Quantitative Structure-Activity Relationships for soil Ecotoxicity

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Summary

Pollution with organic compounds is a global problem, threatening ecosystem structure and function. In order the assess and evaluate the potential risk of industrial compounds to soil organisms and communities statistical toxicity models such as quantitative structure activity relationships (QSARs) provide an effective alternative to exhaustive toxicity tests. QSARs use physical-chemical properties of a series of compounds and correlate them with defined toxicological endpoint concentrations in the environment, such as EC_{50} for the reduction of reproduction of soil invertebrates. Standardized toxicity tests, in particular for *Folsomia candida*, belonging to one of the most sensitive taxa to soil contamination, are the base for QSARs. Traditionally, the n-octanol-water partition coefficient ($logK_{ow}$) was found to be a good descriptor for hydrophobic organic compounds, to assess toxicity and classify compounds, as their main mode of action is the disruption of cell membranes and potential interaction with membrane integrated complexes. The freely dissolved concentration in the soil for ECx values is correlated with the lipophilicity of the compounds.

In chapter two, 28d standard toxicity tests with *F. candida* were performed and QSARs developed to determine the EC_{10} and EC_{50} for the effect of nine chlorobenzenes on the reproduction *F. candida*, in natural standard soil LUFA2.2 and OECD artificial soil. For both endpoints, two individual QSAR regression models were obtained, based on different sorption behaviour of the compounds towards the soil organic matter. Estimated free soil interstitial water concentrations for both endpoints were measured with solid-phase microextraction (SPME) in LUFA2.2 soil in order to validate estimated concentrations. However, measured concentrations, though QSAR were developed for it, did not confirm estimated concentrations, indicating the need for exact determination of soil sorption coefficients and further investigation of additional processes.

In chapter three, aniline and 5 chlorinated anilines were used in a similar way to develop QSARs in LUFA2.2 and OECD soil for effects on *F. candida*. For both endpoints and soil regression models showed correlations with their $logK_{ow}$. After SPME measurements for the dichloroaniline, trichloroaniline, tetrachloroaniline and pentachloroaniline, estimated concentrations were only confirmed for the two highest chlorinated

congeners. The losses of bioavailability for dichloroaniline were so extensive that QSARs for measured concentrations were not developed.

Toxicity models for environmental risk assessment of organic compounds use mostly initial nominal concentrations. Yet, the freely dissolved fraction of hydrophobic compounds undergoes dynamic processes, such as biodegradation, sorption and volatilisation. Chapter four addresses this problem by measuring EC_{10} and EC_{50} values for eight chlorobenzenes and four chloroanilines, for *F. candida* at 0, 14 and 28 days, covering the total duration of a standardized toxicity test. Lower chlorinated compounds showed significant losses over time, while compounds with higher chloride substitution and $logK_{ow}$ were stable in the soil interstitial water. QSARs were calculated for the geometric mean concentration, as a measure of the average effective concentration over time, for the set of chlorobenzenes. Conversely, for the chloroanilines, QSARs were not developed due to substantial losses of dichloroaniline, while concentrations of tetra- and pentachloroaniline were stabile over the 28-day test period.

The $logK_{ow}$ as descriptor for the lipophilicity of a compound and the $logK_{oc}$ for the sorption towards organic carbon were often used to explain differences in the toxicity of compounds and interstitial water concentrations in test soils. In order to optimize QSARs for the subset of chlorobenzenes (non-polar narcosis) and chloroanilines (polar narcosis), liposome-water partition coefficients ($logK_{lipw}$) as alternative to the $logK_{ow}$ and soil-specific $logK_{oc}$ values were determined for the organic matter of LUFA2.2 and OECD soil and a model based on measured concentrations was developed in chapter five. SPME measurements revealed substantial differences in freely dissolved compound concentrations, only explainable by the varying water concentrations in the soil. In chapter five, a unified QSAR for two soils and both compound sets was accomplished after concentrations in the water were corrected for the water volume of both soils.

In chapter six, a microarray study was used to generate a gene-response profile of *F. candida* after 2-day exposure to concentrations corresponding with predetermined EC_{50}s concentration of aniline and five chloroanilines for potential proton chain inhibition, 1,2,3,4-tetrachlorobenenze as control group for non-polar narcosis acting compounds. Based on the specific response of classifier gene clusters, tetrachloroaniline was identified as uncoupler, while lower chlorinated

anilines showed no significant differences in their molecular response in comparison to inert compounds. Pentachloroaniline showed trends towards similar reaction of tetrachloroaniline, but remained in the cluster of non-polar compounds.

This thesis describes the validation and optimization process of QSARs for soil toxicity tests. It shows that reliable QSARs do not only have to take the structures and properties of a given compound into account, but also characteristics of the matrices used for testing. Furthermore, it demonstrates that the classification of the mode of action can ultimately only be determined by analysing physiological and molecular responses of the organisms. Finally, none of these studies can solely explain toxicity or risk, however, their integration builds a stronghold for future research and evaluation processes.