

**Abstract****[Project Information]**

Project Title :	Development of Ecological Risk Assessment Methods for Multiple Chemicals Based on the Similarity of Activity / Structure and Exposure Profile
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**[Abstract]**

The mixture effects of three groups of organic chemical substances with similar actions and structures and six metals with relatively high ecological risk were assessed by comparing with the prediction from their individual toxicities. For organic chemicals, (sub)grouping was examined from the perspective of ecotoxicity profiles, their physical-chemical characteristics, and the mechanism of action suggested by the database/literature, and case study results were obtained for phthalic esters, mitochondrial electron transport complex inhibitors, and cationic surfactants. For phthalate esters, similarity in effects was suggested over a range of C1-C11 while a gap was identified between C1-C6 and C8+ chains. Additivity was observed for each of the mitochondrial electron transport chain complexes, while inhibitors of each complex showed a certain deviation from the concentration addition (CA) model within the range of 0.5 to 2 times. Similarly, for cationic surfactants, quaternary ammonium, tertiary amine, and tertiary amide with similar structure and use showed a certain deviation from the CA model, but this was within the range of 0.5 to 2 times. In addition, among the substances in the three groups of organic pollutants, the environmental concentrations were predicted, including those for which there was no information on the production, shipping, or emission amounts, and compared with the actual measured environmental concentrations to verify the predictions, and the ecological risks were determined by combining them with ecotoxicity data. Regarding metals, six metals (Ni, Cu, Zn, Pb, Cd, Al) were classified according to their exposure patterns, and a method for evaluating the toxicity of multiple metals considering bioavailability was developed by estimating total organic carbon concentrations. Tests were conducted with metal

mixtures for the three exposure patterns, and the deviations from the CA model were all in the range of 0.5 to 2 times. In theoretical studies, an investigation was conducted into the number of chemicals should be included in risk assessment, and it was suggested that even under fairly conservative assumptions with many oversights, it would be sufficient to consider a risk about twice that of the highest-risk substance. Furthermore, a life table reaction analysis using the flow of individuals and the flow of reproductive values was found to enable the separation and evaluation based on the flows to evaluate individual and multiple chemicals in detail. Finally, when 2 to 20 organic chemicals and metals were examined in the Funnel hypothesis, the results suggest deviations from concentration additivity converge at 10 to 20 substances.

### [References]

Iwasaki, Y., Mano, H., Shinohara, N. (2023). Linking levels of trace-metal concentrations and ambient toxicity to cladocerans to levels of effects on macroinvertebrate communities. *Environmental Advances*, 11:100348. <https://doi.org/10.1016/j.envadv.2023.100348>

Yokomizo, H., Fukaya, K., Lambrinos, J. G., Kawai, Y., Takada, T. (2024). Interstage flow matrices: population statistic derived from matrix population models. *Journal of Ecology*, 112(6), 1326-1338. <https://doi.org/10.1111/1365-2745.14303>

Oda Y., Kawano M., Watanabe H., Yamagishi T., Yamamoto H. (2025). Ecotoxicity assessment of phthalic acid di-alkyl ester mixtures toward aquatic organisms based on results from a series of subchronic toxicity tests, *Environmental Toxicology and Chemistry*, 44(5), 1247–1258. <https://doi.org/10.1093/etojnl/vgae072>

Iwasaki, Y., Naito, W. (2025). Metal exposure profiles at metal-contaminated sites in rivers across Japan, *Environmental Monitoring and Contaminants Research*, 5, 35-39. <https://doi.org/10.5985/emcr.20240039>

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