Molecular and phenotypical toxicological effects of environmental pollutants and their mixtures

A mechanistic approach

av

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Abstract

Current environmental risk assessment of polluted sites primarily relies on single compound evaluation. However, in the environment, organisms are often exposed to complex mixtures of pollutants. To further develop risk assessment of polluted sites and evaluate the risks that mixtures pose to humans and wildlife, a mechanistic understanding of mixture toxicity is needed.

The overall aim of this thesis was to increase our knowledge of the toxic effects caused by chemical mixtures and to develop new approaches to investigate the molecular mechanisms underlying such effects. To reach this aim, a comprehensive set of methods was applied, considering molecular and phenotypical alterations as well as chemical analyses.

The investigations revealed that the acute toxicity caused by mixtures of the pollutants B[*a*]P, PFOS, PCB126, and Arsenate is mainly predictable by concentration addition. The results also showed some specific sublethal effects of the various mixtures that were not observed for the single components. In addition, each mixture caused very specific patterns of behavioral alterations, gene expression changes, altered lipid content, and altered organ growth. A complex environmental mixture from soil contaminated with PACs caused for instance behavioral alterations in zebrafish, in addition to dysfunction of genes that are critical for eye development.

In summary, this thesis contributes to an increased understanding of the mechanistic pathways underlying the mixture toxicity of selected pollutants and environmental samples. In addition, it provides insights for the development of new approaches that may be included in risk assessment, such as image analysis and effect-directed analysis.

Keywords: Environmental pollutants, mixtures, soil, zebrafish, *Danio rerio*, behavior, gene expression, lipidomics, image analysis, PCB126, PFOS, B[*a*]P, Arsenic, risk assessment.