METAL MIXTURES MODELLING

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Fact Sheet Four

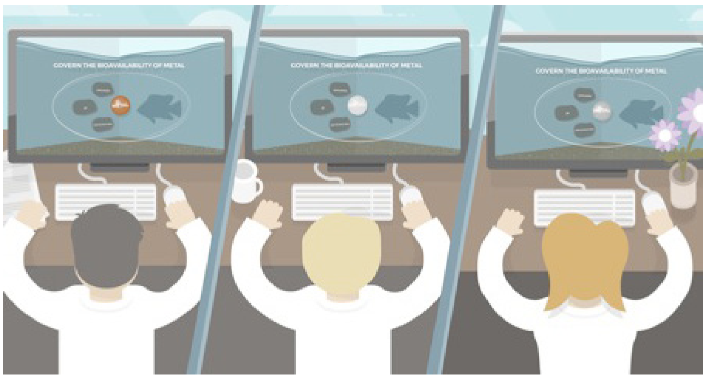
Introduction

Reviews of previous research studies of the toxicity of metal mixtures have not been able to reach a clear consensus about how metals interact together to cause toxicity. Mixtures may have the same effect as their components added together, this is known as an “additive effect”. Alternatively, mixtures may have an effect that is more, or less, than the effect of the components added together. In these cases, the effect would be described as “less than additive” or “more than additive”.

This variability in the way metals interact to cause toxicity creates uncertainty in how best to develop a scientifically robust framework for regulating metal mixtures in the environment. Over the last several years, researchers have been developing promising new methods to solve this problem.

How can models predict the biological effects of metal mixtures?

Speciation modelling based approaches currently represent the most robust approach towards understanding metal toxicity, and provide the best means of further evaluating the toxicity of metal mixtures. Single metal Biotic Ligand Models (BLMs) have proven to be good predictors of metal toxicity over a wide variety of water chemistry conditions, and already accommodate interactions between metals and competing ions such as Ca and Mg that do not cause toxicity. The extension of these types of models to consider multiple metals toxicity is therefore a logical approach.



Figures 1. Consideration of multiple metal exposures with BLMs.

Conceptually, development of mixture BLMs (mBLMs) is relatively straightforward, simply requiring consideration of multiple metals in speciation calculations to estimate metal accumulation at the biotic ligand and then evaluation of how this accumulated metal exerts toxicity. However, there are a number of different options regarding key components of the model framework such as the chemical speciation model selected, the mechanisms of interaction (concentration addition vs. independent interaction), number of metal binding sites (one site for all metals, one site for each metal, or some other configuration), and the dose response model (logistic vs. threshold vs. other). To evaluate these issues, a large international study called the Metal Mixtures Modelling Evaluation (MMME) study was undertaken to begin development of mBLMs.

The MMME evaluated these issues by gathering four groups of scientists that had each developed a preliminary mBLM. The mBLMs were all similar in overall structure, relying on metal speciation calculations to make predictions of metal accumulation at the biotic ligand and then attributing toxicity to this accumulated metal. However, the models varied in the key components described above (speciation model, mechanism of interaction, number of metal binding sites, dose response model). Each research group was provided with a series of metal mixture toxicity data sets against which to test their model. Overall, all four models performed well in predicting both single metal and metal mixture toxicity across a range of aquatic organisms and mixture scenarios. This was despite some significant differences in model parameters such as metal binding affinities, where corresponding differences in, for example, metal potency factors resulted in similar model predictions. In other words, the 4 models were able to correctly develop similar predictions of mixture toxicity, but this was accomplished by different mechanisms across the models evaluated. In general, the models performed well when metal toxicity was additive, but less than additive toxicity was more problematic to predict (more than additive scenarios were not present in the available evaluated dataset). A detailed description of model frameworks and performances can be found in Farley et al. 2015 and Van Genderen et al 2015[1].

Summary and conclusions

Extension of existing single metal BLMs to predict the toxicity of metal mixtures appears to be a promising tool for regulating metal mixtures in the environment. Initial efforts to develop mBLMs have shown promising results[2]. As additional laboratory and field studies evaluating metal mixtures are generated, our understanding of the most appropriate modelling framework for regulating metal mixtures will improve.

[1] Farley KJ, Meyer JS. 2015. Metal mixture modeling evaluation project: 3. Lessons learned and steps forward. Environ Toxicol Chem. 34:821-32. Van Genderen E, Adams W, Dwyer R, Garman E, Gorsuch J. 2015. Modeling and interpreting biological effects of mixtures in the environment: introduction to the metal mixture modeling evaluation project. Environ Toxicol Chem. 34:721-5.

[2] Farley KJ, Meyer JS, Balistrieri LS, De Schamphelaere KA, Iwasaki Y, Janssen CR, Kamo M, Lofts S, Mebane CA, Naito W, Ryan AC. 2015. Metal mixture modeling evaluation project: 2. Comparison of four modeling approaches. Environmental Toxicology and Chemistry. 34:741-53.