Quantitative Structure-Activity Relationships for soil Ecotoxicity

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Chapter 5

Towards a unified Quantitative Structure-Activity Relationship describing toxicity of polar and nonpolar narcotic organic chemicals for the springtail *Folsomia candida* in different soils

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Abstract

The development of a unified Quantitative Structure-Activity Relationship (QSARs) describing the toxicity of polar and non-polar organic compounds in multiple soils was always hampered by two main factors. First, existing QSARs distinguish between narcosis I and II compounds, which exhibit different toxicities when compared with their $\log K_{ow}$ suggesting that polar compounds are more toxic. Second, to predict freely dissolved concentrations, the sorption to soil organic matter of compounds had to be estimated by using organic carbon-water partition coefficients ($\log K_{oc}$). To overcome these problems, in this study the compound interaction with the membrane, the liposome-water partition coefficient ($\log K_{lipw}$), and soil-specific $\log K_{oc}$ were determined for two soils and a compound set of eight chlorobenzenes and four chloroanilines. Solid-phase microextration (SPME) was used to measure actual concentrations in the soil interstitial water at EC_{50} values for the effect on the reproduction of *Folsomia candida*. The QSAR corrected for the determined chemical descriptors still separated between soils, which was in agreement with the difference in the measured concentrations. A unified QSAR, reliably predicting toxicity of all compounds in both soils, was accomplished by the additional incorporation of the total water volume in the soil as an integral compartment of the soil matrix.

Introduction

Originally developed for the effects on aquatic organisms (Könemann, 1981), Quantitative Structure Activity Relationships (QSARs) typically are linear relationships between an aqueous effect concentration (e.g., LC_{50} or EC_{50}) and the compounds' *n*-octanol-water partition coefficient ($logK_{ow}$). QSARs predict toxicity of hydrophobic compounds to increase with increasing hydrophobicity, distinguishing two classes, namely narcosis I and narcosis II (Ramos et al., 1998; Ren, 2002). Narcosis I, or baseline toxicity, applies to inert compounds that exert toxicity only through partitioning into and disturbing cellular membranes. The more polar narcosis II compounds have a higher toxicity, which is believed to be due to potential additional mechanisms, such as proton chain uncoupling or through forming hydrogen bonds. This classification of compounds and the applicability of *n*-octanol as a substitute for lipids, however, have been questioned (Escher et al., 2000a, b; van der Heijden and Jonker, 2009). The difference between *n*-octanol and the actual structure of biological lipids raises the question whether QSARs based on *n*-octanol-water partition coefficients can simulate all interactions of organic compounds. The distinction between polar and non-polar chemicals might perhaps only be an artificial one, due to the fact that *n*-octanol is a suboptimal descriptor. For instance, by using compound-specific artificial membrane (liposome)-water partition coefficients ($logK_{lipw}$), Vaes et al. (1998) optimized QSARs for aquatic systems and showed that the $logK_{ow}$ in fact overestimated the toxicity of polar compounds. Hence, the use of $logK_{ow}$ in QSARs should be viewed with caution.

In soil, the freely dissolved concentration of organic chemicals in the interstitial water is claimed to govern toxicity to soil-dwelling organisms (Van Gestel and Ma, 1988; Van Gestel and Van Dis, 1988). The behavior of hydrophobic compounds in soils, however, deviates from aquatic systems as studied by Vaes et al. (1998), due to the compounds' direct interactions with the soil organic matter. Traditionally, the bioavailable concentration in the interstitial water phase is estimated from the total soil concentration, using the fraction of soil organic carbon (f_{oc}) and the compound-specific organic carbon partition coefficient ($logK_{oc}$) (Droge et al., 2006; Van Gestel and Ma, 1993). QSARs for toxicity to soil organisms also distinguish between

narcosis I and II and recently, we derived four separate regression models when relating the toxicity of chlorobenzenes and chloroanilines to the springtail *Folsomia candida* in two different soils to $\log K_{ow}$ (Giesen et al. 2012; Giesen et al. submitted; Jannsens et al. 2011). The differences observed in toxicity could be partly related to the different modes of action of the non-polar chlorobenzenes and the polar chloroanilines (narcosis type I vs II). However, we also found significantly different QSARs for the different soils, which contradicts the theory that toxic concentrations are comparable across different soils. This discrepancy between theory and experimental observations can be explained by the existence of soil-specific $\log K_{oc}$ values for the tested soils (Rutherford et al., 1992; Sabljic et al., 1995). With the development of solid-phase microextraction (SPME) and other passive sampling methods, it has become possible to measure actual freely dissolved concentrations of organic chemicals in the soil interstitial water directly (Hurdzan and Lanno, 2009; Leslie et al., 2004a; Ouyang and Pawliszyn, 2006; Verbruggen et al., 2000). This allows a comparison of concentrations as estimated according to the traditional way with actual measured ones (Giesen et al., 2012) and may circumvent the indirect step in which aqueous concentrations are estimated from measured total soil concentrations. Therefore, the use of passive samplers also enables a direct comparison between different soils.

The present study aimed at unraveling the differences in the QSARs for the toxicity of chlorobenzenes and chloroanilines for the springtail *F. candida* in different soils, as reported previously (Giesen et al. 2012; Giesen et al. submitted). To this end, liposome-water partition coefficients for eight chlorobenzenes and four chloroanilines, as well as soil-specific organic carbon-water partition coefficients of these compounds in two standard test soils were determined. Additionally, concentrations in the soil interstitial water corresponding to the EC_{50} for the effect on reproduction of *F. candida* were measured with SPME. Based on the results, we demonstrate that it is possible to predict the toxicity of both narcosis type I and II compounds for *F. candida* in different soils with a single, unified QSAR.

Material and Methods

Test substances

The selected chlorobenzene series included all three trichlorobenzene isomers (1,2,3-, 1,2,4-, and 1,3,5-TrCB), all three tetrachlorobenzene isomers (1,2,3,4-, 1,2,3,5-, and 1,2,4,5-TeCB), pentachlorobenzene (PeCB), and hexachlorobenzene (HCB). Compounds were purchased from Sigma-Aldrich, except for 1,2,4-trichlorobenzene, which was obtained from Acros Organics. The minimum purity was 98%. Chloroanilines included 3,5-dichloroaniline (3,5-DCA), ordered from Aldrich, 2,3,4-trichloroaniline (2,3,4-TrCA) from TCI Europe, 2,3,5,6-tetrachloroaniline (2,3,5,6-TeCA) from Chemos, and pentachloroaniline (PCA) from Sigma Aldrich. Purity of the individual compounds was ≥97%.

Test soils

Standardized natural LUFA2.2 soil (Landwirtschaftliche Untersuchungs- und Forschungsanstalt (LUFA), Speyer, Germany) was used, which is classified as a sandy loam soil (particle size distribution: 50-2,000 μm, 75.3%; 2-50 μm, 16.6%, and < 2 μm, 8.1%) with 2.2±0.2 % organic carbon. The measured soil pH was 5.5±0.4. The maximum water holding capacity (WHC) was 38% (w/w). Artificial soil was prepared according to OECD guideline 207 with 70% quartz sand (Praxis, Amsterdam, The Netherlands), 20% kaolin clay (China clay, CH112, Keramikos, Haarlem, The Netherlands), and 10% dried and ground Sphagnum peat (Jongkind B.V., Aalsmeer, The Netherlands). The pH was adjusted with calcium carbonate to 6.5±0.2. WHC was determined to be 94% of dry weight. Both soils were oven dried at 60°C for 24 hours and passed through a 2 mm sieve prior to use. Subsequently, they were spiked with a cocktail solution of all test compounds in acetone, to obtain solid phase concentrations corresponding to the EC_{50}s for reproduction of *F. candida,* as determined in our previous study (see Table 1). Ten percent of the total amounts of dry soil needed for treatment were pre-spiked with 10 mL of the spike solution, shaken for one hour, and stored overnight in the dark. After evaporation of the acetone under a mild air stream, the remaining amount of soil was added and the mixture was thoroughly mixed and moistened to 50% of the respective WHC with demineralized water. Jars were closed with

methanol-cleaned screw caps and stored in the dark at 20°C. Twelve hours after the spiking, freely dissolved concentrations in the soil interstitial water were determined with solid phase microextraction (SPME), as described below.

Table 1. Effective concentrations of chlorobenzenes and chloroanilines causing 50% reduction of the reproduction of *Folsomia candida* (estimated EC_{50}; mg/kg) in natural standard LUFA2.2 soil and OECD artificial soil as determined in previous work and concentrations spiked into the soils in the present study for the benefit of SPME analyses.

	LUFA		**OECD**	
Compound	Estimated EC_{50}	spiked concentration	Estimated EC_{50}	spiked concentration
Chlorobenzenes				
1,2.3-TrCB	78	78	68	68
1,2,4-TrCB	88	88	80	80
1,3,5-TrCB	56	56	40	40
1,2.3.4-TeCB	60	60	40	40
1,2,3,5-TeCB	68	68	62	62
1,2,4,5-TeCB	60	65	40	43
PeCB	54	59	40	43
Chloroanilines				
3,5-DCA	23	23	12	12
2,3,4-TCA	30	30	20	20
2,3,5,6-TeCA	40	40	28	28
PeCA	52	57	44	48

Freely dissolved concentrations in soil

SPME measurements were performed in twelve-fold in each soil. For each of the replicates, 2 grams of soil were mixed in 7 mL amber-colored vials with 6.5 mL of Millipore water containing 0.01 M calcium chloride and 50 mg/L sodium azide. A single 2 cm long 30 µm polyacrylate-coated SPME fiber (Poly Micro Industries, Phoenix, USA) was then introduced into each vial and the systems were agitated for 4 weeks on a “Rock-and-Roller” apparatus (Snijders Scientific) in the dark. At the end of this period, fibers were removed, cleaned with millipore water wetted tissue, and transferred to

cyclohexane (volume fit to expected concentrations). Finally, internal standard solution (10 mg/L PCB-31 in cyclohexane) was added.

Liposome – water partition coefficients

Liposome-water partition coefficients (K_{lipw}) for all test compounds were determined in six-fold as described by van der Heijden and Jonker (2009). In short, a dispersion of 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphatidylcholine (POPC) in an aqueous medium of Millipore water containing 50 mg/L of sodium azide and 0.01 M of calcium chloride was made from a POPC stock solution in chloroform, as supplied by Avanti Polar Lipids (Alabaster, AL, USA). An aliquot of the dispersion was weighed into an amber-colored all-glass bottle of 100 mL, which was then filled with the above-mentioned aqueous medium. Then, 5 cm of polyacrylate-coated (30 μm) SPME fiber was added and the system was spiked with 100 μL of a cocktail solution of the test compounds in acetone. Systems were placed on a shaker (150 rpm) in the dark and equilibrated for 4 weeks at 20°C. Upon equilibration, SPME fibers were collected, cleaned with a wet tissue, and placed in amber-colored autosampler vials filled with 180 μL of cyclohexane in an insert. Finally, 20 μL of the PCB-31 internal standard solution was added. Final results were adjusted for procedural blanks (n=3; containing liposomes, but no spike).

Organic carbon-water partition coefficients

Organic carbon-water distribution coefficients (K_{oc}) for all test compounds were determined in five-fold using both natural standard LUFA2.2 soil and OECD artificial soil in a similar fashion as the K_{lipw}. In this case, three (LUFA soil) or one (OECD soil) gram was weighed into the bottles, and after adding the aqueous medium and the fibers (3 cm for LUFA and 5 cm for OECD soil), the systems were spiked with 100 μL of the spike solution. Equilibration and ending the systems was as described above and final results were adjusted for soil-specific blank determinations (n=3 for each soil).

GC analysis

Concentrations in the fiber extracts were determined by GC-ECD (GC 8000 gas chromatograph; Fisons Instruments, Milan, Italy), equipped with a CombiPAL autosampler system (CTC Analytics, Zwingen, Switzerland), a Rtx-5 amine column (30 m length, coating thickness 25 µm, internal diameter 0.25 µm), a deactivated fused silica pre-column (length 2 m), and a ^{63}Ni electron capture detector. Chromatographic data were analyzed with Chromcard 1.21 (CE Instruments).

Data analysis

Concentrations in the fiber extracts were translated to concentrations in the fibers (C_f), which were then used to calculate freely dissolved chlorobenzene and chloroaniline concentrations in the soil interstitial water (C_w^{meas}), using polyacrylate fiber-water partition coefficients (K_{fiber}) as reported by Giesen et al. 2012 and Giesen et al. submitted, i.e., $C_w^{meas} = C_f/K_{fiber}$. These aqueous concentrations were used as explaining variables in linear structure-activity relationship regression analysis. QSARs derived for both soils and both effect concentrations were analyzed with an F-distribution test. Differences between soil-specific logK_{oc} values were compared with student t-test. Statistical analyses were performed in SPSS (Version 15.00; SPSS Chicago, US).

Results and Discussion

Partition coefficients

Soil-specific organic carbon-water partition coefficients and liposome-water partition coefficients determined for the chlorobenzenes and chloroanilines are presented in Table 2. LogK_{oc} values for the OECD soil are consistently higher than those for the LUFA 2.2 soil, i.e., by an average factor of 1.65. This difference was significant ($p<0.001$) in a two-sided student t test. Nevertheless, the log K_{oc} values generally are in good agreement with literature data (Sabljic et al., 1995).

Table 2. Soil-specific organic carbon-water partition coefficient (log K_{oc}) for natural LUFA2.2 soil and OECD artificial soil and liposome-water partition coefficients ($logK_{lipw}$) for the chlorobenzenes and chloroanilines tested in this study. Also included are $logK_{oc}$ and $logK_{ow}$ values taken from the literature.

	log K_{oc}				**$logK_{lipw}$**		Literature[a]	
Compounds	**LUFA**	stdev	**OECD**	stdev	**$logK_{lipw}$**	stdev	$logK_{oc}$	$logK_{ow}$
Chlorobenzenes								
1,2,3-TrCB	**3.06**	0.01	**3.24**	0.03	**4.16**	0.06	3.31	4.13
1,2,4-TrCB	**3.18**	0.00	**3.40**	0.01	**3.86**	0.09	3.29	4.05
1,3,5-TrCB	**3.18**	0.01	**3.38**	0.02	**4.27**	0.07	3.39	4.18
1,2,3,4-TeCB	**3.82**	0.02	**4.00**	0.02	**4.75**	0.02	3.59	4.64
1,2,3,5-TeCB	**3.68**	0.03	**3.90**	0.02	**4.56**	0.03	3.64	4.65
1,2,4,5-TeCB	**3.75**	0.01	**3.97**	0.02	**4.44**	0.02	3.61	4.60
PeCB	**4.31**	0.01	**4.53**	0.02	**5.15**	0.01	3.93	5.18
HCB	**4.94**	0.01	**5.17**	0.01	**5.63**	0.01	4.24	5.73
Chloroanilines								
3,5-DCA	**2.87**	0.07	**3.19**	0.03	**3.24**	0.02	2.49	2.90
2,3,4-TCA	**3.21**	0.01	**3.45**	0.02	**4.04**	0.05	3.03	3.68
2,3,5,6-TeCA	**3.92**	0.02	**4.12**	0.02	**4.66**	0.02	3.94	4.69
PeCA	**4.45**	0.01	**4.63**	0.02	**5.52**	0.06	4.62	5.08

[a] Sablic et al, 1996

The difference in $logK_{oc}$ values between the soils will be due to the fact that the organic matter in the two soils is derived from totally different sources (Kile et al., 1999). LUFA2.2 is a natural soil with its organic fraction being composed of diverse plant and animal remains, as well as embedded fungal and microbial biomass. The acid sphagnum peat used in the OECD artificial soil originates from a freshwater system. Because of this difference, application of generic, literature-derived $logK_{oc}$ values to different soils is not expected to result in similar and reliable estimations of aqueous EC_{50}s (Chiou and Kile, 1994; Rutherford et al., 1992).

For the non-polar chlorobenzenes, the $logK_{lipw}$ values showed a good 1:1 relationship with $logK_{ow}$, suggesting *n*-octanol to be a good model solvent for mimicking interactions of inert compounds with biological membranes. These results confirm findings by other authors (Droge et al., 2006; Sverdrup et al., 2001) showing that $logK_{ow}$ can be used as a descriptor for non-polar compounds in toxicity models. The chloroanilines on the other hand (with the exception of 2,3,5,6-TeCA) had a significantly stronger affinity for the phospholipids than for octanol. Thus, $logK_{ow}$ does not seem to accurately reflect the interactions of narcosis type II compounds with biological membranes. Therefore, a differentiation into narcosis type I and II acting compounds most probably is based on an artifact caused by the application of inappropriate partition coefficients (van Wezel and Opperhuizen, 1995). The generalized use of $logK_{ow}$ as such may enhance the risk of misinterpretation of toxicity data and may over- or underestimate the potential risk towards organisms in the environment. $LogK_{ow}$ also is commonly used as a parameter to model bioaccumulation, which is considered justified by the good correlation with body concentrations of inert compounds. Still, the use of *n*-octanol appears to be based mainly on scientific tradition rather than on an actual interaction mechanism. Obviously, QSARs that are developed on the basis of biological endpoints preferably need to apply partition coefficients that optimally mimic the assumed target side. For general assessment of narcosis-inducing compounds, artificial membranes (liposomes) therefore are more suitable surrogates than a solvent. The determined $logK_{lipw}$ is an optimal parameter that eliminates the difference in the toxicity – partition coefficient relationship between polar chloroanilines and non-polar chlorobenzenes. This does not explain where in the membrane matrix, polar head groups or alkyl chains, the compounds do exert their effects. In terms of risk assessment or ecotoxicological modeling this however ultimately makes no difference. Physiological responses can differ between compounds, even within isomer groups or congeners, but their median toxic effects may still be predicted by a QSAR (Janssens et al., 2011).

Bioavailable concentrations

The measured freely dissolved concentrations in the soil interstitial water corresponding to the approximate EC_{50} values in soil obtained in earlier toxicity tests with *F. candida* in LUFA2.2 and OECD artificial soil are given in Table 3. Though based on nominal concentrations and close to the original EC_{50} values presented in Table 1, bioavailable concentrations differed substantially between the two test soils, with a maximum difference of a factor of 3.2 (Table 3).

Table 3. Average concentrations of chlorobenzenes and chloroanilines (in µg/L; with corresponding standard deviations; n=12) as measured in the interstitial water of natural standard LUFA2.2 soil and OECD artificial soil with SPME. Soils were spiked with concentrations corresponding to the EC_{50}s for the effect on the reproduction of *Folsomia candida*.

	LUFA		**OECD**	
Compound	**Average**	stdev	**Average**	stdev
Chlorobenzenes				
1,2.3-TrCB	**1792**	72	**700**	17
1,2,4-TrCB	**2024**	88	**900**	20
1,3,5-TrCB	**1013**	35	**396**	18
1,2.3.4-TeCB	**367**	12	**140**	5
1,2,3,5-TeCB	**569**	29	**186**	5
1,2,4,5-TeCB	**545**	25	**194**	7
PeCB	**146**	6	**45**	2
Chloroanilines				
3,5-DCA	**339**	13	**170**	12
2,3,4-TCA	**755**	24	**304**	7
2,3,5,6-TeCA	**237**	6	**90**	4
PeCA	**137**	4	**51**	1

As argued above, when related to the soil interstitial water, effect concentrations should be essentially the same, because the physiological reaction of the organism to a pollutant does not depend on the soil itself, but on the bioavailable concentration in the soil interstitial water. The pore-water hypothesis states that toxicity in terms of freely dissolved aqueous

concentrations is the same for each soil (McCarty and Mackay, 1993; Northcott and Jones, 2001). The application here of a compound mixture instead of individual compounds cannot explain the differences, as previous studies for chlorobenzenes and chloroanilines found similar freely dissolved concentrations at their respective soil-based EC_{50} (Giesen et al 2012, Giesen et al. submitted).

An alternative explanation derives from the composition of the tested soils. Standardized toxicity tests with *F. candida*, as used here, typically are performed at a soil moisture content corresponding to approximately 50% of the water holding capacity. This means that although the volume of available water is similar, the total volume of water in both soils is different. In QSARs, bioavailable concentrations are given in mmol/l interstitial water, however, without correcting for the total amount of water in the soil. OECD artificial soil has 2.54 times more water per unit of dry soil than LUFA2.2 soil. In this study, the difference between the measured interstitial water concentrations for LUFA2.2 and OECD soil also amounts an average factor of approximately 2.5. Such effects have not been taken into account in previous studies. The three-phase porewater hypothesis or equilibrium partitioning model was simply adopted from sediment toxicity studies, in which there is always an excess of water and differences in water volume do not really matter. Soil ecological and ecotoxicological studies on the other hand have to deal with varying volumes of water, associated with differences in soil type. With the main focus on the partition coefficients in the past, the total water volume as the imminent soil compartment containing the pollutant was neglected in the calculation of available chemical concentrations.

Unified QSAR

QSAR models for LUFA2.2 and OECD soil, based on estimated bioavailable chlorobenzene and chloroaniline concentrations using the newly determined $\log K_{oc}$ values are plotted against $\log K_{ow}$ values in Figure 1. The resulting four regression models (i.e, two compound groups in two soils) all show a similar negative relationship between toxicity and hydrophobicity.

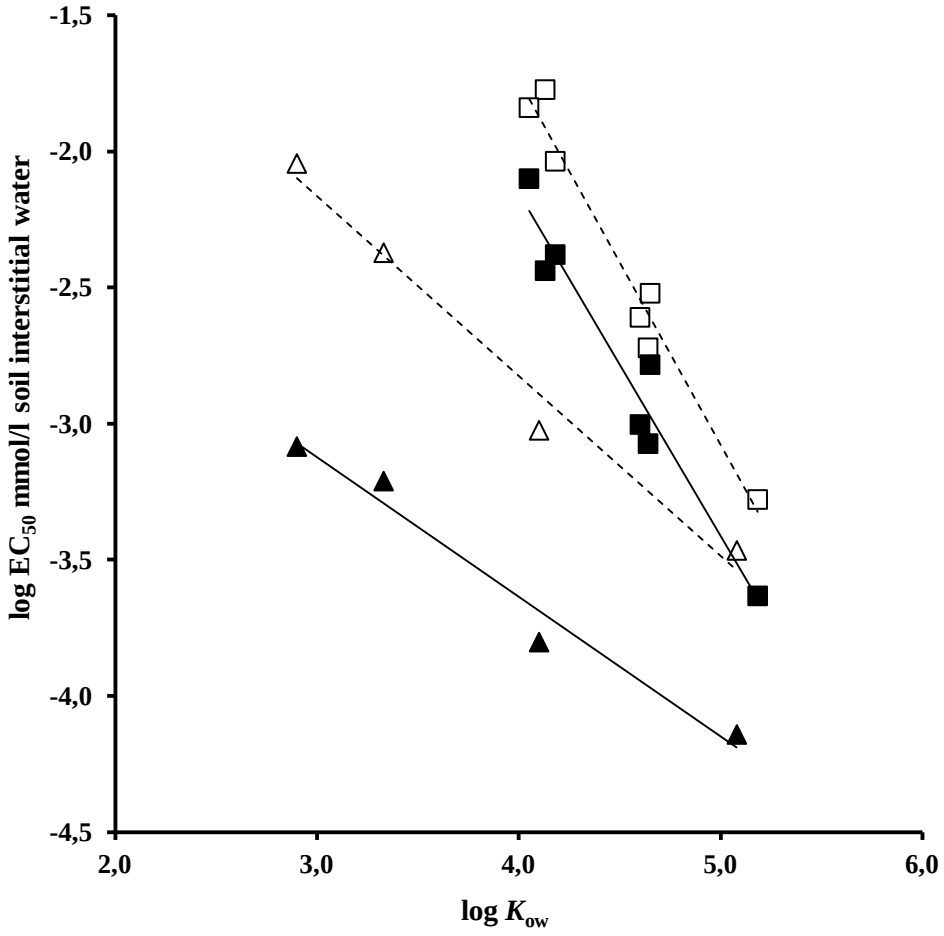

Figure 1. QSAR regression models of i) chlorobenzenes in LUFA2.2 natural soil (white squares); ii) chlorobenzenes in OECD artificial soil (black squares); iii) chloroanilines in LUFA2.2 soil (white triangles), and iv) chloroanilines in OECD soil (black triangles), based on the relationships between median effective concentration (EC_{50}) values, in mmol per liter of interstitial water, for the effect on reproduction of *Folsomia candida*. The QSAR was optimized with experimentally determined $\log K_{oc}$ values.

However, although corrected for soil-specific $logK_{oc}$ values they clearly show differences between non-polar and polar compounds, as well as between the two soils. As a next step, we applied the soil-specific $logK_{oc}$ values as well as the compound-specific $logK_{lipw}$ values in a model based on EC_{50} values calculated from SPME-measured freely dissolved concentrations, which remarkably lead to a single QSAR model:

$EC_{50} = 0.885 * (logK_{lipw}) + 1.40$ $r^2 = 0.861$ $p<0.001$

with EC_{50} expressed on the basis of molar concentrations (mmol l^{-1}) corrected for the amount of soil interstitial water. The EC_{50}s showed a significant negative relationship with $logK_{lipw}$ (Figure 2).

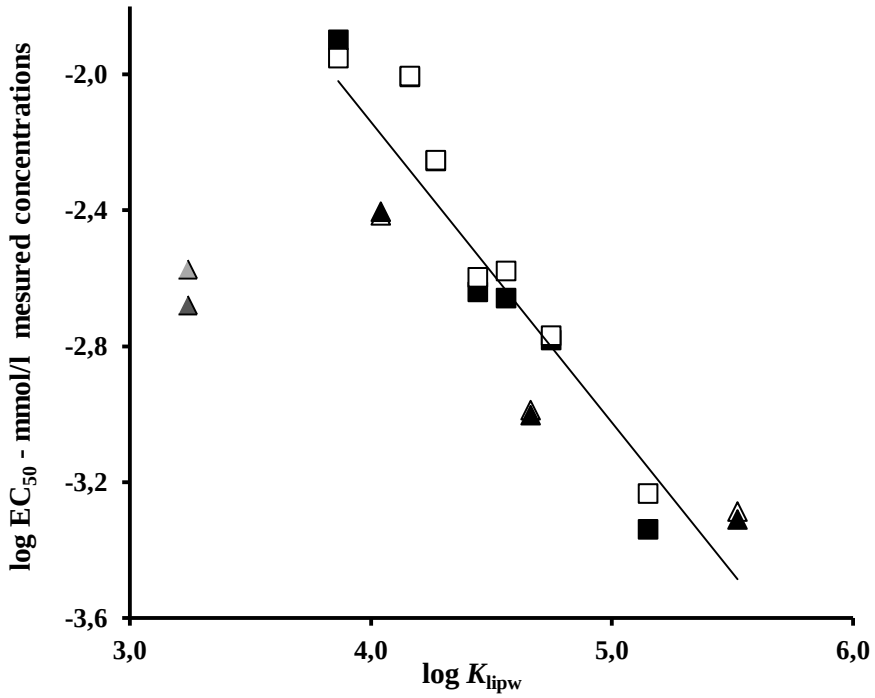

Figure 2. Unified QSAR based on SPME-measured concentrations in interstitial water, corresponding to the EC_{50} of chlorobenzenes in LUFA2.2 soil (white squares), chlorobenzenes in OECD soil (black squares), chloroanilines in LUFA2.2 soil (white triangles), and chloroanilines in QECD soil (black triangles) against experimentally determined liposome-water partition coefficients, including a correction for the total water content of LUFA2.2 and OECD soil. Ommited from both QSARs is 3,5-DiCA in LUFA2.2 and OECD soil (grey triangles).

A distinction between narcosis type I and II compounds as observed in the QSARs based on $\log K_{ow}$ in Figure 1 and in previous studies (Giesen et al 2012, Giesen et al. submitted) interestingly does no longer exist. The toxicity of all chlorinated anilines and benzenes can be described by a single regression model. When correcting for the differences between measured and spiked concentrations, which were highest for 1,2,4,5-TeCB, PeCB, and PeCA (Table 1), this QSAR was further improved to read:

$EC_{50} = 0.910 * (\log K_{lipw}) + 1.50$ $r^2 = 0.867$ $p<0.001$

Note that because of its deviating behavior, 3,5-DiCA was omitted from the QSAR (grey symbols in Figure 2). For this volatile compound, undoubtedly significant evaporative losses occurred during the EC_{50} determinations. Such losses will not have occurred during K_{oc} determinations and the measurements of freely dissolved concentrations in soil interstitial water as these were performed in closed systems. Consequently, for both soils sorption behavior to organic carbon was in agreement with expectations based on the $\log K_{oc}$-$\log K_{ow}$ relationship of the other congeners. Chemical or enzymatic integration in soil organic matter, as described for organic pollutants like aniline and its lower chlorinated analogues (Thorn et al., 1996; Weber and Huang, 2003), as well as bio-degradation can therefore also be excluded, all the more since a biocide was added during these tests. Losses due to evaporation during the spiking procedure and storage lead to significantly lower concentrations in the interstitial water than predicted. This is also supported by the comparable deviations from the QSAR (being ascribed to loss) in both soils, which would rather be expected to be different if the aforementioned reactions would have occurred.

This study presents the first QSAR in which artificial membrane-water partition coefficients are applied as compound descriptor. For the aquatic environment, QSARs based on liposome-water partition coefficients were already developed and even for a larger compound series. Vaes et al. (1998) developed such a QSARs for 19 compounds with $\log K_{ow}$ values for non-polar compounds between 0.83 (2-butoxyethanol) and 4.78 (2,4,5-trichlorotoluene) and for polar chemicals between 0.9 (aniline) and 4.24 (4-n-pentylphenol). It should be stressed however that the heterogeneity of soils constitutes more obstacles for the unification of QSAR models than

encountered in the aquatic environment, which obviously is far more homogeneous. The integration of liposome-water partitioning of polar and non-polar organic compounds and the correction for the bioavailable concentration in soils as presented here should be considered a starting point for further QSAR optimization for soils. The different sensitivities of species can be investigated under the same directive, with the addition of the total lipid content of the organism (Droge et al., 2006; Hurdzan and Lanno, 2011; Leon Paumen et al., 2009; Sverdrup et al., 2002b). Developing comprehensive QSARs for multiple soils, different test organisms, and diverse compound series would clearly support future environmental risk assessments for soils.

Concluding the findings of this study, it is clear that separate QSARs for polar and non-polar narcotic chemicals should not be developed, as the distinction in toxicity between the compound groups most probably is not based on a factual biochemical mechanism. Furthermore, toxicity models that are based on biological endpoints and that are developed for environmental risk assessment call for the optimization of chemical descriptors that are bio-mimetic and the specific analysis of the major routes of exposure. Combining measurements of available concentrations with passive samplers and the determination of compound interactions with the target site domains (e.g., membranes) may account for both factors. Their application should therefore be seriously considered for future evaluations, and so should be the influence of water content of soils as a modifying factor.