

## **A physiological and developmental analysis of metal mixture toxicity in adult and early-life stages of the zebrafish**

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A number of metals are key to life while others do not appear to fulfil essential functions and both become toxic at elevated concentrations. Although the effects of metals on biological systems are well documented on the macroscopic scale, our understanding of the molecular, biochemical and physiological mechanisms of metal toxicity is still limited. Especially the effects of metal mixtures remain very poorly documented and understood.

Within this context we are performing experiments with early life stages and adult zebrafish to investigate the effects of single and combined exposures to Cu and Cd. In adults, effects on survival and behavioural responses were followed up to 28 days and the body burdens of both metals and the major cations were analysed. In zebrafish embryo acute toxicity tests survival and a number of sub-lethal endpoints, including swim bladder inflation, heart rate, mobility and malformations were recorded up to 120 hours post fertilization.

In general, both zebrafish embryos and adults were much more sensitive to Cu than to Cd in single metal exposures on the basis of the observed mortalities. Exposure to Cu and Cd together showed interactions pointing to strong synergistic effects. The metal uptake measured in the adult fish showed a clear dose-response relationship, however neither the metal uptake rates nor body burdens in individual or mixture exposures explain the observed effects.

Analysis of the major body cations showed that a loss of cations, in particular sodium has a large impact on the observed mortality in adults. The results obtained so far with early life stages show a high sensitivity of the development of the posterior swim bladder chamber to the exposure to Cu and Cd compared to other endpoints. In addition to the development of the swim bladder, a co-exposure to Cu and Cd greatly impaired hatching.

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