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Research Paper

Quantifying the interactions among metal mixtures in toxicodynamic process with generalized linear model

Jianfeng Feng [a] [1] ✉, Yongfei Gao [b, 1], Yijun Ji [a], Lin Zhu [a]

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Highlights

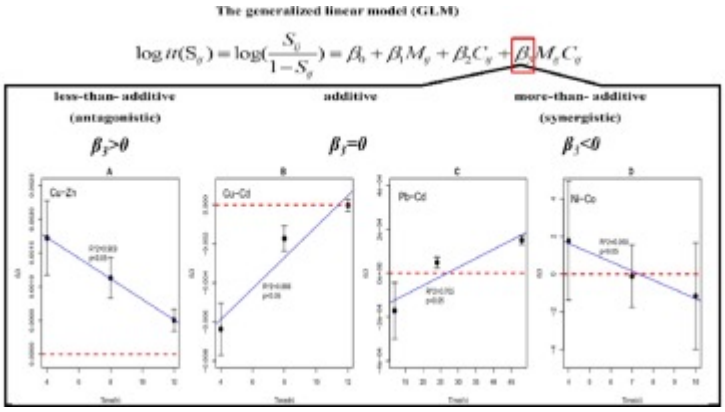
- GLM was used to quantify the metal interactions in toxicodyamics process.
- Joint actions occur among Cu–Zn, Cu–Cd, Cd–Pb, and Ni–Co in toxicodyamics process.
- The interaction types among Cu–Zn, Cu–Cd, Cd–Pb, and Ni–Co were time dependent.
- GLM is a powerful tool for assessing the toxicities of interacting chemical mixtures.

Abstract

Predicting the toxicity of chemical mixtures is difficult because of the additive, antagonistic, or synergistic interactions among the mixture components. Antagonistic and synergistic interactions are dominant in metal mixtures, and their distributions may correlate with exposure

concentrations. However, whether the interaction types of metal mixtures change at different time points during toxicodynamic (TD) processes is undetermined because of insufficient appropriate models and metal bioaccumulation data at different time points. In the present study, the generalized linear model (GLM) was used to illustrate the combined toxicities of binary metal mixtures, such as Cu–Zn, Cu–Cd, and Cd–Pb, to zebrafish larvae (*Danio rerio*). GLM was also used to identify possible interaction types among these method for the traditional concentration addition (CA) and independent action (IA) models. Then the GLM were applied to quantify the different possible interaction types for metal mixture toxicity (Cu–Zn, Cu–Cd, and Cd–Pb to *D. rerio* and Ni–Co to Oligochaeta *Enchytraeus crypticus*) during the TD process at different exposure times. We found different metal interaction responses in the TD process and interactive coefficients significantly changed at different exposure times ($p < 0.05$), which indicated that the interaction types among Cu–Zn, Cu–Cd, Cd–Pb and Ni–Co were time dependent. Our analysis highlighted the importance of considering joint actions in the TD process to understand and predict metal mixture toxicology on organisms. Moreover, care should be taken when evaluating interactions in toxicity prediction because results may vary at different time points. The GLM could be an alternative or complementary approach for BLM to analyze and predict metal mixture toxicity.

Graphical abstract



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Abbreviations

TK-TD model, toxicokinetic–toxicodynamic model; TK model, toxicokinetic model; TD model, toxicodynamic model; GLM, generalized linear model; CA, concentration

addition model; IA, independent action model

Keywords

Toxicodynamic; Generalized linear model; Interaction types; Toxicity; Metal mixtures

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