concentrations of individual components in EC_{50} mixture samples, we utilized the known concentrations of the individual components in the binary mixtures used to determine the EC_{50} dose and effect (e.g., immobilization). Based on these parameters, two dose-response curves were obtained for each component of the binary mixture. The individual concentration in the mixture samples was used as the dose, while the response of the binary mixture was used as the response. Using these curves, we determined the concentrations of the mixture components necessary for calculating mixture toxicity indexes in the next step. The calculations were performed using a combined Python and R script with the 'drc' package.

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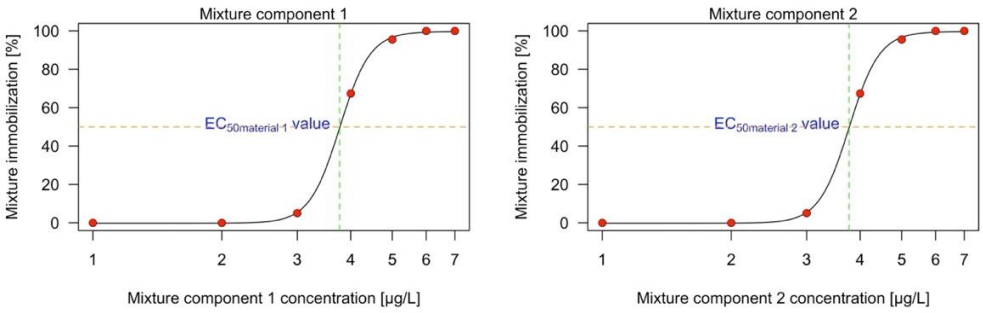

Figure 1 Graphical explanation of two DRC curves method

3. Mixture toxicity indexes calculation

Based on the compositions of binary mixtures of nanoparticles with metal ions available in the literature, the developed approach was utilized to obtain the values necessary for calculating toxicity indices. Four toxicity indices were calculated: Sum of Toxic Units (STU), Additivity Index (AI), Mixture Toxicity Index (MTI), and Model Deviation Ratio (MDR) to assess modes of action (additivity, synergism, and antagonism) for specific samples. In the next step, the indices were compared and displayed graphically.

4. Conclusions

As a result, we obtained a set of 17 binary mixtures of nanoparticles (NPs) and metal ions, characterized by four toxicity indices: Sum of Toxic Units (STU), Additivity Index (AI), Mixture Toxicity Index (MTI), and Model Deviation Ratio (MDR). Primarily, the binary mixtures of nanoparticles with ions exhibited an antagonistic effect, but in four analyses, the effect was synergistic. The effects of toxicity as characterized by these indices were also compared. In 11 of the 17 samples, different types of indices yielded the same toxicity results.

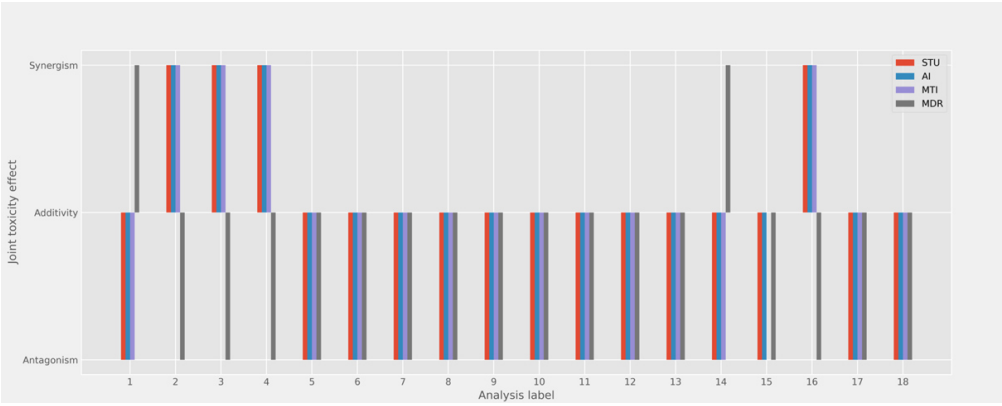

Figure 2 Joint toxicity effect indicate by 4 types of toxicity indexes (STU, AI, MTI, MDR)

5. References

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