Experimental Evaluation and Modeling of Sorption Behavior of Neutral Organic Chemicals in Storage Lipids

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Abstract

Lipids can be seen as an important, if not even the dominating part for bioaccumulation of neutral organic chemicals in organisms. This circumstance was an incentive for the present, comprehensive study focusing on the partitioning behavior of chemicals in lipids in different matrices.

In the first stage, gas chromatographic headspace experiments with cow milk (raw and homogenized) as well as human milk have been conducted with particular emphasis paid to the influence of fatty acid composition and the fat globule membrane structure to the partitioning of milk fat/water. Therefore, 119 substances have been analyzed. The results revealed no significant differences between all three storage lipids and thus indicate that they do not differ with respect to their sorption behavior. For both, the fatty acid composition of cow and human milk as well as the type of processing which has direct influence on the fat globule membrane, no substantial deviation has been found. Results of numerous measurements of partitioning coefficients of certain lipids having different fatty acid composition (fish oil, linseed oil, soybean oil and goose fat) could not reveal any dissimilarity of the partitioning behavior. In the present study, 319 storage lipid/water coefficients have been determined and combined with olive oil data from literature, whereas arithmetic averaging was done if more than one coefficient per chemical was available. Based on these 247 substances, a polyparameter linear free energy relationships (pp-LFERs) has been calibrated as a model for the lipid/water partitioning at 37 °C showing a root mean square error of 0.2 log units.

Besides gaining access to the partitioning behavior of organic chemicals in storage lipids of humans and mammals at 37 °C, pp-LFER could be further used to evaluate bioaccumulation in fishes and aquatic organism. In this case, it is necessary to predict partitioning at lower temperatures which has been done in case of fish oil at 7 °C. The corresponding enthalpies have been used to calibrate another pp-LFER valid for temperature depending storage lipid/water partitioning. Now, this model allows estimation of partitioning coefficients at variable temperatures present for specific environmental conditions.

The quality of results for partitioning coefficients of complex and multifunctional substances based on a pp-LFER model is directly linked to the quality of the substance descriptors. Their availability in case of more complex substances can be seen as the limiting factor for the usage of the pp-LFER model. Therefore, mechanistically based alternative

predictive methods that only require molecular structure as input information are of utmost importance. In the present study, four models, notably ABSOLV, COSMOtherm, KOWWIN and SPARC have been evaluated in a three step approach with respect to their performance of predicting storage lipid/water partitioning. Here, the superior performance of COSMOtherm has been shown. In particular, the third step of evaluation -the performance in case of substances with more than one functional group-revealed significant differences between the four models. Twenty-five substances including pesticides, hormones and mycotoxins have been predicted much worser by KOWWIN (rmse 1.62), SPARC (1.25) and ABSOLV (1.29) compared to COSMOtherm (0.71).

The results obtained within this study clearly emphasize the use of the developed, temperature corrected pp-LFER model for accurate prediction of storage lipid/water coefficients. The usage of octanol as a surrogate for storage lipid is insufficient. Even though it has been found that the performance of all models tested does not differ in case of simple chemicals, significant differences became apparent when applied to complex chemicals. Complex chemicals are typically those, where empirical data are not available so that predictions become necessary.

Zusammenfassung

Fette sind bei der Bioakkumulation neutral organischer Chemikalien ein wichtiger, wenn nicht sogar der dominierende Part eines Organismus. Diese Tatsache war Anreiz zur Durchführung dieser umfangreichen Studie bezüglich des Verteilungsverhaltens von Chemikalien in Fetten in unterschiedlichen Matrices.

Zunächst wurden gaschromatografische Headspace-Messungen mit Kuhmilch, als roh und homogenisiertes Produkt, sowie Muttermilch durchgeführt. Untersucht wurde dabei der Einfluss der Fettsäurezusammensetzung und des Fettmicellenaufbaus auf die Verteilung Milchfett-Wasser. Hierfür wurden 119 Substanzen analysiert. Diese Ergebnisse deuteten darauf hin, dass sich Speicherfette in ihrem Sorptionsverhalten nicht wesentlich unterscheiden, da zwischen den drei Milchformen keine signifikanten Unterschiede feststellbar waren. Sowohl die unterschiedlichen Fettsäurezusammensetzungen von Kuhmilch und Muttermilch, als auch die Verarbeitungsform mit ihrem Einfluss auf die Fettmicellenwand, ergaben keine nennenswerten Abweichungen. Zahlreiche Messungen des Verteilungskoeffizienten in unterschiedlichen tierischen und pflanzlichen Fetten (Fischöl, Leinenöl, Sojaöl und Gänsefett), die sich in ihrer Fettsäurezusammensetzung deutlich voneinander unterscheiden, zeigten bei den untersuchten Substanzen keine Unterschiede im Verteilungsverhalten. Im Zuge dieser Arbeit wurden 319 Speicherfett/Wasser Koeffizienten gemessen und mit Olivenöldaten aus der Literatur kombiniert. Arithmetisch gemittelt wurde bei mehr als einem Koeffizienten pro Chemikalie. Aus diesen 247 Substanzdaten wurde eine Poly-Parameter lineare freie Energie Beziehung (pp-LFER) als Modell für die Speicherfett/Wasser Verteilung bei 37 °C kalibriert. Für dieses Modell ergab sich für die Wurzel der mittleren Fehlerquadratsumme (rmse) ein Fehler von 0,20 log Einheiten.

Neben dem Anwendungsbereich der pp-LFER zum Verteilungsverhalten organischer Chemikalien in Speicherfetten beim Menschen und anderen Säugetieren 37 °C, ist es für die Beurteilung der Bioakkumulation in Fischen und anderen Wasserorganismen jedoch notwendig, die Verteilung in Lipiden bei niedrigeren Temperaturen vorherzusagen. Dafür wurden Verteilungen von Fischöl bei 7 °C gemessen. Die berechneten Enthalpien wurden zur Kalibrierung einer weiteren pp-LFER zur Temperaturabhängigkeit von Speicherfett/Wasser Verteilung genutzt. Dieses Modell ermöglicht es, den Verteilungskoeffizienten bei gewünschten Temperaturen, die unter typischen Umgebungsbedingungen auftreten, abzuschätzen.

Die Güte der Ergebnisse für die Verteilungskoeffizienten von komplexeren und multifunktionalen Substanzen, unter Anwendung des pp-LFER Modell hängen maßgeblich von der Qualität der Substanz Deskriptoren ab, die zur Berechnung verwendet werden. Für komplexere und multifunktionale Substanzen ist die Verfügbarkeit von experimentellen Deskriptoren der limitierende Faktor für die Anwendbarkeit des pp-LFER Modells. Für diese Fragestellungen werden Vorhersagemethoden benötigt, denen mechanistisch basierte Ansätze zugrunde liegen. In dieser Arbeit wurden vier Modelle (ABSOLV, COSMOtherm, KOWWIN und SPARC) auf ihre Qualität der Vorhersage der Speicherfett/Wasser Verteilung in drei Schritten beurteilt. Dabei zeigte sich, dass COSMOtherm über alle drei Fragestellungen hinweg die beste Leistungsfähigkeit hatte. Besonders der dritte Evaluierungsschritt, Substanzen mit mehreren funktionellen Gruppen, zeigte ein starkes Gefälle im Leistungsvermögen der vier Modelle. Die 25 gemessenen Substanzen darunter unter anderem Pestizide, Hormone und Mykotoxine, wurden von KOWWIN (rmse 1,62), SPARC (1,25) und ABSOLV (1,29) deutlich schlechter vorhergesagt als von COSMOtherm (0,71).

Aus den Ergebnissen dieser Arbeit geht deutlich hervor, dass für eine möglichst genaue Vorhersage des Speicherfett/Wasser Koeffizienten das erarbeitete pp-LFER Modell mit möglicher Temperaturkorrektur verwendet werden sollte. Eine Verwendung von Oktanol als Surrogat für Speicherfett erweist sich als unzureichend. Außerdem konnte gezeigt werden, dass die Leistungsfähigkeit der getesteten Modelle sich bei einfachen Chemikalien nicht stark unterscheiden, aber das wesentliche Unterschiede entstanden, als die Modelle auf komplexe Chemikalien angewandt wurden. Komplexe Chemikalien sind oft diejenigen, für die empirische Daten nicht verfügbar sind und damit Vorhersagen benötigt werden.

Preface

The present work was performed between June 2008 to August 2011 at the Helmholtz Centre for Environmental Research, Leipzig at the Department of Analytical Environmental Chemistry. The thesis was written in a cumulative form and is based on the following articles:

A. Geisler, S. Endo and K.-U. Goss. Partitioning of polar and non-polar neutral organic chemicals into human and cow milk. *Environment International*, 37:1253-1258, 2011.
(SI available at: doi: 10.1016/j.envint.2011.05.014. Epub 2011 Jun 17).

A. Geisler, S. Endo and K.-U. Goss. Partitioning of Organic Chemicals to Storage Lipids: Elucidating the Dependence on Fatty Acid Composition and Temperature. *Environmental Science & Technology*, 46: 9519-9524, 2012.
(SI available at: http://pubs.acs.org/doi/suppl/10.1021/es301921w)

A. Geisler, L. Oemisch, S. Endo and K.-U. Goss. Predicting Storage–Lipid Water Partitioning of Organic Solutes from Molecular Structure. *Environmental Science & Technology*, 49: 5538-5545, 2015.
(SI available at: http://pubs.acs.org/doi/suppl/10.1021/es506336m)

Please note, that text passages and tables in the summary are partly taken from the original publication without further indication. The original publications were included. Supporting Information are available at the specified internet address.

1 Experimental evaluation and modeling of sorption behavior of neutral organic chemicals in storage lipids

1.1 Introduction

Lipids are among the most relevant phases for bioaccumulation of neutral organic chemicals. There are two main types of lipids, storage lipids and membrane lipids, which differ in their sorptive properties [17]. Storage lipids refer to triglycerides, whose fatty acids vary in their chain length (typically between C4 and C22) and the degree of unsaturation. They form an unstructured phase similar to organic solvent. In contrast, membrane lipids form structured bilayers that surround, amongst others, biological cells in organisms. The two types of lipids often have high contributions to the overall sorptive capacity of the organism, and the actual contributions depend on the types of chemical of concern and the content of the two lipids in the organism [16]. Partitioning of organic chemicals to membrane lipids and its prediction has been discussed in detail elsewhere [17][11] and the literature cited therein. Partitioning into storage lipids is thus the focus of the present work.

In the literature, there are numerous experimental partition coefficients for selected chemicals and lipids [13][19][35][49] but only a few data allow for a systematic comparison between different types of storage lipids. The available data generally give an indication that differences in partition coefficients into different types of storage lipids may be small. For example, Mayer et al.[27][24] found that polycyclic aromatic hydrocarbons (PAHs) partition similarly to fish oil, olive oil, rapeseed oil, sunflower oil and polychlorinated biphenyls (PCBs) to olive oil, tobis fish oil and seal oil. However, this work did not cover any organic chemicals with functional groups. Niimi [32] reported similar solubilities of various, mainly hydrophobic organic chemicals in triolein and cod liver oil. In fact, a systematic investigation is still lacking. Recently, van der Heijden and Jonker reported a significant interspecies variability in partitioning of PCBs to homogenates of aquatic worms and sticklebacks when normalized to total lipid content [47]. On the basis of this observation, Jonker [25] noted that field-observed biomagnification through a food

chain could be explained by differing accumulation capacities of lipids in organisms. This notion emphasizes a need for further studies on the variability of accumulation properties of lipids.

Lipid/water partition coefficients are typically measured at 37 °C for the relevance to humans and other mammals, or around 25 °C for experimental convenience. However, for assessment of bioaccumulation in fish and other aquatic organisms it is necessary to predict partitioning to lipids at lower temperatures. Considering the temperature variability in the environment, it is desirable to establish a model for the temperature dependence of lipid partitioning.

The logarithm of a partition coefficient is a free energy related property and can be described with a solvation parameter model named polyparameter linear free energy relationships (pp-LFERs). The partitioning of neutral organic chemicals between two condensed phases can be described by each of the following two equations:

$$\log K_{i1/2} = e_{1/2}E_i + s_{1/2}S_i + a_{1/2}A_i + b_{1/2}B_i + v_{1/2}V_i + c_{1/2} \tag{1.1}$$

$$\log K_{i1/2} = l_{1/2}L_i + s_{1/2}S_i + a_{1/2}A_i + b_{1/2}B_i + v_{1/2}V_i + c_{1/2} \tag{1.2}$$

The dependent variable in eqs 1.1 and 1.2, $\log K_{i1/2}$, is the partition coefficient of substance i between two phases 1 and 2. The solute descriptors in capital letters ($E_i, L_i, S_i, A_i, B_i, V_i$) describe the extent to which a given solute undergoes molecular interactions in condensed phases. The corresponding phase descriptors lower case letters ($e_{1/2}, l_{1/2}, s_{1/2}, a_{1/2}, b_{1/2}, v_{1/2}$) describe the difference in capacity between the two phases with regard to intermolecular interactions. The five descriptor pairs quantify the intermolecular interactions that govern the partition process: polar interactions ($s_{1/2}S_i$), van der Waals interactions and cavity formation ($v_{1/2}V_i, e_{1/2}E_i, l_{1/2}L_i$) and H-bond interactions ($a_{1/2}A_i, b_{1/2}B_i$). These phase descriptors are calibrated with experimental $\log K_{i1/2}$ by linear multiple regression analysis. Equation 1.1 was established by Abraham and co-workers [5], while a modified version of this equation (eq 1.2) was proposed by Goss [21]. These two equations generally give the same quality of fit.

Calibrated pp-LFER system parameters are available for a multitude of environmental systems. A typical error margin for pp-LFER models that are applied to homogenous phases such as solvents and technical polymers are 0.2 to 0.3 [37][4][7]. In comparison, pp-LFER models for complex phases such as soil organic matter and serum albumin typically show higher rmse values (> 0.3 log units) [12][15].

Solute descriptors have been reported in the literature for at least 2000 compounds [18]. For chemicals whose descriptors are unavailable, however, the descriptors have to be determined by time-consuming experiments [8][36][3][45]. For a fast screening of the bioaccumulation potential for tens of thousands of organic compounds, we thus need other predictive methods that only require molecular structure as input information.

Therefore, we evaluated four such models, KOWWIN, ABSOLV, COSMOtherm, and SPARC. The three latter methods allow a direct prediction of the partition coefficient from water to triglycerides. In contrast, the first approach, KOWWIN only predicts the partition coefficient from water to octanol (K_{ow}). Nevertheless, we included KOWWIN in the evaluation because octanol is often used as surrogate for lipids and KOWWIN is among the most widely used tools for the prediction of bioaccumulation [41].

1.2 Objective of this study

The main goal of the present work was to test the variability of storage lipids from different animals and plants with regard to their capacity to accumulate organic chemicals. To this end, a diverse set of polar and non-polar chemicals were tested for their partitioning into various storage lipids that cover a wide range of fatty acid compositions. In a next step, these new partitioning data were combined with existing data in the literature to yield a comprehensive data set at 37 °C, which was used to refine a model for predicting partitioning to storage lipids in general.

In addition, to extend the applicability of the model equation to other temperatures we determined partition coefficients into fish oil at 7 °C. Enthalpies were calculated from the partition coefficients at 7 °C and 37 °C and were then used to derive a model that predicts the temperature dependence of partitioning into storage lipids.

Finally, we evaluated the performance for four predictive models, ABSOLV, COSMOtherm, KOWWIN and SPARC to calculate storage lipid-water partition coefficients. We tested their robustness in three steps. To this end, we used a data set with 305 chemicals, which are mostly monofunctional compounds and we measured and evaluated additional compounds with higher complexity in the molecular structure such as hormones, mycotoxins and pesticides. Due to their multifunctionality, these compounds pose a special challenge for predictive models.

1.3 Materials

The chemicals used as calibration substances and analytes were purchased from Sigma-Aldrich Chemie GmbH (Steinheim, Germany), Alfa-Aesar GmbH & Co. KG (Karlsruhe, Germany) or Dr. Ehrenstorfer GmbH (Augsburg, Germany) and their purity was at least 97%. Solvents (purity at least 99%) were purchased from Merck KGaA (Darmstadt, Germany). All solutes were first dissolved in methanol (LiChrosolv quality). Pure water produced by a Milli-Q Gradient A10 system (Millipore GmbH, Schwalbach, Germany) was used. The processed milk, linseed oil (Kunella) and the goose fat (LARU) were standard products from the local grocery store. The raw cow milk (raw milk) was freshly obtained directly from a farmer for each experimental set. The human milk was not taken within the first 2 weeks after birth. The fish oil (cod liver oil, Caelo) was obtained

from the pharmacy. Polyacrylate-(PA) and polydimethylsiloxane-(PDMS) coated glass fibers produced by Polymicro Technologies (Phoenix, AZ, USA) were used in the fiber experiments. The PDMS tubes produced by A-M Systems, (Sequim, WA, USA) were obtained from Biomedical Instruments (Zöllnitz, Germany).

1.4 Experimental work

Equilibrium partition coefficients were determined at 37 °C ± 1 °C with batch sorption experiments either using headspace measurements or using a solid phase micro extraction (SPME) technique. In both methods, two sets of vials were prepared: one filled with milk or oil and the other with water. For the headspace measurements, 20 ml headspace vials, whose exact volume had been determined gravimetrically, were filled with water, milk or oil. Both vials were spiked and immediately closed with a crimp cap and a polytetrafluoroethylene-(PTFE) or aluminium-lined silicon septum to prevent loss of solute. After equilibration for 4 h in a temperature controlled horizontal shaker, the headspace was analyzed with GC. All experiments were done in replicates, only results with a repeatability better than 10% were used for further calculations. The partition coefficient was determined from the comparison of peak areas between milk vial or oil vial and water vial.

Experiments at 7 °C were carried out using fish oil with the same headspace method as described above but equilibration and analysis took place at 7 °C and the equilibration time was 18 h. Fish oil was liquid at 7 °C.

The SPME measurements were performed analogous to the headspace measurements. Again, vials with milk and water were prepared with a defined portion of the fibres and spiked. After equilibration, the fibres were collected from the vials and carefully wiped with clean tissue. The fibres were extracted and analyzed with GC.

For the silicon membrane equilibrator method (SMEM) [33], a PDMS tube was placed within a vial that contained soybean oil spiked with the substance under investigation. Water was filled into the tube whereby an equilibrium partitioning from the oil phase to the water phase was established via the PDMS. If the target substance can significantly deprotonate around neutral pH, water was acidified before filled into the PDMS tube. After equilibration, the water phase was sampled and analyzed for the concentration of the substance.

1.5 Experimental determination of pp-LFER system parameters

1.5.1 Similarity of different storage lipids

It has been shown, that the experimental $K_{\text{milk fat/water}}$ values for almost all compounds differ only by < 0.3 log units between human and cow milk. Thus, one can conclude that the differences in fatty acid composition of human and cow milk have no significant influence on the respective sorption properties. Also, the processing status appears to have little influence on $K_{\text{milk fat/water}}$ as can be seen from the agreement between raw and processed cow milk (Fig. 1.1).

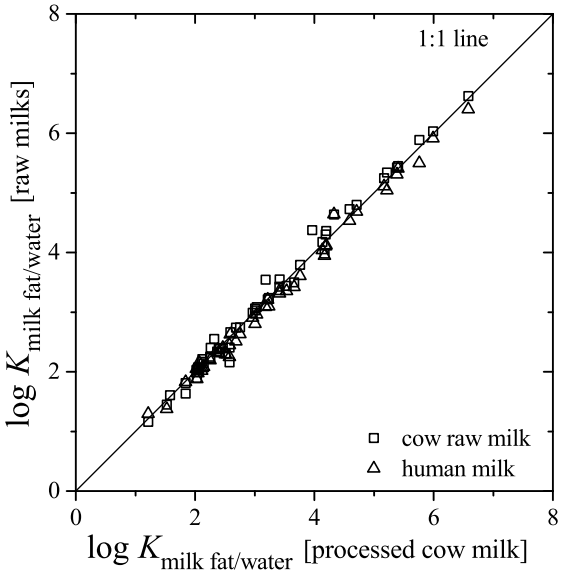

Fig. 1.1: Partition coefficients for human milk ($n = 73$) and cow raw milk ($n = 54$) compared to processed cow milk (experimental data, 37 °C)

For 89 organic compounds $K_{\text{storage lipid/water}}$ equilibrium partition data for more than one type of storage lipid have been obtained. In addition to the three types of storage lipids (fish oil, linseed oil and goose fat), data for milk fat and olive oil from the literature [1] were considered. The five storage lipids considered here represent those from animal and plant origins and differ considerably in their fatty acid composition (Tab. 1.1). Table 1.2 shows the experimental results exemplarily for a selection of diverse chemicals. It can be seen that the $K_{\text{storage lipid/water}}$ values for all chemicals, including non-polar, H-bond donor, and H-bond acceptor chemicals, vary typically within $\pm$ 0.1 log units across the different lipids. Moreover, no systematic trend could be observed. The same is true for the complete data set, which is reported in Tab. 1.6 (for comfortable reading this table is provided separately in section 1.9). Thus, all available data so far indicate that no substantial differences exist between different storage lipids in terms of their partitioning properties. Because the storage lipids considered here include a wide variability of fatty acid compositions (Tab. 1.1), this conclusion is likely valid generally for storage lipids.

Tab. 1.1: Typical fatty acid compositions of investigated animal and plant oils and fats as mass percent of total lipids

fatty acid	4 : 0	6 : 0	8 : 0	10 : 0	12 : 0	14 : 0	16 : 0	16 : 1	18 : 0	
olive oil [10]	-	-	-	-	-	-	11.5	1.5	2.5	
linseed oil [10]	-	-	-	-	-	-	6.5	-	3.5	
milk fat (cow) [46]	3.3	1.6	1.3	3.0	3.6	9.5	26.3	2.3	14.6	
milk fat (human) [46]	-	traces	traces	1.3	3.1	5.1	20.2	5.7	5.9	
fish oil [22]	-	-	-	-	-	3.7	9.7	8.5	2.1	
goose fat [10]	-	-	-	-	-	0.5	21.0	2.5	6.5	
soybean oil [10]	-	-	-	-	-	-	10.0	-	5.0	
fatty acid	18 : 1	18 : 2	18 : 3	20 : 0	20 : 1	20 : 4	20 : 5	22 : 1	22 : 5	22 : 6
olive oil [10]	75.5	7.5	1.0	0.5	-	-	-	-	-	-
linseed oil [10]	18.0	14.0	58.0	-	-	-	-	-	-	-
milk fat (cow) [46]	29.8	2.4	0.8	-	-	-	-	-	-	-
milk fat (human) [46]	46.4	13.0	1.4	-	-	-	-	-	-	
fish oil [22]	22.4	2.0	1.0	-	14.4	0.9	9.5	7.5	1.3	12.7
goose fat [10]	58.0	9.5	2.0	-	-	-	-	-	-	-
soybean oil [10]	21.0	53.0	8.0	0.5	0.5	-	-	-	-	-

Tab. 1.2: Selected chemicals from various compound classes with their experimental storage lipid/water partition coefficients and the corresponding average values

	exp. log $K_{\text{storage lipid/water}}$					
Substance	olive oil ref [1]	milk fat	fish oil	linseed oil	goose fat	average ± SD
1-Chloropentane	3.51	3.41	3.47	3.54	3.48	3.48 ± 0.05
1-Nitropropane	0.90	0.99	0.97	1.06	0.94	0.97 ± 0.06
Pentafluorobenzene	2.46	2.30	2.19	2.27	2.32	2.31 ± 0.10
Propyl acetate	1.12	0.97	1.03	1.06	0.93	1.02 ± 0.08
1-Nonanol	-	3.00[1]	-	3.01	-	3.01
Propylbenzene	3.77	3.76	3.6	3.54	3.58	3.65 ± 0.11
Toluene	2.68	2.75	2.65	2.63	2.63	2.67 ± 0.05
2-Hexanone	1.04	1.21	1.25	1.31	1.16	1.19 ± 0.10
Cyclohexane	4.01	4.01	4.08	4.06	4.08	4.05 ± 0.04
Carbon tetrachloride	3.14	3.22	3.20	3.19	3.17	3.18 ± 0.03
2-Nitrotoluene	-	2.51	2.43	2.45	2.21	2.40 ± 0.13
Halothane	2.26	2.40	2.25	2.26	2.23	2.28 ± 0.07
4-Ethyl-3-hexanol	-	2.07[1]	1.91	1.93	1.93	1.92 ± 0.07
Decane	6.52	6.58	6.28	6.25	6.33	6.39 ± 0.15
Ethyl tert-butyl ether	1.31	1.43	1.36	1.35	1.39	1.37 ± 0.04

[1] Milk fat data were not included in the average because of possible impact of milk proteins on the values

1.5.2 Calibration of an universal pp-LFER for storage lipids

Abraham et al. [1][42] have presented pp-LFERs for partitioning to olive oil. On the basis of the similarity of different lipids that was demonstrated above, this equation might seem suitable as a predictive model for storage lipids in general. However, H-bond donor compounds as well as large non-polar compounds were underrepresented in their calibration data set. This suggests that the model equations in refs [1] and [42] may have a low prediction power for these types of compounds. We therefore measured a number of alcohols and PAHs in the experiments presented here. In addition, the data for five phenolic compounds measured with a silicone tube equilibrator method (similar to a method in ref [27]) were included [33]. For a comprehensive calibration data set, 198 data for partitioning to olive oil [1] and 95 for milk fat were also used. A list of 247 compounds used for the calibration of the pp-LFER equations is presented in Tab. 1.6 (section 1.8) together with the respective descriptors.

We used arithmetic mean values of the $\log K_{\text{storage lipid/water}}$ at 37 °C if values for more than one lipid were available for a specific compound (see section 1.8). The experimental data of $\log K_{\text{storage lipid/water}}$ range from −2.66 to 9.88. The fitting of the two forms of the pp-LFER (eqs 1.1 and 1.2) yields, respectively:

$$\begin{aligned}\log K_{\text{storage lipid/water}} =&(0.70 \pm\ 0.06)E_i - (1.08 \pm\ 0.08)S_i - (1.72 \pm\ 0.13)A_i \\ &- (4.14 \pm\ 0.09)B_i + (4.11 \pm\ 0.06)V_i - (0.07 \pm\ 0.07)\end{aligned} \tag{1.3}$$

$$SD : 0.29, n = 247, R^2 = 0.977$$

$$\begin{aligned}\log K_{\text{storage lipid/water}} =&(0.58 \pm\ 0.03)L_i - (1.62 \pm\ 0.07)S_i - (1.93 \pm\ 0.10)A_i \\ &- (4.15 \pm\ 0.07)B_i + (1.99 \pm\ 0.11)V_i - (0.55 \pm\ 0.06)\end{aligned} \tag{1.4}$$

$$SD : 0.20, n = 247, R^2 = 0.988$$

It appears that both forms of the equation fit the experimental values well, with slightly better statistics for eq 1.4. A comparison between measured and calculated values is given in Fig. 1.2. The figure displays all measured 517 values for 247 chemicals in all storage lipids and thus demonstrates not only the excellent model fit but also the small variation between different storage lipids. The data cover 12 orders of magnitude. The predicted values have a root mean squared error (rmse) of only 0.20 log units. This is a typical error margin for pp-LFER models that are applied to homogenous phases such as solvents and technical polymers [37][4][7]. In comparison, pp-LFER models for complex phases such as soil organic matter and serum albumin typically show higher rmse values (> 0.3 log units) [12][15]. Thus, storage lipids are certainly among the phases that are most accurately predictable in the environment.

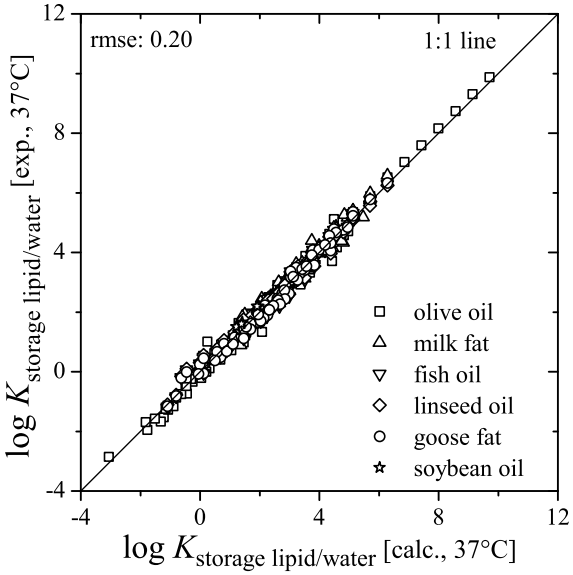

Fig. 1.2: Experimental storage lipid/water partition coefficients for all compounds and all lipids versus storage lipid/water partition coefficient calculated with eq 1.4; 517 data points

1.5.3 Octanol as a surrogate for storage lipid

Traditionally, octanol has often been used in sorption studies as a surrogate for storage lipids [14][9][39]. However, the intermolecular interactions that govern any partition behaviour must be expected to be different between octanol which is an alcohol and storage lipid that consists of esters. Alcohols like octanol possess an H-bond donor and -acceptor function whereas storage lipids that are comprised of triacyl esters only exhibit an H-bond acceptor function. It is therefore not surprising that a plot of all experimental storage lipid data versus experimental octanol data (Fig. 1.3) shows more scatter (rmse of 0.48) than the storage lipid pp-LFER model (rmse of 0.20) (Fig. 1.2). A closer look at the deviations reveals a systematic trend: especially compounds with a H-bond donor property such as alcohols or phenols tend to partition more into octanol than into storage lipid. In addition, differences in fitting coefficients of the pp-LFER equations that describe the octanol-water and storage lipid-water partition systems also suggest that octanol may not always be a good surrogate for storage lipids (Tab. 1.3). The pp-LFERs indicate that H-bond donor solutes will sorb stronger to octanol than to storage lipids.

Tab. 1.3: pp-LFER equation coefficients for storage lipid and octanol

	l	s	a	b	v	c
storage lipid/water 37 °C	0.58	-1.62	-1.93	-4.15	1.99	0.55
octanol/water 25 °C [21]	0.43	-1.41	-0.18	-3.45	2.41	0.34

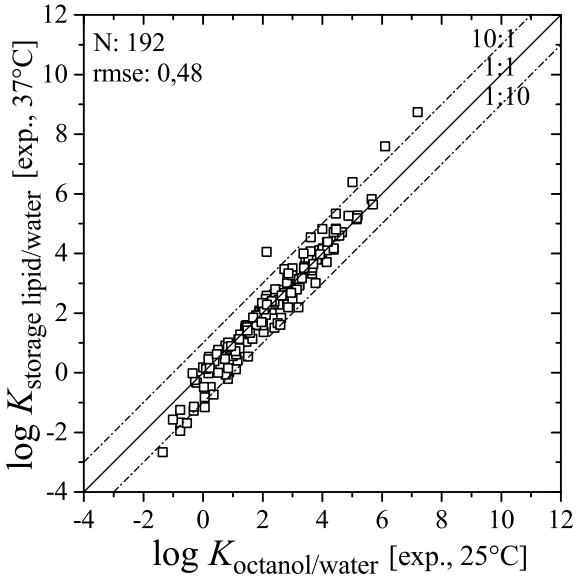

Fig. 1.3: Experimental storage lipid/water partition coefficients versus experimental octanol/water partition coefficient ($n = 192$)

1.6 Temperature dependence

Experimental fish oil/water partition coefficients at 7 °C ($K_{i\,\text{fish oil/water}[7\,°\text{C}]}$) were used in combination with the corresponding data at 37 °C ($K_{i\,\text{fish oil/water}[37\,°\text{C}]}$) to calculate the enthalpies of partitioning (ΔH_i) based on the van´t Hoff equation.

$$\Delta H_i = \frac{\log K_{i\,\text{fish oil/water}[7\,°\text{C}]} - \log K_{i\,\text{fish oil/water}[37\,°\text{C}]}}{\left[\frac{1}{280.13\,\text{K}} - \frac{1}{310.13\,\text{K}}\right]} \cdot R \cdot 2.303 \tag{1.5}$$

The resulting enthalpies are reported in Tab. 1.7 (section 1.8). It has been shown before that enthalpies of partitioning can often be fitted with the same descriptors that are used in the pp-LFER equations [31][30][29]. The respective fitting based on the descriptor combination L_i, S_i, A_i, B_i and V_i is given in eq 1.6.

$$\begin{aligned}\Delta H_i =&(10.51 \pm\ 3.74)L_i - (49.29 \pm\ 6.26)S_i - (16.36 \pm\ 8.71)A_i \\ &- (70.39 \pm\ 6.27)B_i + (66.19 \pm\ 12.51)V_i - (38.95 \pm\ 4.73)\end{aligned} \tag{1.6}$$

$$SD : 5.96, n = 46, R^2 = 0.83$$

Figure 1.4 shows the goodness of fit for this equation. It must be noted that the calibration set for (ΔH_i) is far less diverse than that for log $K_{\text{storage lipid/water}}$ (eq 1.4), and the experimental uncertainty for (ΔH_i) is larger than for log $K_{\text{storage lipid/water}}$, because ($\Delta H_i$) is based on two experimental log $K_{\text{storage lipid/water}}$ values at different temperatures. This explains why the scatter is larger in Fig. 1.4 than in Fig. 1.2. Fortunately, the temperature dependence for many compounds is small (ΔH_i close to zero) and, in practice, temperature extrapolations are needed for only small temperature ranges under typical

environmental conditions. Therefore, estimations based on eq 1.6 should be sufficient for most applications.

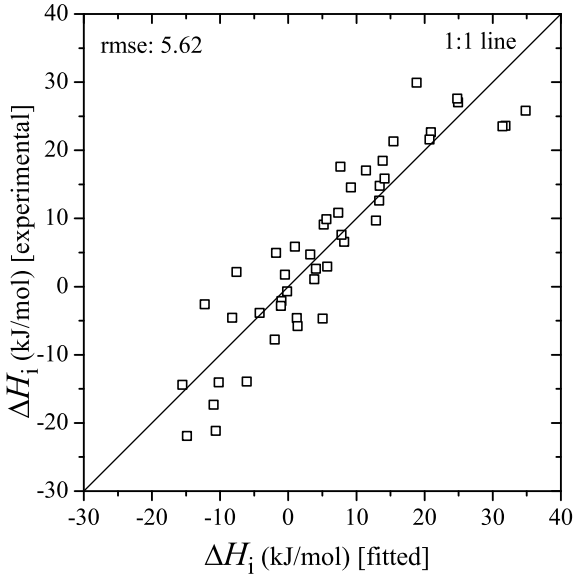

Fig. 1.4: Experimental enthalpy versus fitted enthalpy for fish oil/water partitioning; 46 data points

By using the general equation for predicting storage lipid/water partitioning at 37 °C (eq 1.4) and extrapolating these values to the actual temperature based on the enthalpy predicted with eq 1.6, $K_{\text{storage lipid/water}}$ at a desired temperature can be calculated. From our own measurements at 7 °C in fish oil, there are data for six compounds that were not used for calibration of eq 1.6 (because of lacking values at 37 °C) and that can be used for validation of this predictive approach. In addition, data from the literature [27][24] for the partitioning of PAHs and PCBs at 21 °C in two oils, which had not been among the oils used here (i.e. rapeseed oil and seal oil), were also used to validate the approach. Figure 1.5 compares these validation data with calculated values that result from the combined predictions of eqs 1.4 and 1.6. Calibration data for eq 1.6 are also presented in Fig. 1.5 for comparison. The predicted values agree well with the experimental data, validating the models presented here.

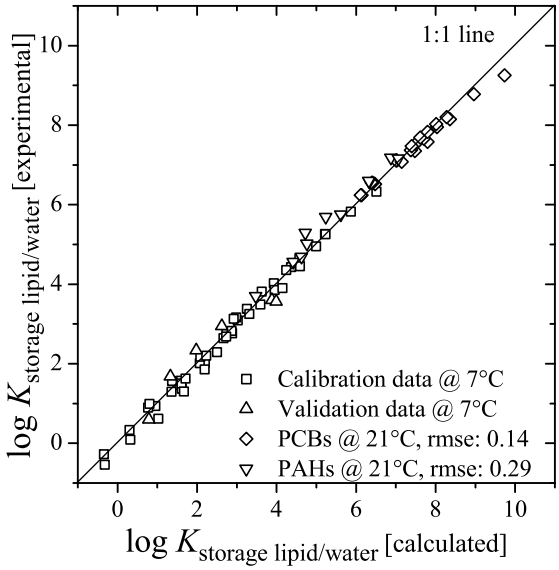

Fig. 1.5: Experimental and calculated log $K_{\text{storage lipid/water}}$. Calibration data for temperature dependence and validation data from this study are presented. Data from PAHs are from [27], data for PCBs from [24].

1.7 Validation of COSMOtherm, ABSOLV, KOWWIN and SPARC

1.7.1 Prediction models

KOWWIN, the standard method for predicting the storage lipid-water partition coefficient, is to predict K_{ow} with an existing quantitative structure activity relationship (QSAR) and assume that there is little difference between octanol and storage lipid (i.e., $K_{\text{storage lipid/water}} = K_{\text{ow}}$) [20][28][40][38]. KOWWIN uses the molecular structure of the partitioning chemical in the form of a SMILES string as input information. The model is based on an atom and fragment contribution method and has been calibrated with K_{ow} data for 2447 training compounds. ABSOLV is a QSAR model that predicts the pp-LFER solute descriptors for chemicals. Chemicals are entered in SMILES notation. ABSOLV is based on a fragment-contribution method that is calibrated with a large number of experimentally determined solute descriptors [34]. ABSOLV seems to include some additional (undisclosed) adjustments for improved predictions [6]. The predicted solute descriptors can be combined with existing pp-LFER equations for predicting equilibrium partition coefficients. In this study, we used the ABSOLV-predicted descriptors together with the calibrated pp-LFER equation for storage lipid-water partitioning at 37 °C (eq 1.4). For a validation of the ability to predict temperature dependence, we used ABSOLV-predicted descriptors in combination with the pp-LFER equation for the enthalpy of the storage lipid-water partitioning process (eq 1.6). COSMOtherm predicts various chemical properties based on the COSMO-RS theory [26]. COSMOtherm requires three-dimensional cosmo files generated by a quantum-chemical dielectric continuum solvation calculation.

A cosmo file encompasses information for interaction properties of the molecule. Using cosmo files, COSMOtherm performs a statistical thermodynamics treatment of surface interactions and can predict equilibrium partition coefficients. The prediction can be performed for any solute in any partition system at desired temperature, provided that the solute and solvents have defined molecular structures. SPARC estimates the molecular interactions (e.g. van der Waals, H-bonds) that are responsible for a partition process based on a molecular fragment approach. Fragment values are from an extensive calibration with existing partition data [23]. It calculates equilibrium partition constants for organic compounds at any temperature and in any partition system whose molecular structure is known and can be provided in SMILES notation. Nonanoic acid triglyceride (NTG; i.e. trinonanoylglycerol) were used as model structures for storage lipids in the COSMOtherm and SPARC calculations.

1.7.2 Experimental data for model evaluation

In a first validation step (*Step 1*), we considered all log $K_{\text{storage lipid/water}}$ data that were used to calibrate the pp-LFER model (eq 1.4) plus some additional data mostly for hydrophobic compounds such as polychlorinated biphenyls (PCBs) [24] and polycyclic aromatic hydrocarbons [27]. All data are for 37 °C and for the neutral species in case chemicals are ionizable, although the molecular structure of the chemicals is relatively simple, typically with no or only one polar functional group. A sub-selection of 51 H-bond donor substances taken from this first validation data set were used for *Step 2* of our evaluation, because a comparison of the pp-LFER equations for octanol and storage lipids reveals substantial differences in the aA-term (see section 1.5). This implies that H-bond donor compounds should partition differently to octanol and storage lipid phases and could exhibit systematic errors when K_{ow} is assumed to equal $K_{\text{storage lipid/water}}$. For *Step 3* of our evaluation, we used experimental data for 31 complex compounds with more than one polar functional group per molecule. The model evaluation with the complex chemical structures possessing more than one functional group is instructive because many of the thousands of chemicals that have to be assessed by regulatory authorities concerning their environmental behavior also possess such complex structures. For prediction methods, such complex structures typically pose a challenge because neighboring functional groups often do not contribute additively to the free energy of partitioning due to intramolecular interactions.

1.7.3 Validation results

Step 1 – Simply Structured Substances. Model evaluation with the 305 literature data reveals good overall agreement between experimental data and predictions from all models (rmse from 0.45 log units to 0.61 log units; see Tab. 1.4 and Fig. 1.6a-d). The data were predicted within an accuracy of 1 log units for most of the compounds. Two

distinct outliers were found with the SPARC v4.5 method: triethylphosphate, the only compound with a phosphate group in the *Step 1* data set, and PCB 209, the largest of the PCBs. Predictions for phosphates appear to be generally inaccurate with SPARC v4.5 and v 4.6 [43][45]. Prediction errors for PCBs by SPARC v4.5 appear to increase with increasing size of PCBs and similar trends also exist for ABSOLV and KOWWIN though to a lesser extent. While it is obvious that accurate measurements of partition coefficients for large PCBs are generally challenging, the data used were measured with a passive sampling method, which is the state-of-the-art approach for hydrophobic chemicals, and the difference of 3 log units between experimental and predicted values is too large to be ascribed only to experimental uncertainty. The relatively large errors for PCBs may rather be related to the bulkiness of PCB molecules which may not accurately be modeled by incremental methods [48]. The evaluation further indicates systematic errors for long alkanes in the KOWWIN prediction. Such systematic deviations as found for SPARC v4.5, ABSOLV, and KOWWIN were not observed for COSMOtherm.

Tab. 1.4: Statistic values for all models and validation steps. Root-mean-square errors (rmse) are given for the logarithmic partition coefficients.

		ABSOLV	COSMOtherm	KOWWIN (K_{ow} at 25 °C)	SPARC (v4.5)
Step 1	number of chemicals	304[1]	304[1]	305	302[1]
	rmse	0.61	0.45	0.6	0.54
Step 2	number of chemicals	51	51	51	51
	rmse	0.91	0.35	0.84	0.42
Step 3	number of chemicals	24	24	24	24
	rmse	1.29	0.71	1.62	1.25

[1] ABSOLV, COSMOtherm, and SPARC v4.5 do not calculate the value for SF_6. SPARC v4.5 does not calculate CS_2 and $CH_3CH_2CClF_2$ either

Step 2 – H-bond donor Substances. As outlined above, one expects a systematically poorer performance of the K_{ow}-based approach to predict $K_{\text{storage lipid/water}}$ for H-bond donor chemicals, and thus an evaluation of the four prediction models with respect to H-bond donor chemicals was of particular interest. Therefore, in the second step, we limited the evaluation to a subset of 51 H-bond donor compounds (all compounds with an experimental H-bond donor descriptor A > 0.3). The results for KOWWIN do indeed show a strong systematic overestimation of $K_{\text{storage lipid/water}}$ (Fig. 7c) and an rmse that is higher than for the complete data set (Tab. 1.4). We note that this systematic error is not attributed to the uncertainty of KOWWIN to predict K_{ow} but to the use of octanol as a surrogate for storage lipids. Thus, the same systematic error should occur no matter which K_{ow} estimation model is used, even in the case of experimental K_{ow}. Interestingly, the results for ABSOLV (Fig. 1.7a) also show a poorer prediction for H-bond donor compounds (rmse = 0.91) as compared to the complete data set (rmse = 0.61). This systematic error cannot be due to an insufficient calibration of the pp-LFER equation used

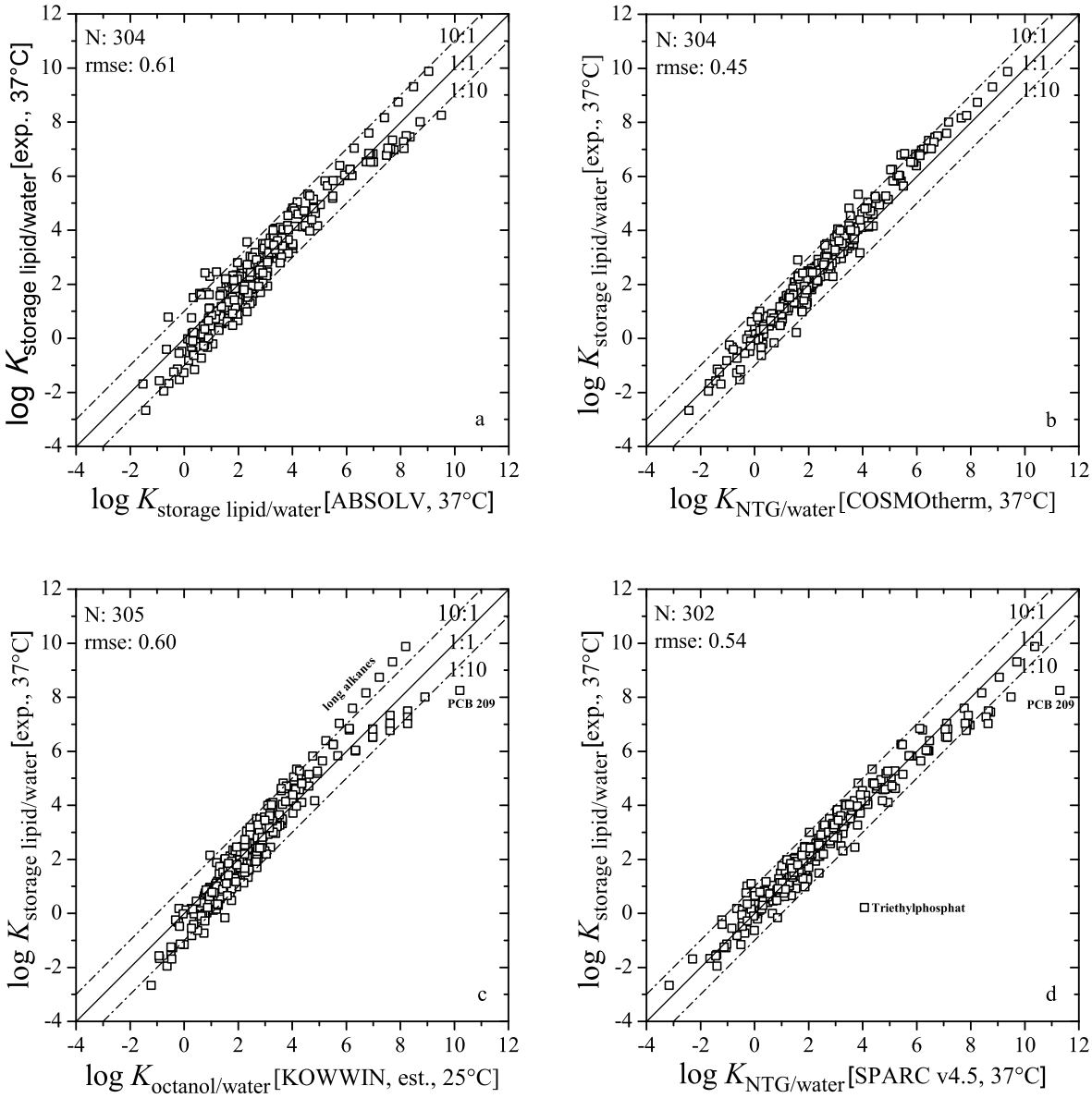

Fig. 1.6: Experimental storage lipid-water partition coefficients for all literature compounds versus predictions by four different models (*Step 1* evaluation)

in combination with the ABSOLV descriptors, because all 51 experimental values had been part of the calibration. While most of the values are overestimated by the ABSOLV approach, the values for all halogenated phenols are underestimated. It is currently unknown why ABSOLV exhibits relatively large errors for H-bond donor compounds. The other two models, COSMOtherm and SPARC v4.5, show a substantially better prediction for H-bond donor compounds (rmse of 0.35 and 0.42, respectively) than KOWWIN and ABSOLV, suggesting the robustness of COSMOtherm and SPARC v4.5 for such polar compounds.

Step 3 – Complex substances. In this section, chemicals that contain more than one functional group and have more complex molecular structure than those considered above are under consideration. The selected compounds cover hormones and hormone

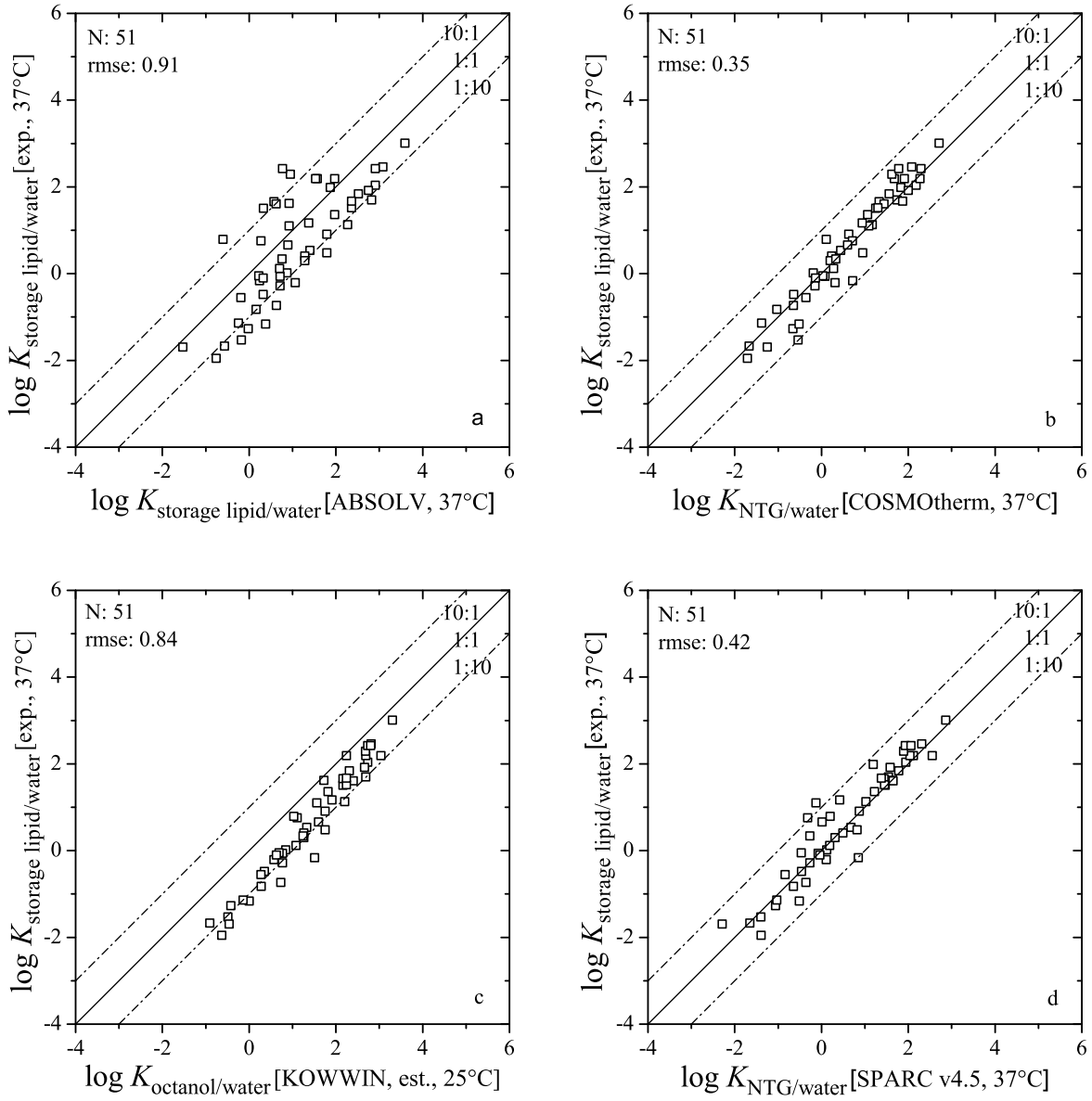

Fig. 1.7: Experimental storage lipid-water partition coefficients for H-bond donor substances versus model-predicted values (*Step 2* evaluation)

active compounds (e.g., estrone, bisphenol A, phthalate esters), fungicides, herbicides, and mycotoxins. Functional groups that are represented include alcohol, amide, carbonyl, nitrile, ester, epoxide, and phenyl groups. A list of all 31 experimental data is provided in Tab. 1.5.

For 7 out of the 31 measured chemicals (all 7 chemicals are mycotoxins), we can only report an upper limit for $K_{\text{storage lipid/water}}$ because the value appears to be too small to measure with the SMEM method [33]. Still, these values can at least be used for a partial validation of the predictive methods. Experimental and predicted $K_{\text{storage lipid/water}}$ values for the complex chemicals are compared in Fig. 1.8. Performance of KOWWIN appears to be the weakest of the four models considered. The predicted values for 12 compounds are 1 log units to 2.4 log units higher than the experimental values and the prediction for

one chemical (verrucarin) is as much as 5 log units too low. Nine of the 12 chemicals overestimated by KOWWIN are strong H-bond donors (ABSOLV-predicted $A = 0.31 - 1.00$), indicating that, again, the principal chemical difference between octanol and storage lipids is a reason for the observed inaccurate predictions. Interestingly, however, predictions for two overestimated chemicals, flusilazole and penconazole, which are no H-bond donors, also differ by more than 2 log units from the experimental values. For these two chemicals and verrucarin, the poor performance of the K_{ow} prediction itself with KOWWIN is likely to be the main reason for the observed discrepancy, indicating a weakness in covering complex structures. This interpretation is further corroborated by the predictions of log K_{ow} by COSMOtherm, ABSOLV, and SPARC v4.5, which often differ by more than one log unit from KOWWIN-predicted log K_{ow}.

Tab. 1.5: The 31 $K_{\text{storage lipid/water}}$ values for complex compounds (*Step 3*)

Compound	log $K_{\text{storage lipid/water}}$	Compound	log $K_{\text{storage lipid/water}}$
Bromoxynil	2.19	Deoxycorticosterone	2.10
Ioxynil	2.84	Metconazole	3.43
Testosterone	1.96	3-Acetyl-DON	< 0.0
Estrone	2.65	Aflatoxin B1	< 0.8
Penconazole	2.30	Aflatoxin B2	< 0.7
Malathion	2.88	Aflatoxin G1	< 0.5
Flusilazole	2.88	Aflatoxin M1	< 0.5
Methidathion	2.43	Alternariol	1.98
Methiocarb	2.54	Altenuene	< 0.5
Lenacil	1.26	Fusarenone-X	< 0.0
Progesterone	3.18	Verrucarin	1.91
Monuron	0.78[1]	Atrazine	1.81[1]
Carbamazepine	0.50[1]	Diethyl phthalate	2.36
Estradiol	2.42[1]	dipropyl phthalate	3.36
Bisphenol A	1.75[1]	Dipentyl phthalate	5.38
Carbazole	3.49[1]		

[1] Data from Oemisch [33]

Among the three other models, COSMOtherm shows the best performance with an rmse of 0.71. Prediction errors were around one log unit in the worst case. Due to its fundamental and least empirical nature, it is reasonable that COSMOtherm possesses the widest application range of all models tested here. Nevertheless, an rmse of 0.71 is higher than the rmse for the large evaluation data set of simple structures (Step 1, shown above). The fact that COSMOtherm predictions are, on average, less accurate for complex chemicals than simple chemicals has already been pointed out before [43][44]. The performance of ABSOLV and SPARC v4.5 for the complex chemicals is substantially worse (rmse of 1.29 and 1.25, respectively) but with no clear systematic trend with respect to the type of chemical structure. The relatively large errors suggest that some of the

tested chemicals are out of the applicability domain of these two models that is restricted by their empirical calibration.

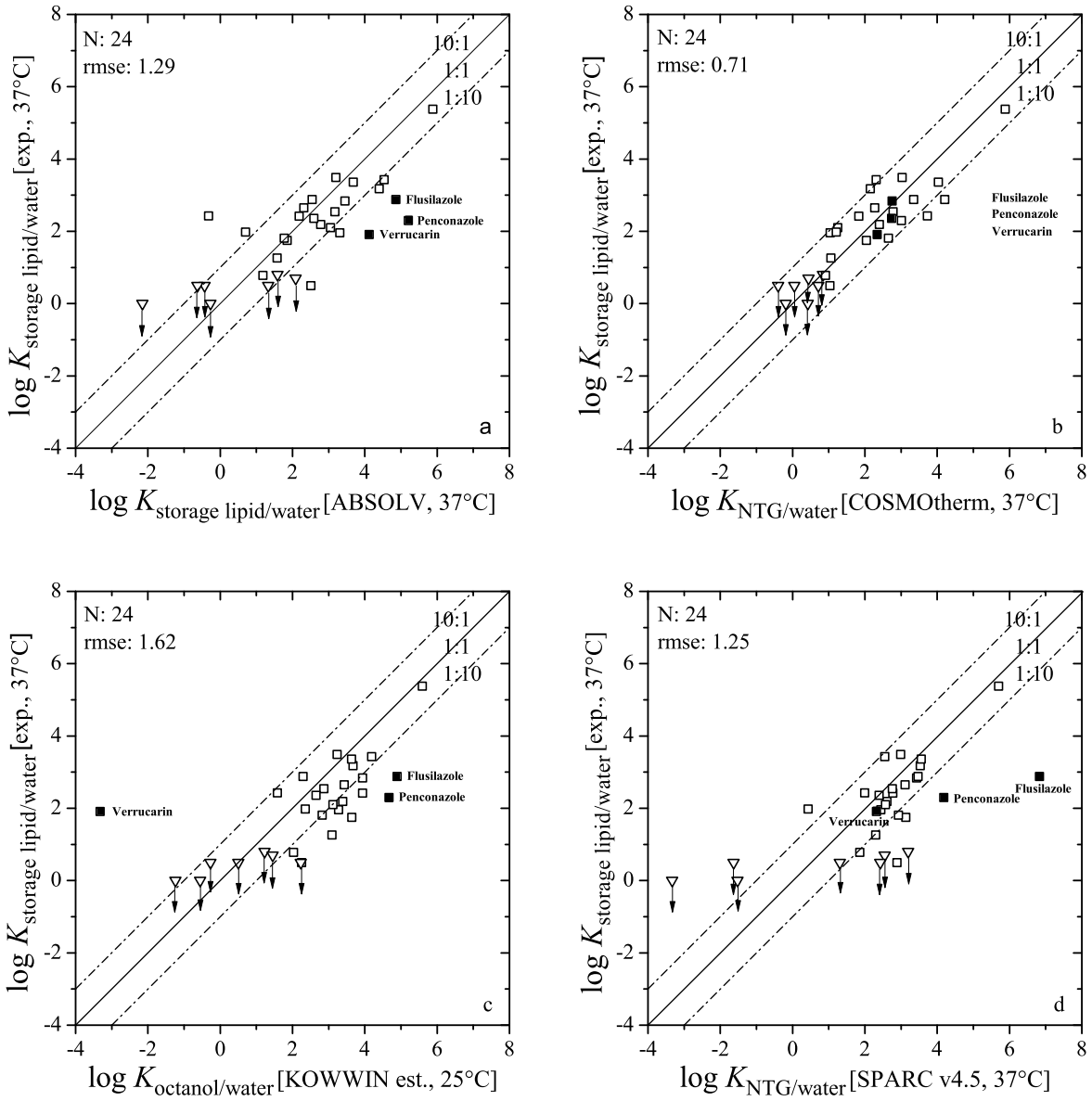

Fig. 1.8: Experimental storage lipid-water partition coefficients for 31 complex compounds versus predictions with four different models (*Step 3* evaluation). Filled squares indicate data for three chemicals denoted within the figure, triangles with arrows indicate experimental values that can only be reported as upper limits (see text) and open squares indicate the rest of the data. The rmse is calculated for 24 substances which were shown as squares.

Note that for poikilotherm organisms it would also be important to be able to predict the temperature dependence of $K_{\text{storage lipid/water}}$. COSMOtherm and SPARC can calculate $K_{\text{storage lipid/water}}$ at different temperatures. For ABSOLV the calibrated pp-LFER equation for enthalpies (ΔH_i) of transfer from water to storage lipid (eq 1.6) can be used to predict the temperature dependence of $K_{\text{storage lipid/water}}$ using the van´t Hoff equation. KOWWIN is out of consideration here because it predicts K_{ow} at only one temperature (25 °C).

1.8 Conclusions

The results of this work have important implications for the modeling and understanding of bioaccumulation of neutral organic chemicals.

First, storage lipids from different origins do not differ in their accumulation properties for various polar and non-polar organic chemicals. This is important for the prediction of bioaccumulation and for the normalization of measured bioaccumulation data. Inter-species differences in lipid-normalized biota-water partition coefficients as observed by van der Heijden and Jonker [47] for PCBs cannot be explained by the different types of storage lipids. An alternative explanation may come from the membrane lipids, which also contribute significantly to the sorption capacity of organisms. Note, however, that partition coefficients of many hydrophobic compounds to storage lipids and to a model membrane (phosphatidylcholine liposome) have been shown to be similar as well [17]. Thus, to elucidate the inter-species differences, further studies on partitioning into various biological membranes are suggested.

Second, the presented pp-LFER model refines an existing model from the literature and allows more accurate predictions for neutral chemicals, provided that the respective compound descriptors are available. This model was amended by the calibration of a predictive equation for the enthalpies of the partitioning process, which enables the prediction of temperature dependent partition coefficients into storage lipids. The presented results will help to improve the accuracy of predictions for the partitioning in biological systems and account for temperature dependent differences between mammals (homeotherm) and fish (poikilotherm). However, for high accuracy of the model predictions, a high quality of the experimental solute descriptors is a requirement. For many organic chemicals of environmental concern, such high quality experimental descriptors do not exist.

Third, the performance of models for predicting the physico-chemical properties of complex compounds is of general interest and goes far beyond the storage lipid-water partitioning discussed here. The presented work showed that performance of the tested models was not largely different for structurally simple chemicals, but that substantial differences emerged when the models were applied to complex chemicals. Complex chemicals are often those for which empirical data are unavailable and thus predictions are needed. While this work suggests an advantage of mechanistic models to predict partition coefficients of complex chemicals, more experimental data for the general evaluation of COSMOtherm, ABSOLV and SPARC with complex, multifunctional chemicals are desirable.

1.9 Physicochemical properties and experimental results for the chemicals in section 1.5 and 1.6

Literature data for olive oil/air partitioning [1] were transformed to olive oil/water with air/water partition coefficients from [2].

Tab. 1.6: Physicochemical properties and experimental results for the chemicals in the section 1.5.

CAS	Solute	compound descriptors						exp. $\log K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
630-20-6	1,1,1,2-Tetrachloroethane	0.54	0.63	0.10	0.08	0.88	3.64	2.85					2.85
71-55-6	1,1,1-Trichloroethane	0.37	0.41	0.00	0.09	0.76	2.73	2.66					2.66
79-34-5	1,1,2,2-Tetrachloroethane	0.60	0.76	0.16	0.12	0.88	3.8	2.56	2.58	2.33	2.38		2.46
79-00-5	1,1,2-Trichloroethane	0.50	0.68	0.13	0.13	0.76	3.29	2.09					2.09
1717-00-6	1,1-Dichloro-1-fluoroethane	0.84	0.43	0.01	0.05	0.67	1.92	1.34					1.34
75-34-3	1,1-Dichloroethane	0.32	0.49	0.10	0.10	0.64	2.32	1.74					1.74
75-35-4	1,1-Dichloroethene	0.36	0.34	0.00	0.05	0.59	2.11	2.19					2.19
526-73-8	1,2,3-Trimethylbenzene	0.73	0.61	0.00	0.19	1.14	4.57	3.32					3.32
367-23-7	1,2,4-Trifluorobenzene	0.31	0.65	0.00	0.02	0.83	2.85	2.67					2.67
95-63-6	1,2,4-Trimethylbenzene	0.68	0.56	0.00	0.19	1.14	4.44	3.43					3.43
106-93-4	1,2-Dibromoethane	0.75	0.76	0.10	0.17	0.74	3.38	1.67					1.67
95-50-1	1,2-Dichlorobenzene	0.87	0.78	0.00	0.04	0.96	4.32	3.88	3.53				3.71
107-06-2	1,2-Dichloroethane	0.42	0.64	0.10	0.11	0.64	2.57	1.6					1.60
78-87-5	1,2-Dichloropropane	0.37	0.68	0.00	0.15	0.78	2.87	1.99					1.99
367-11-3	1,2-Difluorobenzene	0.39	0.63	0.00	0.06	0.79	2.84	2.62					2.62
372-38-3	1,3,5-Trifluorobenzene	0.27	0.49	0.00	0.00	0.83	2.66	2.93					2.93

Continued on next page

CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
108-67-8	1,3,5-Trimethylbenzene	0.65	0.52	0.00	0.19	1.14	4.34	3.49					3.49
541-73-1	1,3-Dichlorobenzene	0.85	0.73	0.00	0.02	0.96	4.41	4.02	3.66				3.84
540-36-3	1,4-Difluorobenzene	0.38	0.60	0.00	0.06	0.79	2.77	2.58					2.58
107-04-0	1-Bromo-2-chloroethane	0.08	0.70	0.10	0.09	0.69	2.98	2.07					2.07
71-36-3	1-Butanol	0.22	0.42	0.37	0.48	0.73	2.60	0.18		-0.05	0.00	-0.05	0.02
109-69-3	1-Chlorobutane	0.21	0.40	0.00	0.10	0.79	2.72	2.78					2.78
543-59-9	1-Chloropentane	0.21	0.38	0.00	0.09	0.94	3.22	3.51	3.41	3.47	3.54	3.48	3.48
540-54-5	1-Chloropropane	0.22	0.40	0.00	0.10	0.65	2.20	2.22					2.22
111-27-3	1-Hexanol	0.21	0.42	0.37	0.48	1.01	3.61	1.36					1.36
107-98-2	1-Methoxy-2-propanol	0.22	0.54	0.31	0.82	0.79	2.66	-1.53					-1.53
108-03-2	1-Nitropropane	0.24	0.95	0.00	0.31	0.71	2.89	0.90	0.99	0.97	1.06	0.94	0.97
71-41-0	1-Pentanol	0.22	0.42	0.37	0.48	0.87	3.11	0.62		0.50	0.56	0.49	0.54
71-23-8	1-Propanol	0.24	0.42	0.37	0.48	0.59	2.03	-0.48					-0.48
540-84-1	2,2,4-Trimethylpentane	0.00	0.00	0.00	0.00	1.24	3.11	4.72	4.33	4.70	4.68	4.76	4.64
306-83-2	2,2-Dichloro-1,1,1-trifluoroethane	-0.16	0.40	0.22	0.00	0.75	1.75	1.81					1.81
75-83-2	2,2-Dimethylbutane	0.00	0.00	0.00	0.00	0.95	2.35	3.79					3.79
565-75-3	2,3,4-Trimethylpentane	0.00	0.00	0.00	0.00	1.24	3.48	5.05					5.05
111-76-2	2-Butoxyethanol	0.20	0.50	0.30	0.83	1.07	3.81	-0.21					-0.21
75-29-6	2-Chloropropane	0.18	0.35	0.00	0.12	0.65	1.97	2.03					2.03
110-80-5	2-Ethoxyethanol	0.24	0.52	0.31	0.81	0.79	2.79	-1.27					-1.27
420-26-8	2-Fluoropropane	0.00	0.32	0.00	0.10	0.57	1.07	1.38					1.38
110-43-0	2-Heptanone	0.12	0.68	0.00	0.51	1.11	3.76	1.95	1.84	1.77	1.85	1.62	1.81
591-78-6	2-Hexanone	0.14	0.68	0.00	0.51	0.97	3.29	1.04	1.21	1.25	1.31	1.16	1.19

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
109-59-1	2-Isopropoxyethanol	0.20	0.47	0.30	0.91	0.93	3.17	-1.16					-1.16
109-86-4	2-Methoxyethanol	0.27	0.50	0.30	0.84	0.79	2.49	-1.67					-1.67
78-83-1	2-Methyl-1-propanol	0.22	0.39	0.37	0.48	0.73	2.41	-0.06					-0.06
75-65-0	2-Methyl-2-propanol	0.28	0.30	0.31	0.60	0.73	1.96	-0.73					-0.73
107-83-5	2-Methylpentane	0.00	0.00	0.00	0.00	0.95	2.50	3.99					3.99
79-46-9	2-Nitropropane	0.22	0.92	0.00	0.33	0.71	2.55	0.61					0.61
107-87-9	2-Pentanone	0.14	0.68	0.00	0.51	0.83	2.76	0.47		0.72	0.76	0.67	0.65
67-63-0	2-Propanol	0.21	0.36	0.33	0.56	0.59	1.76	-0.87		-0.83	-0.78	-0.81	-0.82
123-51-3	3-Methyl-1-butanol	0.19	0.39	0.37	0.48	0.87	3.01	0.41					0.41
589-34-4	3-Methylhexane	0.00	0.00	0.00	0.00	1.09	3.04	4.61					4.61
96-14-0	3-Methylpentane	0.00	0.00	0.00	0.00	0.95	2.58	4.07					4.07
96-22-0	3-Pentanone	0.15	0.66	0.00	0.51	0.83	2.81	0.56					0.56
108-10-1	4-Methyl-2-pentanone	0.11	0.65	0.00	0.51	0.97	3.09	1.05					1.05
67-64-1	Acetone	0.18	0.70	0.04	0.49	0.55	1.70	-0.75		-0.19	-0.15	-0.21	-0.32
300-57-2	Allylbenzene	0.72	0.60	0.00	0.22	1.10	4.14	2.96					2.96
71-43-2	Benzene	0.61	0.52	0.00	0.14	0.72	2.79	2.08	2.25	2.09	2.10	2.08	2.12
74-97-5	Bromochloromethane	0.54	0.80	0.01	0.06	0.55	2.45	1.49					1.49
78-93-3	2-Butanone	0.17	0.70	0.00	0.51	0.69	2.29	-0.07		0.27	0.31	0.24	0.18
106-97-8	Butane	0.00	0.00	0.00	0.00	0.67	1.62	3.03					3.03
123-86-4	Butyl acetate	0.07	0.60	0.00	0.45	1.03	3.35	1.72	1.58	1.59	1.65	1.43	1.59
56-23-5	Carbon tetrachloride	0.46	0.38	0.00	0.00	0.74	2.82	3.14	3.22	3.20	3.19	3.17	3.18
76-14-2	1,2-Dichlorotetrafluoroethane	-0.19	0.05	0.00	0.00	0.79	1.43	3.00					3.00
377-36-6	1,1,2,2,3,3,4,4-Octafluorobutane	-0.79	0.08	0.15	0.15	0.97	1.46	2.50					2.50

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					average
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	
680-00-2	1,1,2,2,3,3-Hexafluoropropane	-0.59	0.21	0.15	0.10	0.76	0.62	1.49					1.49
359-35-3	1,1,2,2-Tetrafluoroethane	-0.39	0.24	0.10	0.12	0.54	0.39	0.92					0.92
75-37-6	1,1-Difluoroethane	-0.25	0.49	0.04	0.05	0.47	0.52	0.91					0.91
151-67-7	Halothane	0.10	0.39	0.13	0.05	0.80	1.95	2.26	2.40	2.25	2.26	2.23	2.28
124-72-1	Teflurane	-0.07	0.21	0.20	0.02	0.72	1.37	1.80					1.80
811-97-2	1,1,1,2-Tetrafluoroethane	-0.39	0.16	0.16	0.05	0.54	0.40	1.03					1.03
406-90-6	Fluroxene	0.18	0.30	0.00	0.27	0.80	1.60	1.26					1.26
75-73-0	Carbon tetrafluoride	-0.58	-0.26	0.00	0.00	0.40	-0.82	1.12					1.12
462-39-5	1,3-Difluoropropane	-0.20	0.55	0.12	0.21	0.61	1.35	0.66					0.66
13838-16-9	Enflurane	-0.24	0.54	0.01	0.10	0.90	2.01	2.11	2.05	1.98	1.98		2.03
26675-46-7	Isoflurane	-0.24	0.56	0.00	0.08	0.90	1.97	2.12	2.14	1.85	1.94	1.91	1.99
57041-67-5	Desflurane	-0.47	0.38	0.05	0.04	0.82	0.99	1.88					1.88
28523-86-6	Sevoflurane	-0.47	0.56	0.00	0.10	0.99	1.50	1.87					1.87
108-90-7	Chlorobenzene	0.72	0.65	0.00	0.07	0.84	3.66	2.93	2.96	2.53	2.60	2.62	2.73
124-48-1	Chlorodibromomethane	0.78	0.68	0.12	0.10	0.72	3.30	2.12					2.12
75-00-3	Chloroethane	0.23	0.40	0.00	0.10	0.51	1.68	1.58					1.58
67-66-3	Chloroform	0.43	0.49	0.15	0.02	0.62	2.48	2.17	2.02	1.97	1.99	1.96	2.02
156-59-2	cis-1,2-Dichloroethene	0.44	0.61	0.11	0.05	0.59	2.44	1.59					1.59
291-64-5	Cycloheptane	0.35	0.10	0.00	0.00	0.99	3.70	5.12	4.71	4.75	4.71	4.79	4.82
110-82-7	Cyclohexane	0.31	0.10	0.00	0.00	0.85	2.96	4.01	4.01	4.08	4.06	4.08	4.05
287-92-3	Cyclopentane	0.26	0.10	0.00	0.00	0.70	2.48	3.50	3.62	3.43	3.45	3.49	3.50
75-19-4	Cyclopropane	0.41	0.23	0.00	0.00	0.42	1.31	1.73					1.73
124-18-5	Decane	0.00	0.00	0.00	0.00	1.52	4.69	6.52	6.58	6.28	6.25	6.33	6.39

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
74-95-3	Dibromethane	0.71	0.69	0.11	0.07	0.60	2.89	1.76					1.76
75-09-2	Dichloromethane	0.39	0.57	0.10	0.05	0.49	2.02	1.47		1.21	1.24	1.20	1.28
60-29-7	Diethyl ether	0.00	0.25	0.00	0.45	0.73	2.02	1.03		0.72	0.72	0.69	0.79
75-10-5	Difluoromethane	-0.32	0.49	0.06	0.05	0.32	0.04	0.53					0.53
109-93-3	Divinyl ether	0.26	0.39	0.00	0.13	0.64	1.76	1.69					1.69
74-84-0	Ethane	0.00	0.00	0.00	0.00	0.39	0.49	1.73					1.73
64-17-5	Ethanol	0.25	0.42	0.37	0.48	0.45	1.49	-1.14		-1.17	-1.10	-1.16	-1.14
74-85-1	Ethene	0.11	0.10	0.00	0.07	0.35	0.29	0.84					0.84
141-78-6	Ethyl acetate	0.11	0.62	0.00	0.45	0.75	2.31	0.50		0.47	0.48	0.38	0.46
637-92-3	Ethyl tert-butyl ether	-0.02	0.16	0.00	0.60	1.01	2.72	1.31	1.43	1.36	1.35	1.39	1.37
919-94-8	Ethyl tert-pentyl ether	0.00	0.16	0.00	0.61	1.15	3.26	1.64	2.03	1.99	1.99	2.01	1.93
100-41-4	Ethylbenzene	0.61	0.51	0.00	0.15	1.00	3.78	3.21	3.24	3.12	3.08	3.08	3.14
462-06-6	Fluorobenzene	0.48	0.57	0.00	0.10	0.75	2.79	2.41					2.41
353-36-6	Fluoroethane	0.05	0.35	0.00	0.10	0.43	0.58	0.62					0.62
593-70-4	Fluorochloromethane	0.04	0.61	0.07	0.04	0.41	0.98	0.77					0.77
142-82-5	Heptane	0.00	0.00	0.00	0.00	1.09	3.17	4.76	4.87	4.64	4.62	4.67	4.71
392-56-3	Hexafluorobenzene	0.09	0.56	0.00	0.01	0.82	2.35	2.65	2.45	2.30	2.39	2.46	2.45
110-54-3	Hexane	0.00	0.00	0.00	0.00	0.95	2.67	4.18	4.23	4.04	4.02	4.09	4.11
110-19-0	Isobutyl acetate	0.05	0.57	0.00	0.47	1.03	3.16	1.60					1.60
123-92-2	Isopentyl acetate	0.05	0.57	0.00	0.47	1.17	3.74	2.11					2.11
108-21-4	Isopropyl acetate	0.06	0.57	0.00	0.47	0.89	2.55	1.02					1.02
98-82-8	Isopropylbenzene	0.06	0.49	0.00	0.16	1.14	4.08	3.52					3.52
76-38-0	Methoxyflurane	0.11	0.67	0.07	0.14	0.91	2.86	2.18	2.25	2.03	2.07	1.99	2.11

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
74-82-8	Methane	0.00	0.00	0.00	0.00	0.25	-0.32	0.75					0.75
67-56-1	Methanol	0.28	0.44	0.43	0.47	0.31	0.97	-1.95					-1.95
79-20-9	Methyl acetate	0.14	0.64	0.00	0.45	0.61	1.91	-0.02		-0.01	0.00	-0.07	-0.02
74-87-3	Methyl chloride	0.25	0.43	0.00	0.08	0.37	1.16	0.80					0.80
96-37-7	Methylcyclopentane	0.23	0.10	0.00	0.00	0.85	2.91	3.91	4.40	3.89	3.88	3.91	4.00
771-56-2	Methylpentafluorobenzene	0.06	0.59	0.00	0.01	1.05	3.24	3.59	3.13	3.08	3.15	3.41	3.27
100-80-1	m-Methylstyrene	0.87	0.65	0.00	0.18	1.10	4.38	3.23					3.23
108-38-3	m-Xylene	0.62	0.52	0.00	0.16	1.00	3.84	3.16					3.16
111-84-2	Nonane	0.00	0.00	0.00	0.00	1.38	4.18	5.89	5.99	5.74	5.71	5.78	5.82
95-47-6	o-Xylene	0.66	0.56	0.00	0.16	1.00	3.94	3.12					3.12
106-42-3	p-Xylene	0.61	0.52	0.00	0.16	1.00	3.84	3.16					3.16
76-01-7	Pentachloroethane	0.65	0.66	0.17	0.06	1.00	4.27	2.93					2.93
363-72-4	Pentafluorobenzene	0.15	0.68	0.00	0.02	0.90	2.58	2.46	2.30	2.19	2.27	2.32	2.31
109-66-0	Pentane	0.00	0.00	0.00	0.00	0.81	2.16	3.61	3.66	3.39	3.34	3.44	3.49
628-63-7	Pentyl acetate	0.07	0.60	0.00	0.45	1.17	3.84	2.17	2.25	2.08	2.18	1.9	2.11
622-97-9	p-Methylstyrene	0.87	0.65	0.00	0.18	1.10	4.40	3.21					3.21
74-98-6	Propane	0.00	0.00	0.00	0.00	0.53	1.05	2.35					2.35
109-60-4	Propyl acetate	0.09	0.60	0.00	0.45	0.89	2.82	1.12	0.97	1.03	1.06	0.93	1.02
103-65-1	Propylbenzene	0.60	0.50	0.00	0.15	1.14	4.23	3.77	3.76	3.60	3.54	3.58	3.65
127-18-4	Tetrachloroethene	0.64	0.44	0.00	0.00	0.84	3.58	3.68	3.59	3.52	3.49	3.54	3.57
108-88-3	Toluene	0.60	0.52	0.00	0.14	0.86	3.33	2.68	2.75	2.65	2.63	2.63	2.67
156-60-5	trans-1,2-Dichloroethene	0.43	0.41	0.09	0.05	0.59	2.28	2.06					2.06
79-01-6	Trichloroethene	0.52	0.37	0.08	0.03	0.71	3.00	2.95	2.85	2.74	2.73	2.74	2.80

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
629-50-5	tridecane	0.00	0.00	0.00	0.00	1.94	6.20	8.16					8.16
121-44-8	triethylamine	0.10	0.15	0.00	0.79	1.05	3.04	1.04					1.04
1120-21-4	undecane	0.00	0.00	0.00	0.00	1.66	5.19	7.03					7.03
7785-26-4	alpha-pinene	0.45	0.14	0.00	0.12	1.26	4.31	4.58					4.58
110-71-4	1,2-dimethoxyethane	0.12	0.67	0.00	0.68	0.79	2.65	-0.33					-0.33
123-91-1	1,4-dioxane	0.33	0.75	0.00	0.64	0.68	2.89	-0.24					-0.24
111-70-6	1-heptanol	0.21	0.42	0.37	0.48	1.15	4.12	1.84	1.84 [1]				1.84
109-06-8	2-methylpyridine	0.60	0.75	0.00	0.58	0.82	3.42	0.61					0.61
108-99-6	3-methylpyridine	0.63	0.81	0.00	0.54	0.82	3.63	0.84					0.84
108-89-4	4-methylpyridine	0.63	0.82	0.00	0.54	0.82	3.64	0.82					0.82
100-51-6	benzyl alcohol	0.80	0.87	0.39	0.56	0.92	4.22	0.12					0.12
108-86-1	bromobenzene	0.88	0.73	0.00	0.09	0.89	4.04	3.27					3.27
592-84-7	butyl formate	0.12	0.63	0.00	0.38	0.89	2.96	1.46					1.46
590-01-2	butyl propanoate	0.06	0.56	0.00	0.47	1.17	3.83	2.35					2.35
104-51-8	butylbenzene	0.60	0.51	0.00	0.15	1.28	4.73	4.38	4.2	4.07	3.96	4.06	4.13
359-10-4	1,1-difluoro-2-chloroethene	-0.34	0.29	0.15	0.00	0.55	0.72	1.63					1.63
75-88-7	1-chloro-2,2,2-trifluoroethane	0.01	0.4	0.15	0.00	0.63	1.17	1.34					1.34
333-36-8	bis-(2,2,2-trifluoroethyl)ether	-0.51	0.03	0.08	0.36	0.96	1.42	1.92					1.92
110-83-8	cyclohexene	0.40	0.28	0.00	0.09	0.80	2.95	3.22	3.34	3.36	3.35	3.37	3.33
120-92-3	cyclopentanone	0.37	0.86	0.00	0.52	0.72	3.22	0.39					0.39
75-45-6	difluorochloromethane	0.00	0.25	0.20	0.00	0.45	0.69	0.72					0.72
108-20-3	diisopropyl ether	-0.06	0.16	0.00	0.58	1.01	2.53	1.26	0.89	1.42	1.44	1.44	1.29
109-87-5	dimethoxymethane	0.10	0.46	0.00	0.52	0.65	1.89	0.18					0.18

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					average
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	
115-10-6	dimethyl ether	0.00	0.27	0.00	0.41	0.45	1.29	0.13					0.13
127-19-5	dimethylacetamide	0.36	1.35	0.00	0.77	0.79	3.64	-1.25					-1.25
68-12-2	dimethylformamide	0.37	1.31	0.00	0.74	0.65	3.17	-1.57					-1.57
142-96-1	di-n-butyl ether	0.00	0.25	0.00	0.45	1.29	3.92	3.13	3.18	3.10	3.12	3.19	3.14
109-94-4	ethyl formate	0.15	0.66	0.00	0.38	0.61	1.85	0.16					0.16
105-37-3	ethyl propanoate	0.09	0.58	0.00	0.45	0.89	2.81	1.13					1.13
75-03-6	iodoethane	0.64	0.40	0.00	0.14	0.65	2.57	1.85					1.85
75-69-4	fluorotrichloromethane	0.21	0.24	0.00	0.07	0.65	1.95	2.28					2.28
107-31-3	methyl formate	0.19	0.68	0.00	0.38	0.46	1.29	-0.48					-0.48
108-87-2	methylcyclohexane	0.24	0.06	0.00	0.00	0.99	3.32	4.62	4.48	4.54	4.52	4.56	4.54
79-24-3	nitroethane	0.27	0.95	0.02	0.33	0.56	2.41	0.31		0.50	0.56	0.45	0.45
75-52-5	nitromethane	0.31	0.95	0.06	0.31	0.42	1.89	-0.23		0.07	0.10	-0.01	-0.02
121-69-7	N,N-dimethylaniline	0.96	0.81	0.00	0.41	1.10	4.70	2.29					2.29
629-62-9	pentadecane	0.00	0.00	0.00	0.00	2.22	7.21	9.31					9.31
110-89-4	piperidine	0.42	0.46	0.13	0.68	0.80	3.30	1.01					1.01
106-94-5	propyl bromide	0.37	0.40	0.00	0.12	0.71	2.62	2.47					2.47
110-74-7	propyl formate	0.13	0.63	0.00	0.38	0.75	2.43	0.87					0.87
110-86-1	pyridine	0.63	0.84	0.00	0.52	0.68	3.02	0.15					0.15
629-59-4	tetradecane	0.00	0.00	0.00	0.00	2.08	6.71	8.74					8.74
109-99-9	tetrahydrofuran	0.29	0.52	0.00	0.48	0.62	2.64	0.62					0.62
679-84-5	halopropane	-0.07	0.28	0.20	0.00	0.86	2.03	2.91					2.91
56885-28-0	CF3CHFOCHFCl	-0.24	0.50	0.00	0.11	0.90	1.87	2.15					2.15
292-64-8	Cyclooctane	0.41	0.10	0.00	0.00	1.13	4.33		5.39	5.32	5.29	5.36	5.34

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
111-87-5	Octan-1-ol	0.20	0.42	0.37	0.48	1.29	4.62		2.42 [1]		2.46		2.46
143-08-8	Nonan-1-ol	0.19	0.42	0.37	0.48	1.44	5.12		3.00 [1]		3.01		3.01
66-25-1	Hexanal	0.15	0.65	0.00	0.45	0.97	3.36		1.92				1.92
111-71-7	Heptanal	0.14	0.65	0.00	0.45	1.11	3.87		2.46				2.46
124-13-0	Octanal	0.16	0.65	0.00	0.45	1.25	4.36		3.01				3.01
124-19-6	Nonanal / n-Nonyl Aldehyde	0.15	0.65	0.00	0.45	1.39	4.86		3.42				3.42
629-06-1	1-Chloroheptane	0.19	0.40	0.00	0.10	1.22	4.28		4.47	4.33	4.38	4.32	4.37
111-85-3	1-Chlorooctane	0.19	0.40	0.00	0.10	1.36	4.77		5.17	4.86	4.91	4.85	4.95
592-41-6	1-Hexene	0.08	0.08	0.00	0.07	0.91	2.57		3.54	3.50	3.49		3.51
592-76-7	1-Heptene	0.09	0.08	0.00	0.07	1.05	3.06		4.02	4.06	4.04		4.04
111-66-0	1-Octene	0.09	0.08	0.00	0.07	1.19	3.57		4.59	4.62	4.59		4.60
124-11-8	1-Nonene	0.09	0.08	0.00	0.07	1.33	4.07		5.22	5.13	5.10		5.15
872-05-9	1-Decene	0.09	0.08	0.00	0.07	1.47	4.57		5.76	5.60	5.57		5.64
120-82-1	1,2,4-Trichlorobenzene	0.98	0.81	0.00	0.00	1.08	5.25		4.17				4.17
111-43-3	Di-n-propyl ether	0.01	0.25	0.00	0.45	1.01	2.95		2.07	2.04	2.05	2.07	2.06
693-65-2	Dipentyl ether	0.00	0.25	0.00	0.45	1.58	4.80		4.19	4.06	4.12	4.25	4.16
111-13-7	2-octanone	0.11	0.68	0.00	0.51	1.25	4.26		2.46	2.29	2.40	2.08	2.31
821-55-6	2-nonanone	0.12	0.68	0.00	0.51	1.39	4.74		3.03	2.78	2.91	2.44	2.79
627-05-4	1-Nitrobutane	0.23	0.95	0.00	0.29	0.85	3.42		1.53	1.55	1.60	1.44	1.53
646-14-0	1-Nitrohexane	0.20	0.95	0.00	0.29	1.13	4.42		2.68	2.59	2.62	2.40	2.58
536-75-4	4-Ethylpyridine	0.63	0.80	0.00	0.57	0.96	4.12		1.14				1.14
100-00-5	1-Chloro-4-nitrobenzene	0.98	1.18	0.00	0.24	1.01	5.22		2.58	2.32	2.34	2.27	2.38
98-95-3	Nitrobenzene	0.87	1.11	0.00	0.28	0.89	4.56		2.03	1.95	1.93	1.75	1.92

Continued on next page

CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					average
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	
88-72-2	2-Nitrotoluene	0.87	1.11	0.00	0.28	1.03	4.88		2.51	2.43	2.45	2.21	2.40
606-20-2	2,6-Dinitrotoluene	1.15	1.60	0.00	0.45	1.21	6.30		2.37	1.76	1.82	1.81	1.94
100-17-4	4-Nitroanisole	0.97	1.21	0.00	0.40	1.09	5.85		2.32				2.32
150-78-7	1,4-Dimethoxybenzene	0.81	1.00	0.00	0.50	1.12	5.04		2.12				2.12
106-48-9	4-Chlorophenol	0.92	1.08	0.67	0.20	0.90	4.78		1.68 [2]	1.51 [3]			1.51
93-89-0	Ethyl benzoate	0.69	0.85	0.00	0.46	1.21	5.20		2.59				2.59
104-76-7	2-Ethyl-1-hexanol	0.21	0.39	0.37	0.48	1.29	4.38		2.26 [1]	1.99	2.04	2.08	2.04
597-76-2	3-Ethyl-3-hexanol	0.20	0.30	0.31	0.60	1.29	4.29		1.85 [1]	1.69	1.71	1.71	1.70
19780-44-0	4-Ethyl-3-hexanol	0.17	0.36	0.33	0.57	1.29	4.18		2.07 [1]	1.91	1.93	1.92	1.92
597-49-9	3-Ethyl-3-pentanol	0.20	0.30	0.31	0.60	1.15	3.79		1.19 [1]	1.11	1.15	1.12	1.13
121-14-2	2,4-Dinitrotoluene	1.15	1.60	0.00	0.47	1.21	6.26		2.34				2.34
33018-78-9	CF3CH2OCF2Cl	-0.24	0.14	0.00	0.06	0.90	1.58	2.73					2.73
430-55-7	1-fluropropane	0.03	0.35	0.00	0.13	0.69	1.10	0.98					0.98
67-72-1	Hexachloroethane	0.68	0.68	0.00	0.00	1.12	4.72	3.71					3.71
92-52-4	Biphenyl	1.36	0.99	0.00	0.26	1.32	6.01		4.14				4.14
75995-72-1	1,1,1,2,3,4,4,4-Octafluorobutane	-0.79	0.20	0.13	0.05	0.97	1.10	2.44					2.44
544-76-3	hexadecane	0.00	0.00	0.00	0.00	2.36	7.71	9.88					9.88
75-26-3	isopropyl bromide	0.33	0.35	0.00	0.14	0.71	2.39	2.28					2.28
375-17-7	1,1,1,2,2,3,3,4,4-nonafluorobutane	-0.78	-0.30	0.10	0.10	1.01	0.42	2.82					2.82
127-91-3	beta-pinene	0.53	0.24	0.00	0.19	1.26	4.39	4.11					4.11
5989-27-5	limonene	0.49	0.28	0.00	0.21	1.32	4.73	4.17					4.17
593-53-3	Fluoromethane	0.07	0.35	0.00	0.09	0.29	0.06	0.00					0.00
2825-83-4	Tricyclo[5.2.1.0(2,6)]decane	0.59	0.45	0.00	0.06	1.19	4.84	4.62					4.62

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CAS	Solute	compound descriptors						exp. log $K_{\text{storage lipid/water}}$					
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	average
1634-04-4	Methyl tert-butyl ether	0.02	0.21	0.00	0.59	0.87	2.38	0.89					0.89
2551-62-4	Sulfur hexafluoride	-0.60	-0.20	0.00	0.00	0.58	-0.12	1.85					1.85
75-01-4	vinyl chloride	0.26	0.38	0.00	0.05	0.47	1.40	1.58					1.58
67-68-5	dimethyl sulfoxide	0.52	1.72	0.00	0.97	0.61	3.46	-2.85					-2.66
64-18-6	formic acid	0.34	0.75	0.76	0.33	0.32	1.55	-1.69					-1.69
13466-78-9	3-carene	0.51	0.22	0.00	0.10	1.26	4.65	4.71					4.71
593-60-2	vinyl bromide	0.56	0.50	0.00	0.07	0.52	1.85	1.34					1.34
106-47-8	4-Chloroaniline	1.06	1.13	0.30	0.31	0.94	4.89		1.62 [2]				-
107-05-1	allyl chloride	0.33	0.56	0.00	0.05	0.61	2.11	1.84					1.84
100-42-5	Styrene	0.85	0.65	0.00	0.16	0.96	3.86	2.68					2.68
111-65-9	Octane	0.00	0.00	0.00	0.00	1.24	3.68	5.35	5.41	5.19	5.16	5.23	5.27
108-43-0	3-Chlorophenol	0.91	1.06	0.69	0.15	0.90	4.77		1.84 [2]	1.66 [3]			1.66
140-11-4	Benzyl acetate	0.80	1.06	0.00	0.65	1.21	5.01			1.65	1.75		1.70
90-15-3	1-Naphthol	1.52	1.05	0.61	0.37	1.14	6.13		2.47 [2]	2.19 [3]			2.19
106-41-2	4-bromophenol	1.08	1.17	0.67	0.20	0.95	5.14		1.91 [2]	1.61 [3]			1.61
540-37-4	4-Iodoaniline	1.53	1.28	0.31	0.40	1.07	5.70		2.19 [2]				-
91-66-7	N,N-Diethylaniline	0.95	0.80	0.00	0.50	1.38	5.29		3.17				3.17
645-56-7	4-n-Propylphenol	0.79	0.88	0.55	0.37	1.20	5.19		2.35 [2]	2.19 [3]			2.19
540-38-5	4-iodophenol	1.38	1.22	0.68	0.20	1.03	5.49		2.29 [2]				-
99-65-0	1,3-Dinitrobenzene	1.15	1.60	0.00	0.47	1.06	5.90			1.32		1.51	1.42
120-12-7	Anthracene	2.29	1.34	0.00	0.28	1.45	7.57		4.83				4.83
85-01-8	Phenanthrene	2.06	1.29	0.00	0.29	1.45	7.63		4.80				4.80
206-44-0	Fluoranthene	2.38	1.55	0.00	0.20	1.58	8.83		5.18				5.18

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CAS	Solute	compound descriptors						exp. $\log K_{\text{storage lipid/water}}$					average
		E	S	A	B	V	L	olive oil [1]	milk fat	fish oil	linseed oil	goose fat	
129-00-0	Pyrene	2.81	1.71	0.00	0.29	1.58	8.83		5.26				5.26
86-73-7	Fluorene	1.59	1.03	0.00	0.20	1.36	6.92		4.39				4.39
83-32-9	Acenaphthene	1.60	1.04	0.00	0.20	1.26	6.47		3.97				3.97

[1] Milk fat data were not included in the average because of possible impact of milk proteins on the values

[2] These milk fat data have been corrected for protein binding but were not included in the average

[3] Data measured in soybean oil from [33]

Tab. 1.7: Physicochemical properties and experimental results for the chemicals in section 1.6

CAS	Substance	compound descriptors						exp. $\log K_{\text{fish oil/water}}37\,^{\circ}\text{C}$	enthalpy(kJ/mol)
		E	S	A	B	V	L		
123-86-4	n-Butyl acetate	0.07	0.60	0.00	0.45	1.03	3.35	1.47	6.60
628-63-7	n-Pentyl acetate	0.07	0.60	0.00	0.45	1.17	3.84	2.03	2.61
71-36-3	Butan-1-ol	0.22	0.42	0.37	0.48	0.73	2.60	-0.54	27.06
71-41-0	Pentan-1-ol	0.22	0.42	0.37	0.48	0.87	3.11	0.09	22.65
111-70-6	Heptan-1-ol	0.21	0.42	0.37	0.48	1.15	4.12	1.37	9.69
110-54-3	n-Hexane	0.00	0.00	0.00	0.00	0.95	2.67	4.02	1.08
142-82-5	n-Heptane	0.00	0.00	0.00	0.00	1.09	3.17	4.65	-0.68
111-65-9	n-Octane	0.00	0.00	0.00	0.00	1.24	3.68	5.26	-3.86
111-84-2	n-Nonane	0.00	0.00	0.00	0.00	1.38	4.18	5.83	-4.57
124-18-5	n-Decane	0.00	0.00	0.00	0.00	1.52	4.69	6.33	-2.60
75-09-2	Dichloromethane	0.39	0.57	0.10	0.05	0.49	2.02	1.30	-4.61

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		compound descriptors							
CAS	Substance	E	S	A	B	V	L	exp. $\log K_{\text{fish oil/water}} 37\,^{\circ}\text{C}$	enthalpy(kJ/mol)
67-66-3	Trichloromethane	0.43	0.49	0.15	0.02	0.62	2.48	2.01	-2.13
56-23-5	Tetrachloromethane	0.46	0.38	0.00	0.00	0.74	2.82	3.09	5.88
79-34-5	1.1.2.2-Tetrachloroethane	0.60	0.76	0.16	0.12	0.88	3.80	2.64	-17.32
543-59-9	1-Chloropentane	0.21	0.40	0.00	0.10	0.94	3.22	3.38	4.96
111-85-3	1-Chlorooctane	0.19	0.40	0.00	0.09	1.36	4.71	5.26	-21.9
71-43-2	Benzene	0.61	0.52	0.00	0.14	0.72	2.79	2.18	-4.67
108-88-3	Toluene	0.60	0.52	0.00	0.14	0.86	3.33	2.75	-5.79
100-41-4	Ethylbenzene	0.61	0.51	0.00	0.15	1.00	3.78	3.26	-7.74
103-65-1	n-Propylbenzene	0.60	0.5	0.00	0.15	1.14	4.23	3.86	-13.94
104-51-8	n-Butylbenzene	0.60	0.51	0.00	0.15	1.28	4.73	4.45	-21.17
142-96-1	Di-n-butyl ether	0.00	0.25	0.00	0.45	1.29	3.92	2.77	18.46
693-65-2	Dipentyl ether	0.00	0.25	0.00	0.45	1.58	4.88	3.90	9.10
78-93-3	2-Butanone	0.17	0.70	0.00	0.51	0.69	2.29	-0.27	29.91
107-87-9	2-pentanone	0.14	0.68	0.00	0.51	0.83	2.76	0.33	21.33
591-78-6	2-hexanone	0.14	0.68	0.00	0.51	0.97	3.26	0.94	17.04
110-43-0	2-heptanone	0.12	0.68	0.00	0.51	1.11	3.76	1.57	10.86
111-13-7	2-octanone	0.11	0.68	0.00	0.51	1.25	4.26	2.2	4.73
821-55-6	2-nonanone	0.12	0.68	0.00	0.51	1.39	4.74	2.83	-2.81
627-05-4	1-Nitrobutane	0.23	0.95	0.00	0.29	0.85	3.42	1.51	2.15
287-92-3	Cyclopentane	0.26	0.10	0.00	0.00	0.70	2.48	3.16	14.78
110-82-7	Cyclohexane	0.31	0.10	0.00	0.00	0.85	2.96	3.81	14.54
291-64-5	Cycloheptane	0.35	0.10	0.00	0.00	0.99	3.70	4.43	17.62
110-83-8	cyclohexene	0.40	0.20	0.00	0.09	0.80	2.95	3.13	12.64
108-87-2	methylcyclohexane	0.24	0.06	0.00	0.00	0.99	3.32	4.36	9.91

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		compound descriptors							
CAS	Substance	E	S	A	B	V	L	exp. $\log K_{\text{fish oil/water}} 37\,^{\circ}\text{C}$	enthalpy(kJ/mol)
637-92-3	Ethyl tert-butyl ether	-0.02	0.16	0.00	0.60	1.01	2.72	0.90	25.81
919-94-8	Ethyl tert-pentyl ether	0.00	0.16	0.00	0.61	1.15	3.26	1.57	23.62
76-38-0	Methoxyflurane	0.11	0.67	0.07	0.14	0.91	2.86	2.29	-14.41
104-76-7	2-Ethyl-1-hexanol	0.21	0.39	0.37	0.48	1.29	4.38	1.86	7.59
597-76-2	3-Ethyl-3-hexanol	0.20	0.30	0.31	0.60	1.29	4.29	1.30	21.60
19780-44-0	4-Ethyl-3-hexanol	0.17	0.36	0.33	0.57	1.29	4.18	1.62	15.86
597-49-9	3-Ethyl-3-pentanol	0.20	0.30	0.31	0.60	1.15	3.79	0.62	27.60
127-18-4	Tetrachloroethene	0.64	0.44	0.00	0.00	0.84	3.58	3.49	1.74
79-01-6	Trichloroethene	0.52	0.37	0.08	0.03	0.71	3.00	2.68	2.95
540-84-1	2.2.4-Trimethylpentane	0.00	0.00	0.00	0.00	1.24	3.11	4.95	-14.05
108-20-3	diisopropyl ether	-0.06	0.16	0.00	0.58	1.01	2.53	0.99	23.55
920-66-1	1.1.1.3.3.3-Hexafluoro-2-propanol	-0.24	0.55	0.77	0.10	0.82	1.39	0.60	-
95-50-1	1.2-Dichlorobenzene	0.87	0.78	0.00	0.04	0.96	4.52	3.61	-
541-73-1	1.3-Dichlorobenzene	0.85	0.73	0.00	0.02	0.96	4.41	3.56	-
66-25-1	Hexanal	0.15	0.65	0.00	0.45	0.97	3.36	1.68	-
111-71-7	Heptanal	0.14	0.65	0.00	0.45	1.11	3.87	2.34	-
124-13-0	Octanal	0.16	0.65	0.00	0.45	1.25	4.36	2.95	-

2 Abstracts of the original publications

Partitioning of polar and non-polar neutral organic chemicals into human and cow milk

A. Geisler, S. Endo and K.-U. Goss

Environment International, 37:1253-1258, 2011
DOI: 10.1016/j.envint.2011.05.014

Abstract The aim of this work was to develop a predictive model for milk/water partition coefficients of neutral organic compounds. Batch experiments were performed for 119 diverse organic chemicals in human milk and raw and processed cow milk at 37 °C. No differences (< 0.3 log units) in the partition coefficients of these types of milk were observed. The polyparameter linear free energy relationship model fit the calibration data well (SD = 0.22 log units). An experimental validation data set including hormones and hormone active compounds was predicted satisfactorily by the model. An alternative modelling approach based on log Kow revealed a poorer performance. The model presented here provides a significant improvement in predicting enrichment of potentially hazardous chemicals in milk. In combination with physiologically based pharmacokinetic modelling this improvement in the estimation of milk/water partitioning coefficients may allow a better risk assessment for a wide range of neutral organic chemicals.

Partitioning of Organic Chemicals to Storage Lipids: Elucidating the Dependence on Fatty Acid Composition and Temperature

A. Geisler, S. Endo and K.-U. Goss

Environmental Science & Technology, 46: 9519-9524, 2012
DOI: 10.1021/es301921w

Abstract Lipids serve as important compartments in partitioning of neutral organic chemicals into organisms. Storage lipids, made up of triglycerides with various fatty acids, are among the major classes of lipids. Here, we present experimental equilibrium partition data for diverse chemicals in fish oil, linseed oil, and goose fat at 37 °C. These data, in combination with data from the literature for olive oil and milk fat, show that the fatty acid composition of triglycerides has no significant influence on the partition coefficient. This result allows the derivation of a general predictive model for partitioning into storage lipids. We have collected storage lipid/water partition coefficients for 247 compounds to calibrate polyparameter linear free energy relationships (pp-LFERs) for 37 °C, which achieved a model fit with a root mean squared error of 0.20 log units. To extend the applicability of this model toward the aquatic food chain, we also measured fish oil partition data at 7 °C. The resulting enthalpies were used to calibrate an additional pp-LFER for the temperature dependence of storage lipid/water partitioning. This model allows us to estimate partition coefficients at desired temperatures that occur under typical ambient conditions.

Predicting Storage–Lipid Water Partitioning of Organic Solutes from Molecular Structure

A. Geisler, L. Oemisch, S. Endo and K.-U. Goss

Environmental Science & Technology, 49: 5538-5545, 2015
DOI: 10.1021/es506336m

Abstract Partitioning to storage fat is the major process for bioaccumulation of many neutral organic chemicals. In this work, we evaluated the performance of four predictive models, ABSOLV, COSMOtherm, KOWWIN, and SPARC to calculate storage lipid-water partition coefficients. In a first step of the validation, we used over 300 literature data for chemicals with relatively simple molecular structures. For these compounds the overall performance was similar for all models with a root-mean-square error (rmse) between 0.45 and 0.61 log units. Clear differences became visible in the second validation step where a subset with only H-bond-donor compounds was used. Here, COSMOtherm and SPARC performed clearly better with an rmse of 0.35 and 0.42 log units, respectively, compared to ABSOLV and KOWWIN with an rmse of 0.91 and 0.85 log units, respectively. The last step in our validation was a comparison with experimental values for 22 complex, multifunctional chemicals (including pesticides, hormones, mycotoxins) that we measured specifically for this validation purpose. For these chemicals, predictions by all models were less accurate than those for simpler chemicals. COSMOtherm performed the best (rmse 0.71 log units) while the other methods showed considerably poorer results (rmse 1.29 (ABSOLV), 1.25 (SPARC), and 1.62 (KOWWIN) log units).

Bibliography

[1] M. H. Abraham and A. Ibrahim. Gas to olive oil partition coefficients: A linear free energy analysis. *Journal Of Chemical Information And Modeling*, 46(4):1735–1741, 2006.

[2] M. H. Abraham, A. Ibrahim, and W. E. Acree. Partition of compounds from gas to water and from gas to physiological saline at 310 k: Linear free energy relationships. *Fluid Phase Equilibria*, 251(2):93–109, 2007.

[3] M. H. Abraham, A. Ibrahim, and A. M. Zissimos. Determination of sets of solute descriptors from chromatographic measurements. *Journal of Chromatography A*, 1037(1-2):29–47, 2004.

[4] M.H. Abraham. *Quantitative Treatments of Solute/Solvent Interactions*, volume 1 of *Theoretical and Computational Chemistry*, book section New Solute Descriptors for Linear Free Energy Relationships and Quantitative Structure-Activity Relationships, pages 83–134. Elsevier, Amstderdam, 1994.

[5] M.H. Abraham, J. Andonian-Haftvan, G.S. Whiting, A. Leo, and R.S. Taft. Hydrogen bonding. part 34. the factors that influence the solubility of gases and vapours in water at 298 k, and a new method for its determination. *Journal of the Chemical Society, Perkin Transactions*, 2(7):1777–1791, 1994.

[6] ACD. Advanced chemistry development. data sheet: Absolv prediction module.

[7] W. E. Acree and M. H. Abraham. Solubility predictions for crystalline polycyclic aromatic hydrocarbons (pahs) dissolved in organic solvents based upon the abraham general solvation model. *Fluid Phase Equilibria*, 201(2):245–258, 2002.

[8] Sanka N. Atapattu and Colin F. Poole. Determination of descriptors for semivolatile organosilicon compounds by gas chromatography and non-aqueous liquid-liquid partition. *Journal of Chromatography A*, 1216(45):7882, 2009.

[9] H. C. Atkinson and E. J. Begg. Relationship between human-milk lipid ultrafiltrate and octanol water partition-coefficients. *Journal Of Pharmaceutical Sciences*, 77(9):796–798, 1988.

[10] H.D. Belitz, W. Grosch, and P. Schieberle. *Lehrbuch der Lebensmittelchemie*. Springer Verlag, Berlin, 5th edition, 2001.

[11] K. Bittermann, S. Spycher, S. Endo, L. Pohler, U. Huniar, K.-U. Goss, and A. Klamt. Prediction of phopholipid-water partition coefficients of ionic organic chemicals using the mechanistic model cosmomic. *Journal of Physical Chemistry B*, 118(51):14833–14842, 2014.

[12] G. Bronner and K.-U. Goss. Predicting sorption of pesticides and other multifunctional organic chemicals to soil organic carbon. *Environmental Science & Technology*, 45:1313–1319, 2011.

[13] C. T. Chiou. Partition-coefficients of organic-compounds in lipid water-systems and correlations with fish bioconcentration factors. *Environmental Science & Technology*, 19(1):57–62, 1985.

[14] G. Czub and M. S. McLachlan. A food chain model to predict the levels of lipophilic organic contaminants in humans. *Environmental Toxicology and Chemistry*, 23(10):2356–2366, 2004.

[15] M. Endo and K.-U. Goss. Serum albumin binding of structurally diverse neutral organic compounds: Data and models. *Chemical Research in Toxicology*, 24(12):2293–2301, 2011.

[16] S. Endo, T. N. Brown, and K.-U. Goss. General model for estimating partition coefficients to organisms and their tissues using the biological compositions and polyparameter linear free energy relationships. *Environmental Science & Technology*, 47(12):6630–6639, 2013.

[17] S. Endo, B. I. Escher, and K.-U. Goss. Capacities of membrane lipids to accumulate neutral organic chemicals. *Environmental Science & Technology*, 45:5912–5921, 2011.

[18] S. Endo, N. Watanabe, N. Ulrich, G. Bronner, and K.-U. Goss. Ufz-lser database v 2.1, 2014.

[19] M. L. Gargas, R. J. Burgess, D. E. Voisard, G. H. Cason, and M. E. Andersen. Partition-coefficients of low-molecular-weight volatile chemicals in various liquids and tissues. *Toxicology And Applied Pharmacology*, 98(1):87–99, 1989.

[20] F.A.P.C. Gobas, J.B. Wilcockson, R.W. Russell, and G.D. Haffner. Mechanism of biomagnification in fish under laboratory and field conditions. *Environmental Science & Technology*, 33:133–141, 1999.

[21] K.-U. Goss. Predicting the equilibrium partitioning of organic compounds using just one linear solvation energy relationship (lser). *Fluid Phase Equilibria*, 233:19–22, 2005.

[22] I.B. Helland, K. Saarem, O.D. Saugstad, and C.A. Drevon. Fatty acid composition in maternal milk and plasma during supplementation with cod liver oil. *European Journal of Clinical Nutrition*, 52:839–845, 1998.

[23] S. H. Hilal, A. N. Saravanaraj, T. Whiteside, and L. A. Carreira. Calculating physical properties of organic compounds for environmental modeling from molecular structure. *Journal Of Computer-Aided Molecular Design*, 21(12):693–708, 2007.

[24] A. Jahnke, M. S. McLachlan, and P. Mayer. Equilibrium sampling: Partitioning of organochlorine compounds from lipids into polydimethylsiloxane. *Chemosphere*, 73(10):1575–1581, 2008.

[25] J. W. Jonker. What is causing biomagnificationof persistent hydrophobic organic chemicals in the aquatic environment? *Environmental Science & Technology*, 46:110–111, 2012.

[26] A. Klamt. *From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design*. Elsevier, Amsterdam, 2005.

[27] P. Mayer, L. Torang, N. Glaesner, and J. A. Jonsson. Silicone membrane equilibrator: Measuring chemical activity of nonpolar chemicals with poly(dimethylsiloxane) microtubes immersed directly in tissue and lipids. *Analytical Chemistry*, 81(4):1536–1542, 2009.

[28] M.S. McLachlan. Bioaccumulation of hydrophobic chemicals in agricultural food chains. *Environmental Science & Technology*, 30(1):252–259, 1996.

[29] C. Mintz, K. Burton, T. Ladlie, M. Clark, W. E. Acree, and M. H. Abraham. Enthalpy of solvation correlations for gaseous solutes dissolved in dibutyl ether and ethyl acetate. *Thermochimica Acta*, 470(1-2):67–76, 2008.

[30] C. Mintz, J. Gibbs, W. E. Acree, and M. H. Abraham. Enthalpy of solvation correlations for organic solutes and gases dissolved in acetonitrile and acetone. *Thermochimica Acta*, 484(1-2):65–69, 2009.

[31] C. Mintz, T. Ladlie, K. Burton, M. Clark, W. E. Acree, and M. H. Abraham. Enthalpy of solvation correlations for gaseous solutes dissolved in alcohol solvents based on the abraham model. *Qsar & Combinatorial Science*, 27(5):627–635, 2008.

[32] A. J. Niimi. Solubility of organic-chemicals in octanol, triolein and cod liver oil and relationships between solubility and partition-coefficients. *Water Research*, 25(12):1515–1521, 1991.

[33] L. Oemisch, S. Endo, and K.-U. Goss. Determination of oil-water partition coefficients of polar compounds: silicone membrane equilibrator vs. spme passive sampler. *Analytical and Bioanalytical Chemistry*, 405:2567–2574, 2013.

[34] J.A. Platts, D. Butina, M.H. Abraham, and A. Hersey. Estimation of molecular linear free energy relation descriptors using a group contribution approach. *Journal of Chemical Information and Computer Sciences*, 39:835–845, 1999.

[35] P. Pollien and D. Roberts. Use of solid-phase microextraction for measuring oil-water partition coefficients and correlation with high-performance liquid chromatographic methods for lipophilicity. *Journal Of Chromatography A*, 864(2):183–189, 1999.

[36] C. F. Poole, S. N. Atapattu, S. K. Poole, and A. K. Bell. Determination of solute descriptors by chromatographic methods. *Analytica Chimica Acta*, 652(1-2):32–53, 2009.

[37] C. F. Poole and S. K. Poole. Separation characteristics of wall-coated open-tubular columns for gas chromatography. *Journal Of Chromatography A*, 1184(1-2):254–280, 2008.

[38] T. Rodgers and M. Rowland. Physiologically based pharmacokinetic modelling 2: Predicting the tissue distribution of acids, very weak bases, neutrals and zwitterions. *Journal Of Pharmaceutical Sciences*, 95(6):1238–1257, 2006.

[39] R. K. Rosenbaum, T. E. McKone, and O. Jolliet. Ckow: A dynamic model for chemical transfer to meat and milk. *Environmental Science & Technology*, 43(21):8191, 2009.

[40] W. Schmitt. General approach for the calculation of tissue to plasma partition coefficients. *Toxicology in Vitro*, 22(2):457, 2008.

[41] R.P. Schwarzenbach, P.M. Gschwend, and D.M. Imboden. *Environmental Organic Chemistry*. John Wiley & Sons, 2nd edition, 2003.

[42] L. M. Sprunger, W. E. Acree, and M. H. Abraham. Mathematical correlations for gas-to-olive oil, gas-to-saline solution, and saline solution-to-olive oil partition coefficients based on the goss modified abraham model. *Qsar & Combinatorial Science*, 27(7):890–900, 2008.

[43] A. Stenzel, M. Endo, and K.-U. Goss. Measurements and predictions of hexadecane/air partition coefficients for 387 environmentally relevant compounds. *Journal of Chromatography A*, 1220:132–142, 2012.

[44] A. Stenzel, S. Endo, and K.-U. Goss. Predicting of partition coefficients for complex environmental contaminants:validation of cosmotherm, absolv and sparc. *Environmental Toxicology and Chemistry*, 33(7):1537–1543, 2014.

[45] A. Stenzel, K.-U. Goss, and S. Endo. Experimental determination of polyparameter linear free energy relationship (pp-lfer) substance descriptors for pesticides and other

contaminants: New measurements and recommendations. *Environmental Science & Technology*, 47(24):14204–14214, 2013.

[46] A. Töpel. *Chemie und Physik der Milch*. B.Behr's Verlag, 1st edition, 1994.

[47] S. A. van der Heijden and M. T. O. Jonker. Intra- and interspecies variation in bioconcentration potential of polychlorinated biphenyls: Are all lipids equal? *Environmental Science & Technology*, 45(24):10408, 2011.

[48] P. C. M. van Noort, J. J. H. Haftka, and J. R. Parsons. Updated abraham solvation parameters for polychlorinated biphenyls. *Environmental Science & Technology*, 44(18):7037, 2010.

[49] S. M. van Ruth, I. Grossmann, M. Geary, and C. M. Delahunty. Interactions between artificial saliva and 20 aroma compounds in water and oil model systems. *Journal Of Agricultural And Food Chemistry*, 49(5):2409–2413, 2001.

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Erklärung

Hiermit versichere ich an Eides statt, dass ich die vorliegende Arbeit selbstständig und ohne fremde Hilfe verfasst, keine anderen als die angegebenen Quellen und Hilfsmittel benutzt und die den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen als solche kenntlich gemacht habe. Weiterhin erkläre ich, dass ich noch keine vergeblichen Promotionsversuche unternommen habe und die Dissertation weder in der gegenwärtigen noch in einer anderen Fassung bereits einer anderen Fakultät vorgelegen hat.

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