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Linear solvation energy relationships (LSERs) for robust prediction of partition coefficients between low density polyethylene and water. Part II: Model evaluation and benchmarking

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ABSTRACT

By neglecting the kinetics of leaching, accumulation of leachables in a clinically relevant medium in contact with plastics is principally driven by the equilibrium partition coefficient between the polymer and the medium phase. Based on experimental partition coefficients for a wide set of chemically diverse compounds between low density polyethylene (LDPE) and water, a linear solvation energy relationship (LSER) model was obtained in part I of this study, reading: $logK_{i,LDPE/W} = -0.529 + 1.098 E_i - 1.557 S_i - 2.991 A_i - 4.617 B_i + 3.886 V_i$. The model was proven accurate and precise (n = 156, $R^2 = 0.991$, RMSE = 0.264).

In this part II of the study, for further evaluation and benchmarking of the LSER model $\sim 33\%$ (n = 52) of the total observations were ascribed to an independent validation set. Calculation of partition coefficients $\log_{i,LDPE/W}$ for this validation set was based on experimental LSER solute descriptors. Linear regression against the corresponding experimental values yielded $R^2 = 0.985$ and RMSE = 0.352. When using LSER solute descriptors predicted from the compound's chemical structure by means of a QSPR prediction tool, instead, $R^2 = 0.984$ and RMSE = 0.511 were obtained. These statistics are considered indicative for extractables with no experimental LSER solute descriptors available. By comparison to LSER models from the literature, a strong correlation between the quality of experimental partition coefficients and the chemical diversity of the training set to the model's predictability was observed, the latter of particular relevance for the application domain of the model.

Further, to tentatively match partitioning into LDPE to partitioning into a liquid phase, partition coefficients $\log K_{i,LDPE/W}$ were converted into $\log K_{i,LDPEamorph/W}$ by considering the amorphous fraction of the polymer as effective phase volume only. A LSER model now recalibrated based on the observations for $\log K_{i,LDPEamorph/W}$ exhibited the constant in the equation above to now read -0.079 instead of -0.529 which rendered the model more similar to a corresponding LSER-model for n-hexadencane/water.

Based on LSER system parameters available, the sorption behavior of LDPE could be efficiently compared to the one of polydimethylsiloxane (PDMS), polyacrylate (PA) and polyoxymethylene (POM). The latter, by offering capabilities for polar interactions due to their heteroatomic building blocks, exhibit stronger sorption than LDPE to the more polar, non-hydrophobic domain of sorbates up to an $\log K_{i,LDPE/W}$ range of 3 to 4. Above that range, all four polymers exhibited a roughly similar sorption behavior.

Overall, LSERs were found to represent an accurate and user-friendly approach for the estimation of equilibrium partition coefficients involving a polymeric phase. All intrinsic input parameters can be retrieved from a free, web-based and curated database along with the outright calculation of the partition coefficient for any given neutral compound with a known structure for a given two-phased system.

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	by utilizing these da
Nomenclature	characterize partitioning
	Solvation Energy Relation
C Molar concentration	brated in part I of this st
E, S, A, B, V, L Abraham-type LSER solute descriptors f Volume fraction (0 - 1) K Volume based molar partition coefficient (L/L) V Phase volume Liter (L)	$\label{eq:kildperiod} \begin{array}{l} \log \ K_{i,LDPE/W} = -0.529 \! + \! 1 \\ n = 156, \ R^2 \! = \! 0 \end{array}$
Subscripts i, 1/2 Solute i, partitioning between phases 1 and 2 LDPE Low density polyethylene LDPEamorph Amorphous fraction of low density polyethylene M (Contacting) Medium	A very good correla 0.264 is considered exce solvent/water partition While LSER(EV) mod related solute transfer
M (Contacting) Medium	form applicable to both

1

0 Octanol phase Р Polymer PE Polvethylene

	- J J
W	Water (or aqueous) phase

Superscripts

Crystalline С

eq	At equilibrium

0 Time zero/ initial

1. Introduction and background

Studies on extractables and leachables (E&L) represent the backbone of a chemical safety risk assessment as required for primary contact plastic materials used in the pharmaceutical industry (EMA, 2005; ISO, 2020; U.S. FDA, 1999). As opposed to safety assessments on plastic materials in direct food contact, regulatory thinking with E&L allocates a high priority on the correlation between extractables and leachables in order to estimate and control the ultimate patient exposure risk from material knowledge, i.e. identity and levels of plastic constituents.

The industry approach to E&L studies is largely driven by experimentally-based, analytical protocols (Jenke, 2018). Hence, relating workflows typically do not leverage information on physicochemical factors which dictate the distribution of compounds in the system under investigation, and thus, ultimately patient exposure (Jenke, 2011).

More recently and in line with modern risk-based thinking (ICH Q9, 2009a; ICH Q8(R2), 2009b), predictive concepts and toolsets to characterize the distribution of potentially leaching compounds have been reported and aim to improve this situation (Jenke and Barge, 2015; Welle, 2014; Egert 2018; Saylor et al., 2019; Paudel et al., 2020; Hauk et al., 2021). By following the general paradigms of these attempts, emphasis of the work presented herein is devoted to the many equilibrium-driven, i. e. partition-controlled situations of use involving primary contact plastic materials. Specifically, in such situations, information on the kinetics of migration can be neglected, i.e. the maximum accumulation of leachables upon equilibration of a system can be projected based on partition coefficients of (potential) leachables and their limiting solubilities, only (Bodai, 2016; Jenke, 2015). To this end, in part I of this work (Egert, 2022), thoroughly determined partition coefficients between low density polyethylene (LDPE) and water for 159 compounds spanning a wide range of chemical diversity, molecular weight, vapor pressure, aqueous solubility and polarity (hydrophobicity) were collected (n = 159, MW: 32 to 722, $\log K_{i,O/W}$: -0.72 to 8.61 and logK_{i,LDPE/W}: -3.35 up to 8.36). With respect to their chemical nature, these compounds are generally considered indicative for the wide universe of compounds potentially leaching from plastics (Ball et al., 2012; Bohrer, 2012; Groh et al., 2019; Jenke, 2008; Wiesinger et al., 2021). LDPE, representative for the family of polyolefines, is a material of particular interest for healthcare applications.

By utilizing these data and striving for a robust predictive model to g LDPE (polymer)/water, two types of Linear onships (LSERs) model were successfully calitudy. First, the LSER(EV) model obtained reads:

$$\begin{array}{l} log \; K_{i,LDPE/W} = -0.529 \! + \! 1.098 \; E_i \! - \! 1.557 \; S_i \! - \! 2.991 \; A_i \! - \! 4.617 \; B_i \! + \! 3.886 \; V_i \\ n \! = \! 156, \; R^2 \! = \! 0.991, \; RMSE \! = \! 0.264, \; F \! = \! 3436 \end{array}$$

(1)

tion was obtained ($R^2 = 0.991$). The RMSE of llent but slightly higher than RMSEs typical for systems (0.10 – 0.20) (Ulrich et al., 2017).

dels are preferred for estimation of free-energy between condensed phases, the more generic form applicable to both condensed and gaseous phases is the LSER(VL) model as devised by (Goss, 2005). Established from the same set of experimental partition coefficients, the LSER(VL)-version reads:

$$\label{eq:constraint} \begin{split} & \log K_{i,LDPE/W} = -0.330 - 1.512 \ S_i - 3.396 \ A_i - 5.069 \ B_i + 2.115 \ V_i + 0.594 \ L_i \\ & n = 138, \ R^2 = 0.988, \ RMSE = 0.308, \ F = 2237 \end{split}$$

(2)

In Eqs. (1) and (2), the five descriptor pairs quantify the molecular interactions that govern the partition process: non-specific van der Waals interactions and cavity formation (vV_i, eE_i or lL_i), and specific polar interactions, i. e. dipolarity/polarizability (sS_i) and hydrogenbonding interactions (aA_i and bB_i). The upper case letters denote the solute descriptors as follows: Ei: excess molar refraction in units of $(cm^3mol^{-1})/10$, S_i: dipolarity/polarizability, A_i: solute hydrogen (H)bond acidity, B_i: solute H-bond basicity, V_i: McGowan characteristic molar volume in units of (cm³ mol⁻¹)/100 (Abraham and McGowan, 1987), and Li: logarithmic hexadecane/air partitioning constant, respectively.

The lower case regression coefficients and regression constant (termed phase descriptors or system parameters) e, s, a, b, v, l and c are obtained by multiple linear (MLR) regression of an experimental set of solute properties (e.g. partition coefficient data) for a specific biphasic system. The regression coefficients and constants reflect the differential properties (or differential potential interactions) the solubilizing phases can undergo. Several excellent reviews exist covering the subtleties and general applications of LSERs ((Abraham et al., 2004; Endo and Goss, 2014; Poole et al., 2009).

LSERs have yet not been explored for the estimation of partition coefficients utilized in the safety evaluation of pharmaceutical - and food contact materials. Notwithstanding, a few reports on LSER models characterizing solute sorption from water to polymers in use for environmental sampling, namely polydimethylsiloxane (PDMS), polyacrylate (PA) and polyoxymethylene (POM) exist and are listed in Table 2.

By expanding on the LSER models constructed in part I, study part II presented herein aims at further exploring the performance of the models and to compare them to experimental data and models for partitioning LDPE/water from the literature. Also, based on LSER - predicted partition coefficients polymer/water, the sorption of a wide array of compounds indicative to extractable compounds from plastics to PDMS, PA and POM is briefly inspected.

2. Results and discussion

2.1. Predictivity of LSER(EV) model for $\log K_{i,LDPE/W}$ - Validation Set

To assess accuracy and robustness of the LSER(EV) model for logK_{i,LDPE/W}, an independent validation set of partition coefficients as listed in Table 1 was generated by randomly selecting ~ 33% of the total observations (n = 52 out of 159 partition coefficients) from the full set of experimental observations for $log K_{i,LDPE/W}$ (this study + literature data). The remaining observations were then ascribed to a calibration set (n =

Table 1

Validation Set – measured logK _{i,LDPE/W}	and LSER calculated	values based on the calibration	set (Eq. (3)).
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VALD Salut Case Compand Messand ISR (clr US) deep) Diff Size clr USA deep) Diff 1 104 225 1730 374 2.5 intentlyinspitulates 4.36 4.37 0.12 4.08 0.23 2 105 1470 374 1.5 intentlyinspitulates 4.14 4.33 0.12 4.08 0.23 5 157 6.877 1.5 intentlyinspitulates 0.31 0.34 0.21 0.13 0.34 0.21 0.13 0.23 0.05 7 6.8 2656/17.2 4.8tylpetaxol cald 1.74 0.61 1.13 0.43 0.56 0.55 7 6.8 2656/17.2 4.8tylpetaxol cald 1.74 0.61 0.18 0.35 0.56 0.01 0.15 0.55 0.55 0.55 0.55 0.55 0.55 0.55 0.56 0.64 0.64 0.64 0.66 0.66 0.56 0.56 0.56 0.56 0.56 0.56 0.56 0.5					$\log K_{i,LDPE/W}$				
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	VAL ID	Solute ID	CAS	Compound	Meas-ured	LSER calc ^a (EXP descr)	Diff	LSER calc ^b (OSAR descr)	Diff
11441444.344.124.024.084.024.084.024.084.024.034.03326173.05170.05170.05170.052.020.081.010.03 <th></th> <th></th> <th></th> <th>r · · · r</th> <th>(1)</th> <th>(2)</th> <th>(2)- (1)</th> <th>(3)</th> <th>(3)-(1)</th>				r · · · r	(1)	(2)	(2)- (1)	(3)	(3)-(1)
2 105 170.37.6 1.empl/fluerene 4.11 4.23 0.12 3.18 0.07 0.03 4 18 94.26.8 Butyl-hydrophenosite 0.14 0.02 0.22 0.23 0.25 0.07 5 17.0 85.57.1 1.Nitroomphtalene 0.13 0.34 0.21 0.13 0.48 0.25 6 106.4 10.47.2 4.01/phathene 0.13 0.34 0.23 8.23 0.65 7 10.4 0.653/7.1 2.3.3.4.5.5.6.6.4 0.42 0.63 8.23 0.63 10 0.4 10.47.2.3 Actionolyhemyl 1.14 4.37 0.43 8.23 0.63 11 0.4 10.47.2.4 Actionolyhemyl 1.14 4.37 0.43 0.44 12 10.9 10.9.1.6.2.9 Handerenee 2.52 2.52 0.44 0.43 0.61 13 8.67.37 Handerenee 2.52 2.52 0.01 1.54 0.57 14 9.29.4.5 Actionolyhemenee 2.52 2.52 0.01 2.54 0.53 0.57 15 8.67.37 Handerenee 2.52 2.52 0.51 0.54 0.53<	1	104	2245-38-7	2,3,5-trimethylnaphthalene	4.36	4.24	0.12	4.08	0.28
3 26 92.6.9 Bitly-hydroxyberazet 0.04 0.08 0.02 0.07 0.03 5 157 85.77 1.Nironaphthalene 2.51 2.92 0.08 0.057 7 0.81 206.07.12 4.Nironaphthalene 1.74 0.61 1.31 0.48 0.65 7 0.81 206.57.7.1 2.7.3.3.4.55.0650xatchirthighent 7.47 0.61 1.33 0.48 0.60 7 145 206.57.7.2 2.7.3.4.55.0650xatchirthighent 7.61 0.61 0.33 0.43 0.61 9 205.16.2.7.2 2.5.3.65.0650xatchirthighent 7.61 0.61 0.51 0.53 0.55 0	2	105	1730-37-6	1-methylfluorene	4.11	4.23	-0.12	3.18	0.93
4 18 108-88-3 1-Nitronghihane 2.10 2.02 0.08 1.81 0.03 6 77 18.51 1-Nitronghihane 0.13 0.34 0.21 0.13 0.48 6 2065.17.1 4-Nitronechi acida 1.74 0.61 1.3 0.43 0.22 0.51 7 18.0 2065.77.1 4-Nitronechi acida 1.74 0.61 0.33 0.33 0.61 10 69 105.73.2 1-Adorobjenery 1.61 4.27 0.16 0.84 0.42 11 60 105.73.2 1-Borochi acida 1.72 5.74 0.16 0.32 12 21 51.50.4 1-Borochi acida 1.81 1.80 0.91 0.11 0.02 13 80 97.50.4 1-Borochi acida 1.81 1.80 0.21 1.64 0.17 14 3 97.80.1 Naphrindiarci 1.50 1.53 0.13 0.67 0.78 0.02 15 13 139.60.8 Nophrindiarci 1.50 1.53 0.13 0.60 0.40 16 97 13.98.0.8 1.99.60.9 Nophrindiarci 1.50 1.50 0.20 <	3	26	94-26-8	Butyl-hydroxybenzoate	0.04	-0.08	0.12	0.07	-0.03
5 157 857.7 1311.3 1.34 0.24 0.22 2.59 0.05 7 68 0561.71.2 Hatylbenzoic acid 1.74 0.61 1.33 0.44 1.26 7 168 5266.77.1 2.7.3.7.55.66.4%0acchbripher) 7.62 6.94 0.12 0.13 0.61 9 145 124.7.2 12.7.5.5.66.4%0acchbripher) 7.66 6.94 0.12 0.12 0.12 0.12 11 96 2051.6.2 4.610070bleny1 7.66 6.94 0.12 0.48 0.44 0.32 12 12 591.50 4.610070bleny1 7.6 5.64 0.48 0.44 0.32 13 97.84 10401ersenee 3.78 3.69 0.48 0.44 0.20 14 97.84 10401ersenee 2.82 2.81 0.01 2.64 0.02 15 80 120.9.34 Actorphicersenee 3.69 3.73 0.13 5.74 0.13 16 120.9.34 Actorphicersenee 3.64 3.74 0.14 3.24 0.20 0.21 17 143 120.9.46 Actorphicersenee 3.45 3.25 0.20 3.6	4	18	108-88-3	Toluene	2.10	2.02	0.08	1.81	0.29
677181131-11.310.methyl phtalate0.130.340.210.180.0517813620651.7.7.14.50.y (a).conachlor tiphenyl7.628.150.638.230.61801047.2.31.65.y (b).conachlor tiphenyl7.628.150.638.530.621069102.9.7.21.61.conachlor tiphenyl4.114.270.168.530.621169102.9.7.21.60.oblenzen2.562.740.188.640.440.7312218.91.50.41.00.oblenzen2.562.740.182.840.670.671439.78.1Hutyl nethacrylate1.811.600.211.640.70158.09.12.9Naphtalenzen1.781.720.031.710.0416389.92.9Naphtalenzen2.601.840.761.330.671714.82.19.9.5.8Naphtalenzen2.601.840.761.330.67189.92.03.9Naphtalenzen2.601.840.761.320.67198.72.03.9.5.7Naphtalenzen2.601.840.761.320.61192.03.9.72.04.9.4Nathalenzen2.602.640.600.620.62105.72.05.9.6Naphtalenzen3.613.70.613.610.610.620.61105.72.05.9	5	157	86-57-7	1-Nitronaphthalene	2.51	2.29	0.22	2.59	-0.08
7 68 06051-71-2 4-Barybenzole acid 1.74 0.61 1.13 0.48 1.26 9 145 10472.3 nedcylbenzene 7.06 6.94 0.12 6.91 0.51 9 145 10472.3 nedcylbenzene 7.06 6.94 0.12 6.91 0.51 11 96 129.72.3 Benzolclpyrene 6.12 5.64 0.48 6.44 0.32 12 13 88 67.37 Incorene 3.78 3.69 0.09 3.11 0.76 13 97.84 n.8uptlmethacrylare 2.82 2.81 0.01 2.84 0.024 15 80 12.03.5 Calcorothane 7.8 7.8 7.83 0.30 1.74 0.02 16 12.91.84 nocrylberzene 5.96 5.83 0.31 5.78 0.31 17 143 12.94.94 nocrylberzene 3.43 3.25 0.20 3.16 0.20 18 87 12.93.94 Anthracene 3.43 3.25 0.20 3.16 0.20 19 12.94.94 nocrylberzene 3.04 3.25 0.20 3.16 0.20 10	6	77	131-11-3	Dimethyl phthalate	-0.13	-0.34	0.21	-0.18	0.05
81365263 7.712.2, 3.3, 4.5, 5.6, 6.4 onachlorbipheny7.628.15-0.538.23-0.6110691207.421.4, 5.7, 6.5, 6.4 onachlorbipheny4.114.27-0.163.850.26119129.79Benzolepyrene6.125.62.74-0.163.850.26122191.950.41Iodoberzene2.562.74-0.182.820.26138886.73Pluorene3.781.600.211.640.7714397.84.1natyli methacylate1.811.600.211.640.721538109.69.3Caloroburane1.751.720.031.710.041638109.69.3nocyli-hydroxytenzate2.601.840.761.930.6717143219.90.40nocyli-hydroxytenzate2.601.840.761.930.671859219.98.41Antracene3.613.470.163.200.6119200.922009.01.913.613.470.163.200.6121219.38.44.metylephyl alcohol3.613.470.163.200.61228153.92.4Antracene3.613.470.163.200.612314015.922.72.161.610.591.620.230.61244710.933.244.610.633.63<	7	68	20651-71-2	4-Butylbenzoic acid	1.74	0.61	1.13	0.48	1.26
9 145 144-23 0.14/2.43 0.12 6.91 0.12 6.91 0.12 6.91 0.12 6.91 0.12 6.91 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.22 11 95 95.4 1000000000000000000000000000000000000	8	136	52663-77-1	2,2',3,3',4,5,5',6,6'-Nonachlorbiphenyl	7.62	8.15	-0.53	8.23	-0.61
10699231-62.94.chlorobiphenyi4.114.270.163.850.26119191-50.4Idobenzene2.562.740.182.820.26122191-50.4Idobenzene2.562.740.182.820.093.110.6714397-88-1	9	145	104-72-3	n-decylbenzene	7.06	6.94	0.12	6.91	0.15
1196192-97.2Benzo[e]pyrene6.125.640.486.440.321212591.50Iolorenene2.562.740.182.820.261388867.37Fluorene3.783.690.093.110.6714378.81-Burg interharylate1.811.600.211.440.17158019.90.3Chorobitane2.822.810.012.440.021613129.96.08nocylbenzene5.965.830.135.780.6717143219.96.08nocylbenzene3.663.250.033.690.40188720.98.96.4Acenaphthylenzozte2.601.840.034.690.40198720.99.96.4Acenaphthylenzozte7.127.170.057.470.02201883.29Acenaphthence7.127.170.057.470.330.61211018.70.32.502.603.840.426.020.420.220.41231015.70.32.502.73.44.555.830.426.020.230.11241010.70.22.502.74.4.555.840.140.160.220.412410.702.502.607.127.170.057.470.501.520.53259720.59.9Benzolylihoznithene6.30 <td< td=""><td>10</td><td>69</td><td>2051-62-9</td><td>4-Chlorobiphenyl</td><td>4.11</td><td>4.27</td><td>-0.16</td><td>3.85</td><td>0.26</td></td<>	10	69	2051-62-9	4-Chlorobiphenyl	4.11	4.27	-0.16	3.85	0.26
122191-90.4Indobenzene2.562.740.182.820.26138886.73.7Fucenes3.783.690.093.110.6714397-88.1n-buryl methacrylate1.811.600.211.640.02163891-90.3Naphthalene2.822.810.012.440.021638109-90.3Calorobutane1.751.720.033.710.0417130219-38.6n-Octyl-4-bydroxybenzoate2.601.840.761.330.622090120-12.7Antracene4.294.260.034.690.020.022181859.444-Methylbenzyl alcohat3.613.470.163.200.022281833.24Acenaphthene3.613.470.163.200.022310717.702.612.462.440.884.834.834.232447107.732.Chicorethane6.305.880.426.022.440.232597205.99.2Benzolb/Honerahter6.306.340.114.280.230.112711616605.91.72.3.5hchitharcane7.824.640.114.230.210.2326972.73.44/7.5/5heptabromodiphenylet7.628.270.651.590.230.120.131.240.230.1127<	11	96	192-97-2	Benzo[e]pyrene	6.12	5.64	0.48	6.44	-0.32
138886-73-7Fluorene3.783.690.093.110.6714397.84n-Barty inerhacry later1.811.600.211.640.021158091-20.3Naphthalene2.822.810.012.840.002151432189-60.8n-octy Denzene5.765.830.135.780.81171432189-60.8n-octy Denzene2.601.840.761.930.671987228-96.8Accanaphthylene3.613.470.160.920.02218183-02.9Accanaphthylene3.613.470.160.920.02228183-32.9Accanaphthene3.613.470.160.920.02231070.572.20 loroethanol-2.06-2.940.481.830.430.232447107.07.32.Chloroethanol6.305.880.426.020.28259720.59.2Berochlikorothenet0.810.930.121.220.412640107.441.874.534.640.114.280.2327107.07.32.Chloroethano0.810.336.641.320.630.372810107.441.874.541.534.640.114.280.252915296.641.650.631.640.511.590.67 <td>12</td> <td>21</td> <td>591-50-4</td> <td>Iodobenzene</td> <td>2.56</td> <td>2.74</td> <td>-0.18</td> <td>2.82</td> <td>-0.26</td>	12	21	591-50-4	Iodobenzene	2.56	2.74	-0.18	2.82	-0.26
14397-88-1n-Butyl methacrylate1.811.600.211.640.0121.640.012158091-203Naphthalene2.822.810.0132.840.0021638109-693Chlorobutane1.751.720.031.710.04217143218-608n-octyl-4-hydroxybenzoate2.605.830.135.780.0291890120-12.7Antiracene4.294.260.034.690.040218859-18.44-Methylbenzyl alcohol0.900.740.143.200.021228183.24Acenaphthere7.127.170.057.470.352310053.70.3Dibenz(a, ja janthracene7.127.170.057.470.352597205.99.2Benzo(b)flouronthene6.305.880.426.020.282597205.99.2Benzo(b)flouronthene0.810.930.121.220.0212611616605-91.72.3Dichlorobipenyl4.534.640.114.280.252711616605-91.72.3Dichlorobipenyl5.265.200.679.510.9130320674-27FTOH 6.21.321.470.679.510.9131146123.01n-dodez/berzene6.844.710.134.240.6032519.51-69Benzoinhazofe<	13	88	86-73-7	Fluorene	3.78	3.69	0.09	3.11	0.67
158091-20.3Naphhalene2.822.810.012.840.02163810-50-8noctylbenzene1.751.720.031.710.04171432189-60-8noctylbenzene5.665.840.135.780.181987208-96-8Acenaphtylene2.601.840.761.330.671987208-96-8Acenaphtylene3.613.453.260.203.160.291010.17Athracene4.294.260.203.160.490.41218839.18.44.Methylbenzyl alcohol3.013.470.160.920.022310053.70.3Dibenz(a,h)antracene7.127.17-0.057.47-0.352447107'0 ⁷ .32.Chloroethanel6.305.880.426.020.282540107'0 ⁴ .401.Bromo-2-chloroethane6.305.880.426.020.282640107'0 ⁴ .401.Bromo-2-chloroethane6.306.820.120.23-0.113032647.42.7FTOH 6.21.321.470.151.590.22311080.62.6Methylmentherylate6.625.200.665.050.02325195.16.9Benzothizzole6.746.560.016.490.230.02331210.262.27,4,4,5/5.6-Hetachlorbighenyl5	14	3	97-88-1	n-Butyl methacrylate	1.81	1.60	0.21	1.64	0.17
1638109-69-3Chlorobutane1,751,720.031,710.04171432169-866.830.135.780.135.780.1818591219-38.1n-Octyl-4hytorybenzoate2.601.840.761.390.672090120-12.7Anthracene3.453.250.034.690.02218183.32.9Acapathene3.613.470.143.200.412310053.70.3Dibert(a)lanthracene7.127.17-0.057.47-0.352597205.99-2Benz(b)lanthracene7.127.17-0.057.47-0.352597205.99-2Benz(b)lanthracene0.810.93-0.121.22-0.242697205.99-2Benz(b)lanthracene0.810.93-0.121.22-0.242711616605-91-72,5 Uchloroblphenyl4.534.64-0.114.28-0.252711616605-91-72,5 Uchloroblphenyl6.611.16-0.11-0.11-0.1129154207122-16-52,7 3,4 4 / 5/ ebentahromodiphenylethe7.608.72-0.679.51-0.97-0.5731166120-13n-doceylhenzene8.368.020.347.99-0.37-0.5131194210-232,7 4,4 / 5/ ebentahromodiphenylethe6.625.010.60-0.55-0.68-0.69-0.	15	80	91-20-3	Naphthalene	2.82	2.81	0.01	2.84	-0.02
171432189-60-8n-octylbenzene5.965.800.135.780.181850129.83n-Octylbenzene2.601.840.761.330.671987208-96-8Acenaphtylene3.643.520.203.160.292090120.12Athracene4.294.260.034.690.040218183-32.9Acenaphthene3.613.470.143.200.021228183-32.9Acenaphthene7.127.170.057.470.352447107-07-32.Chforedtnanl-2.06-2.940.881.830.23259720.59-22Bezzobljhuorathene6.305.880.426.020.282640107-04-01-bromo-2-chlorethane0.810.330.121.220.4127154806-26Methyl methacylate0.120.440.114.280.252816806-26Methyl methacylate0.160.511.590.272915427.34,4/5/5-cheptatromodiphenyletter7.608.270.670.510.912915427.34,4/5/5-cheptatromodiphenyletter7.608.270.670.550.61301650.150.023.477.910.500.550.550.550.550.550.550.550.550.550.550.560.520.56	16	38	109-69-3	Chlorobutane	1.75	1.72	0.03	1.71	0.04
18 59 1219-38-1 n-Octyl-4-hydroxybenzoate 2.60 1.84 0.76 1.93 0.67 90 120-127 Anthracene 3.25 3.25 0.03 4.69 0.40 20 90 120-127 Anthracene 4.29 4.26 0.03 4.69 0.02 21 81 83-32-9 Acenaphthone 3.61 3.47 0.14 3.20 0.41 23 100 5370-3 Dibenz[a,h]anthracene 7.12 7.17 -0.05 7.47 -0.35 24 47 107-07-3 2.Chloroethanol -2.06 -2.94 0.88 -1.83 -0.23 25 97 205-99-2 Benzolb/floronthene 6.30 5.88 0.42 6.02 0.23 -0.11 26 47 1760-0 8.37 -0.67 9.51 1.91 0.33 -0.21 -0.21 -0.21 -0.21 -0.21 -0.21 -0.21 -0.21 -0.21 -0.21 -0.21 <td>17</td> <td>143</td> <td>2189-60-8</td> <td>n-octylbenzene</td> <td>5.96</td> <td>5.83</td> <td>0.13</td> <td>5.78</td> <td>0.18</td>	17	143	2189-60-8	n-octylbenzene	5.96	5.83	0.13	5.78	0.18
19 87 208-96-8 Accamplifylere 3.45 3.25 0.20 3.16 0.29 20 90 12.17 Athracene 4.29 4.26 0.03 4.69 0.401 21 81 83.39 Acemphthene 3.61 3.47 0.16 0.92 0.61 23 100 53.70.3 Dibenz[a,h]anthracene 7.12 7.17 -0.05 7.47 -0.35 24 47 107.07.3 2.Chloroethanel 2.06 2.94 0.88 -1.83 -0.22 0.23 25 97 205.91.2 Schloroethane 0.81 0.33 -0.12 1.22 0.41 26 40 107.04.0 1-Bromo-2-chloroethane 0.81 0.21 0.23 0.21 1.22 0.23 0.21 28 14 80-62-6 Methyl methacrylate 7.60 8.27 -0.12 0.23 0.21 0.23 0.21 30 32 647-42.7 FOH 6.2	18	59	1219-38-1	n-Octyl-4-hydroxybenzoate	2.60	1.84	0.76	1.93	0.67
2090120-12-7Anthracene4.294.260.034.69-0.40128183-29-Acenaphthene3.613.470.16-0.920.02221883-29-Acenaphthene3.613.470.143.200.412310053-70-3Dibenz(a,h)anthracene7.127.170.057.470.352447107-07-32.Chloroethanol2.062.940.881.830.232597205-99-2Benzol/Bluoranthene6.305.880.426.020.28261616065-91-72.3-Dichlorobiphenyl4.534.640.114.280.252711616605-91-72.3-Dichlorobiphenyl7.608.270.679.51-1.1129154207122-1652.2/3,4/,5/,6-heptabromodiphenylether7.608.270.679.51-0.273032647-42-7FTOH 6.21.321.470.151.59-0.27311613.3n-ddecylbenzne8.826.840.027.450.663415060348-6092.2/4,4/5/s-hentahromodiphenylether6.826.840.027.450.61351191660-62-32.4/4,5/s-hentahromodiphenylether6.766.840.023.650.12361293830-01-72.2/4,3/5,6/-Hexathorbiphenyl6.766.840.023.650.1037129384	19	87	208-96-8	Acenaphthylene	3.45	3.25	0.20	3.16	0.29
218589-18-44-Methylbenzyl alcohol-0.90-0.74-0.16-0.92-0.02228183.29Acenaphthen3.613.47-0.163.20-0.142310053.70.3Dibenz(a,h)anthracene7.127.17-0.057.47-0.052447107.07.32.Chloroethanol-2.06-2.940.88-1.83-0.232447107.07.41.From-2-chloroethane0.810.39-0.121.22-0.4125141870m-2-chloroethane0.810.39-0.121.22-0.412640107.04.01.From-2-chloroethane0.810.39-0.121.22-0.41271161870m-2-chloroethane0.810.34-0.120.23-0.111.2228180.62.62.01/12.16.52.7,3,4,4,7,6-heptabromolphenylether7.608.27-0.679.51-0.112915420712.16.52.7,3,4,4,7,5-heptabromolphenylether7.608.120.347.99-0.3731146123.01.3n-dodecylbenzene8.368.10-0.314.24-0.60341506034-60.92.7,4,4,5-hentabromolphenylether6.825.84-0.065.05-0.16341506034-60.92.7,4,4,5-hentabromolphenylether6.825.84-0.06-0.84-0.26341505886.447.100.134.24-0.65-0.16<	20	90	120-12-7	Anthracene	4.29	4.26	0.03	4.69	-0.40
228183-32-9Acenaphtene3.613.470.143.200.41321057.03Diben(a,h)anthracene7.127.170.057.470.352447107-07.32.Chlorochanol-2.06-2.940.881.830.232597205.99.2Benzo[b]fluoranthene6.305.880.426.020.282640107-04.01-Bromo-2-chlorochane0.810.93-0.121.22-0.412711616605-91.72.3-Dichlorobiphenyl4.534.64-0.114.280.252810.7122-1652.2,3.4,4,5/5-heptabromodiphenylether7.608.27-0.679.51-0.1529154207122-1652.2,3.4,4,5/5-heptabromodiphenylether7.608.27-0.611.59-0.2731146120-13n-dodecylbenzne8.868.020.347.990.37325195-16-9Benzothizale0.661.16-0.501.35-0.663415060348-60-92.2,4,4,5-Freintabromodiphenylether6.826.84-0.027.45-0.633415060348-60-92.4,4,4'-5-treintabromodiphenylether6.766.84-0.61-0.78-1.013415060348-60-92.4,4,5'-5-treintabromodiphenylether6.766.84-0.630.661.56-0.52-0.130.66-0.51351293830-01.72.4,4,5	21	8	589-18-4	4-Methylbenzyl alcohol	-0.90	-0.74	-0.16	-0.92	0.02
231005370.3Dibenz(a,b)anthracene7.127.170.057.470.03524471070.732.Chloreethanel2.662.940.881.830.232597205.99.2Benzo[b]fluoranthene6.305.880.426.020.282640107.04.01.brome-2-chloreethane0.810.93-0.121.22-0.412716160.69-10.73.2bichlorobiphenyl6.308.28-0.121.22-0.4128180.62.6Methyl methacrylate0.120.24-0.120.23-0.113032647.42.7FTOH 6:21.321.47-0.151.59-0.2731146123-01.3n-dodecylbenzene8.368.020.347.99-0.373392206.44.0Fluoranthene4.844.710.134.34-0.603415060346.092.4',4',5' Fentabromodiphenylether6.826.84-0.027.45-0.633511916606.02.32.4',5' Tricthoribphenyl5.265.200.065.050.21366475-52.5Nitromethane3.753.83-0.086.490.02371293830-01.72.3',3,6',5' Fentachorbiphenyl6.746.560.186.490.03371293380-01.72.3',3,5,5' Tertachorbiphenyl6.720.816.490.033810251.5<	22	81	83-32-9	Acenaphthene	3.61	3.47	0.14	3.20	0.41
2447107.07.32.Chiorechanol-2.06-2.940.88-1.83-0.23259705.99-2Benzo/bl/loronthene6.305.880.426.020.282640107.04.01.Brono-2.chlorothane0.810.930.121.220.412711616605.91.72,3-bichlorobiphenyl4.534.640.114.280.25271540.27122.1652,7,3,4,4,5,6-heptabromodiphenylether7.608.270.679.51-1.913032647.42.7FTOH 6.21.321.470.131.590.3731146123.01.3n-dodecylbenzene8.608.020.347.990.37325195.16.9Benzothlazole0.661.160.501.350.66339226.44.0Floranthene8.626.840.027.450.63341506348.60.92,2',4,4',5-Pentabromodiphenylether6.826.840.027.450.633511916606.02.32,4',5-Fichlorbiphenyl5.265.200.065.050.210.133712938411.22.22,2',3,5,6'-Hexachlorbiphenyl6.746.560.186.490.020.4138102571.58.4Nitomethane3.753.830.080.180.330.040.140.663810251.580.35,5,5' Florathlorbiphenyl6.315.890.12	23	100	53-70-3	Dibenz[a,h]anthracene	7.12	7.17	-0.05	7.47	-0.35
25 97 205-99-2 Benzolbjlhuoranthene 6.30 5.88 0.42 6.02 0.28 26 40 107 0-40 1-Bromo-2-chlorechtame 0.81 0.93 0.12 1.22 0.41 27 116 16605-91-7 2,3-bichlorobiphenyl 4.53 4.64 -0.11 4.28 0.25 28 1 80-62-6 Methyl methacrylate 0.24 0.22 0.24 -0.12 0.23 -0.11 30 154 27.34,47,57-6-heptabromodiphenylether 7.60 8.27 -0.15 1.59 -0.27 31 146 123-01-3 n-dodecylbenzene 8.36 8.02 0.34 7.99 0.37 32 51 95-16-9 Benzothiazole 0.66 1.16 -0.50 1.35 -0.69 33 92 26-44-0 Fluoranthene 6.82 6.84 -0.01 -0.56 0.28 -0.63 35 119 16666-0.23 2.7,4,7-5-Pentabromighenylether 6.82 6.84 -0.02 -0.64 -0.52 36 12 38411-22-2 2.7,3,5,6/-5-Pentabromighenylether 6.76 6.84 -0.08 6.49 -0.23 37 129 38411-2	24	47	107-07-3	2-Chloroethanol	-2.06	-2.94	0.88	-1.83	-0.23
2640107-04-01-Bromo-2-chloroethane0.810.930.121.221.020.41171161660-51-72.3-Dichlorobiphenyl4.534.640.110.230.1129154207122.1652.2,3.4/t.5/s-heptabromodiphenylether7.008.270.679.511.9129154270122.1652.2,3.4/t.5/s-heptabromodiphenylether7.008.270.679.510.2731146123.01n-dodecylbenzene8.368.020.347.990.37325195.16-9Berzothizzole0.661.16-0.501.35-0.693415060348-6092.2/t.4/t.5-Pentabromodiphenylether6.826.84-0.027.45-0.6335191606-0232.4/t.5-Trichlorbiphenyl5.265.200.065.050.213712938411-222.2/3.3/t.6/tHexachlorbiphenyl6.746.560.186.490.2538102571-58-41.4dimetribinaphtalene3.753.83-0.083.650.10381253380-01-72.2/t.4/t.5-Pentachlorbiphenyl6.276.080.196.230.0441120-92-3Nitromethane1.781.690.220.360.10391253380-01-72.2/t.4/t.5-Pentachlorbiphenyl6.746.560.186.490.200.1141120-92-3Nitromethane1.781.630.62 <td>25</td> <td>97</td> <td>205-99-2</td> <td>Benzo[b]fluoranthene</td> <td>6.30</td> <td>5.88</td> <td>0.42</td> <td>6.02</td> <td>0.28</td>	25	97	205-99-2	Benzo[b]fluoranthene	6.30	5.88	0.42	6.02	0.28
2711616605-91-72,3-bichlorobiphenyl4.534.64-0.114.280.2528180-62-6Methyl methacrylate0.120.24-0.120.23-0.1130154207122.1652,2',3,4',5',5-heptabromodiphenylether7.608.27-0.679.51-1.913032647.42-7FTOH 6.21.321.47-0.151.59-0.2731146123.01-3n-dodecylbenzene8.368.020.347.990.37325195-16-9Benzothiazole0.661.16-0.501.350.693392206.44-0Floranthene6.826.84-0.027.45-0.6334150638-60-92,2',4',5' Petabromodiphenylether6.826.84-0.027.45-0.633511916606-02-32,4',5' Trichlorbiphenyl5.265.200.065.05-0.2136647.52-5Niromethane7.753.83-0.086.490.25371293841-22-22,2',3',6',6' Hexachlorbiphenyl6.746.560.186.490.230.0439125338-04.072,2',4',5',5' Tetrachlorbiphenyl6.746.580.186.490.230.0441120214-17.86Ethyl acetae0.65-0.52-0.13-0.680.03421233284-523,5,5' Tetrachlorbiphenyl6.355.29-0.13-0.68 <td>26</td> <td>40</td> <td>107-04-0</td> <td>1-Bromo-2-chloroethane</td> <td>0.81</td> <td>0.93</td> <td>-0.12</td> <td>1.22</td> <td>-0.41</td>	26	40	107-04-0	1-Bromo-2-chloroethane	0.81	0.93	-0.12	1.22	-0.41
28180-62.6Methyl methacrylate0.210.240.120.230.01129154207122-16-52,2',3,4',5',5-heptabromoliphenylether7.608.27-0.679.51-1.913132647-42-7FTOH 6-21.321.47-0.151.59-0.2731146123.01.3n-dodecylbenzene8.368.020.347.990.373292206-44.0Fluoranthene4.844.710.134.240.603415060346-60-92,2',4,4',5-Pentabromoliphenylether6.826.84-0.027.45-0.63351191606-2.32,4',4,5-Pentabromoliphenylether6.826.84-0.027.45-0.6336647.5-2.5Nitromethane-1.78-1.69-0.09-0.78-1.003712938411-22.22,2',3,3',6,6'-Hexachlorbiphenyl6.746.560.186.490.2538102571-58.41,4-dimethylnaphtalene3.753.83-0.083.650.10444120-92.3Cyclopentanone6.91-0.52-0.13-0.680.09-0.684514122141.78.6Hyl actate-0.61-0.52-0.13-0.68-0.99442140-85.5Entyl actafe0.100.08-0.18-0.23-0.1345156330-34.5Triclosan3.302.021.282.70-0.68 <t< td=""><td>27</td><td>116</td><td>16605-91-7</td><td>2,3-Dichlorobiphenyl</td><td>4.53</td><td>4.64</td><td>-0.11</td><td>4.28</td><td>0.25</td></t<>	27	116	16605-91-7	2,3-Dichlorobiphenyl	4.53	4.64	-0.11	4.28	0.25
194154207122.16.52.2', 3.4, 4', 5', 6.1eptabromodiphenylether7.608.270.679.511.1913032647.42.7FTOH 6.21.321.470.151.590.2731146123.01.3n-doceylbenzene8.368.020.347.990.37325195.16.9Benzothizole6.661.160.501.350.693392206.44.0Fluoranthene6.844.710.134.240.633415060348-60.92.2', 4', 5-Pentabromodiphenylether6.826.840.0027.450.633511916606-02.32.2', 4', 5-Pentabromodiphenylether5.265.200.065.050.213612938411-22.22.2', 3', 6, 6' Hexachlorbiphenyl6.746.550.186.490.253712938411-22.22.2', 3', 6, 6' Hexachlorbiphenyl6.746.560.186.490.2538102571-58.41, 4dimethylapathalene3.753.830.083.650.10391253380-01.72.2', 4', 5-Pentachlorbiphenyl6.050.520.130.680.0941120-92.3Cyclopentanone0.91-1.030.12-1.020.0141120141-78Actarisole0.270.290.020.360.99421233384-523.5,5,5'Tetrachlorbiphenyl0.630.610.020.360.9	28	1	80-62-6	Methyl methacrylate	0.12	0.24	-0.12	0.23	-0.11
30 32 647.427 FOH 6:2 1.32 1.47 -0.15 1.59 -0.27 31 146 123.01.3 n-dodecylenzene 8.36 8.02 0.34 7.99 0.37 32 51 9516-9 Benzothiazole 0.66 1.16 -0.50 1.35 -0.69 33 92 206.44.0 Fluoranthene 4.84 4.71 0.13 4.24 0.60 34 150 60348-60-9 2.2',4,4',5-Pentabromodiphenylether 6.82 6.84 -0.02 7.45 -0.63 35 119 16606-02.3 2.4',5.7Tichlorbiphenyl 5.26 5.20 0.06 5.05 0.21 36 64 75.52.5 Nitromethane 1.78 -1.69 0.09 -0.78 -1.00 37 129 38410-12 2.2',4,4',5-Pentachlorbiphenyl 6.74 6.56 0.18 6.49 0.25 0.06 39 125 3830-01-7 2.2',4,4',5-Pentachlorbiphenyl 6.27 6.08 0.19 6.23 0.01 41 20.93 3284-52.5	29	154	207122-16-5	2,2',3,4,4',5',6-heptabromodiphenylether	7.60	8.27	-0.67	9.51	-1.91
31146123.01.3n-dodecylbenzene8.368.020.347.990.37325195.16-9Benzothiazole0.661.16-0.501.35-0.693392206-44.0Fluoranthene4.844.710.134.240.603415060348.60-92,2',4,4',5-Pentabromodiphenylether6.826.84-0.027.45-0.633511916606.02-32,4',5-Trichorbiphenyl5.265.200.065.050.2136647.55.2Niromethane-1.78-1.690.09-0.78-1.003712938411-22-22,2',3,3',6'.6'Hexachlorbiphenyl6.746.560.186.490.2538102571-58.41,4-dimethylnaphthalene3.753.83-0.083.650.104044120-92.3Cyclopentanone0.91-1.030.12-1.020.114122141.78.6Ehyl acetate-0.65-0.52-0.13-0.680.034353100.061Acetanisole0.270.29-0.420.36-0.09442140.88.5Ehyl acetate-0.100.08-0.18-0.230.1345156380.34.5Triclosan3.022.24-1.32-0.69-0.52441010.97.4Acetanisole0.270.29-0.200.11-1.014112380.35.5Triclosan3	30	32	647-42-7	FTOH 6:2	1.32	1.47	-0.15	1.59	-0.27
32 51 95.16-9 Benzothiazole 0.66 1.16 -0.50 1.35 -0.69 33 92 206.44-0 Fluorantene 4.84 4.71 0.13 4.24 0.63 34 150 60348-60-9 2.2', 4, 4', 5-Pentahormodiphenylether 6.82 6.84 -0.02 7.45 0.63 35 119 16606-02-3 2, 4', 5-Pentahormodiphenyle 5.26 5.20 0.06 5.05 0.21 36 64 7.52.5 Nitromethane -1.78 1.69 0.09 -0.78 0.021 37 129 38411-22-2 2, 2', 3, 3', 6, 6'-Hexachlorbiphenyl 6.74 6.56 0.18 6.49 0.20 38 102 571-58.4 1, 4-dimethylnaphthalene 3.75 3.83 -0.08 0.19 6.23 0.04 40 44 120-92.3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.04 41 126 141-78-6 Ethyl acretate 0.67 0.52 0.13 -0.68 0.03 42 123	31	146	123-01-3	n-dodecylbenzene	8.36	8.02	0.34	7.99	0.37
33 92 206.44.0 Fluoranthene 4.84 4.71 0.13 4.24 0.60 34 150 60348-60-9 2,2',4,4',5-Pentabronodiphenylether 6.82 6.84 -0.02 7.45 0.60 35 119 16606-02-3 2,4',5-Trichlorbiphenyl 5.26 5.20 0.06 5.05 0.21 36 64 75.52-5 Nitromethane -1.78 -1.69 -0.09 -0.78 -1.00 37 129 38411-22-2 2,2',3,3',6,6' Hexachlorbiphenyl 6.74 6.56 0.18 6.49 0.25 38 102 571-58-4 1,4-dimethylnaphthalene 3.75 3.83 -0.08 3.65 0.10 40 44 120-92-3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.11 41 2 141-78-6 Ethyl acetate -0.65 -0.52 -0.13 -0.68 -0.03 42 123 3280-54-5 Trictaxhorbiphenyl 6.31 5.89 0.42 5.88 -0.03 43 53 100-06-1	32	51	95-16-9	Benzothiazole	0.66	1.16	-0.50	1.35	-0.69
34 150 60348-60-9 2,2',4,4',5-Pentabromodiphenylether 6.82 6.84 -0.02 7.45 -0.63 35 119 16606-02-3 2,4',5-Trichlorbiphenyl 5.26 5.20 0.06 5.05 0.21 36 64 75-52-5 Niromethane -1.78 -1.69 0.09 -0.78 -1.00 37 129 38411-22-2 2,2',3,3',6,6'-Hexachlorbiphenyl 6.74 6.56 0.18 6.49 0.25 38 102 571-58-4 1,4-dimethylnaphthalene 3.75 3.83 -0.08 3.65 0.10 39 120 38380-01-7 2,2',4,4',5-Pentachlorbiphenyl 6.27 6.08 0.19 6.23 0.04 41 120-92-3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.11 41 2 141-78-6 Ethyl acetate -0.65 -0.52 -0.13 -0.68 -0.33 42 123 3284-52-5 3,3',5,5'-Tetrachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 43 5 100-06	33	92	206-44-0	Fluoranthene	4.84	4.71	0.13	4.24	0.60
35 119 $16606-02-3$ $2,4',5-Trichlorbiphenyl$ 5.26 5.20 0.06 5.05 0.21 36 64 $75.52-5$ Nitromethane 1.78 1.69 0.09 0.78 1.00 37 129 $38411-22-2$ $2,2',3,3',6'$.Heachlorbiphenyl 6.74 6.56 0.18 6.49 0.21 38 102 $571.58-4$ $1,4$ -dimethylnaphthalene 3.75 3.83 0.08 3.65 0.10 39 125 $3830-01-7$ $2,2',4,4',5$ -Pentachlorbiphenyl 6.27 6.08 0.19 6.23 0.044 40 44 $120-92-3$ Cyclopentanone 0.91 1.03 0.12 1.02 0.11 41 23 $3328+52-5$ $3,5,5,5'.Tetrachlorbiphenyl6.315.890.425.880.434353100-061Acetanisole0.270.290.020.36-0.09442140-88-5Ethyl acrylate0.100.08-0.180.230.1345100-061Acetanisole0.270.290.020.36-0.09442140-88-5Ethyl acrylate0.000.070.180.230.1345156380-34-5Trichosan3.302.021.282.700.63451499.748.4,6-7Tibromophenol2.301.870.432.590.25<$	34	150	60348-60-9	2,2',4,4',5-Pentabromodiphenylether	6.82	6.84	-0.02	7.45	-0.63
36 64 75-52-5 Nitromethane -1.78 -1.69 -0.09 -0.78 -1.00 37 129 38411-22-2 22',3,3',6,6'-Hexachlorbiphenyl 6.74 6.56 0.18 6.49 0.25 38 102 571-58-4 1,4-dimethylnaphthalene 3.75 3.83 0.08 3.65 0.10 40 44 120-92-3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.11 41 22 141-78-6 Ethyl acetate -0.65 -0.52 -0.13 -0.68 0.33 42 123 33284-52-5 3,3',5,5'.7 Etrachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 43 53 100-06-1 Acetanisole 0.27 0.29 -0.22 0.36 -0.09 44 2 140-88-5 Ethyl acrylate 0.10 0.88 -0.12 0.36 -0.23 0.36 45 156 3380-34-5 Triclosan 3.30 2.02 1.28 2.70 0.60 46 61 109-74-0 B	35	119	16606-02-3	2,4',5-Trichlorbiphenyl	5.26	5.20	0.06	5.05	0.21
37 129 $38411-22.2$ $2,2',3,3',6,6'$ $4exchlorbiphenyl6.746.560.186.490.2538102571-58.41,4-dimethylnaphthalene3.753.83-0.083.650.103912538300.172,2',4,4',5-Pentachlorbiphenyl6.276.080.196.230.044044120-92.3Cyclopentanone-0.91-1.030.12-1.020.114122141.78.6Ethyl acetate-0.65-0.52-0.13-0.680.33421233284.52.53,3',5,5'.7etrachlorbiphenyl6.315.890.425.880.434353100-6-1Acetanisole0.270.29-0.120.36-0.09442140-88.5Ethyl acrylate0.100.08-0.120.36-0.09442140-88.5Ethyl acrylate-0.100.08-0.18-0.230.13451563380-34.5Ticlosan3.302.021.282.700.604661109-74.0Butyronitrile-0.90-0.70-0.200.11-1.014775118-79.62,4,6-Tribromophenol2.301.870.432.59-0.2948139100-41.4Ethylbenzene2.485.54-0.06$	36	64	75-52-5	Nitromethane	-1.78	-1.69	-0.09	-0.78	-1.00
38 102 571-58-4 1,4-dimethylnaphthalene 3.75 3.83 -0.08 3.65 0.10 39 125 38380-01-7 2,2',4,',5-Pentachlorbiphenyl 6.27 6.08 0.19 6.23 0.04 40 44 120-92-3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.11 41 22 141-78-6 Ethyl acetate -0.65 -0.52 -0.13 -0.68 0.43 42 123 33284-52-5 3,3',5,5'-Tetrachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 43 53 100-06-1 Acetanisole 0.27 0.29 -0.02 0.36 -0.09 44 2 140-88-5 Ethyl acrylate -0.10 0.08 -0.18 -0.23 0.31 45 156 380-34-5 Triclosan 3.30 2.02 1.28 2.70 0.60 46 61 109-74-0 Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 47 75 118-79-6 2,4,6 Tribromophenol </td <td>37</td> <td>129</td> <td>38411-22-2</td> <td>2,2',3,3',6,6'-Hexachlorbiphenyl</td> <td>6.74</td> <td>6.56</td> <td>0.18</td> <td>6.49</td> <td>0.25</td>	37	129	38411-22-2	2,2',3,3',6,6'-Hexachlorbiphenyl	6.74	6.56	0.18	6.49	0.25
39 125 38380-01-7 2,2',4,4',5-Pentachlorbiphenyl 6.27 6.08 0.19 6.23 0.04 40 44 120-92-3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.11 41 22 141-78-6 Ethyl acetate -0.65 -0.52 -0.13 -0.68 0.42 42 123 33284-52-5 3,3',5,5'-Tetrachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 43 53 100-06-1 Acetanisole 0.27 0.29 -0.18 -0.23 0.36 -0.09 44 2 140-88-5 Ethyl acrylate -0.10 0.08 -0.18 -0.23 0.11 45 156 3380-34-5 Triclosan 3.30 2.02 1.28 2.70 0.60 46 61 109-74-0 Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 47 75 118-79-6 2,4,6 -Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48 139 100-41-4 E	38	102	571-58-4	1,4-dimethylnaphthalene	3.75	3.83	-0.08	3.65	0.10
40 44 120-92.3 Cyclopentanone -0.91 -1.03 0.12 -1.02 0.11 41 22 141-78-6 Ethyl acetate -0.65 -0.52 -0.13 -0.68 0.03 42 123 33284-52-5 3,3',5,5'-Tetrachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 43 53 100-06-1 Acetanisole 0.27 0.29 -0.02 0.36 -0.09 44 2 140-88-5 Ethyl acrylate 0.10 0.08 -0.18 -0.23 0.13 45 156 3380-34-5 Triclosan 3.30 2.02 1.28 2.70 0.60 46 61 109-74-0 Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 47 75 118-79-6 2,4,6-Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48 139 100-41-4 Ethyl acrylatence 2.48 2.54 -0.06 2.53 -0.05 50 29 123 1.4-160xane -1.39	39	125	38380-01-7	2,2',4,4',5-Pentachlorbiphenyl	6.27	6.08	0.19	6.23	0.04
4122141-78-6Ethyl acetate -0.65 -0.52 -0.13 -0.68 0.03 421233284-52-5 $3,3',5,5'$ -Tetrachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 4353100-06-1Acetanisole 0.27 0.29 -0.02 0.36 -0.03 4421408-85Ethyl acrylate 0.10 0.08 -0.12 0.23 0.13 451563380-34-5Triclosan 3.30 2.02 1.28 2.70 0.60 4661109-74-0Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 4775118-79-6 $2,4,6$ -Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48139100-41-4Ethylbenzene 2.48 2.54 -0.06 2.53 -0.05 4912141464-43-1 $2,3,3',4'$ -Tetrachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 5029123-91-1 $1,4$ -Dioxane -1.39 -1.59 0.20 -1.38 -0.01 511061376+18-6 $1,4,6,7$ -tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 5257132-65-0Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53Na1620-98-0 3 -ter-butyl-4-hydroxybenzaldehyde 2.81 $?$ -0.13 -0.13	40	44	120-92-3	Cyclopentanone	-0.91	-1.03	0.12	-1.02	0.11
42 123 $33284-52-5$ $3,3',5,5'$ -tertachlorbiphenyl 6.31 5.89 0.42 5.88 0.43 43 53 $100-0-1$ Acetanisole 0.27 0.29 -0.02 0.36 -0.09 44 2 $140-88-5$ Ethyl acrylate -0.10 0.08 -0.18 -0.23 0.13 45 156 $330-34-5$ Triclosan 3.30 2.02 1.28 2.70 0.60 46 61 $109-74-0$ Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 47 75 $118-79-6$ $2,4,6$ -Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48 139 $100-41-4$ Ethylbenzene 2.48 2.54 -0.06 2.53 -0.05 49 121 $41464.43-1$ $2,3,3'4'$ -Tertachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 50 29 $123-91-1$ $1,4-10$ xame -1.39 -1.59 0.20 -1.38 -0.05 51 106 $13764.18-6$ $1,4,6,7$ -tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 $132-65-0$ Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na $1620-98-0$ 3 -ter-butyl-4-hydroxybenzaldehyde 2.81 $?$ $ 2.78$ 0.03	41	22	141-78-6	Ethyl acetate	-0.65	-0.52	-0.13	-0.68	0.03
4353100-06-1Acetanisole0.270.29-0.020.36-0.09442140-88-5Ethyl acrylate-0.100.08-0.18-0.230.13451563380-34-5Triclosan3.302.021.282.700.604661109-74-0Butyronitrile-0.90-0.70-0.200.11-1.014775118-79-62.4,6-Tribronophenol2.301.870.432.59-0.2948139100-41-4Ethylbarzene2.482.54-0.062.53-0.054912141464-4312,3,3',4'-Tetrachlorbiphenyl5.865.720.145.610.255029123-91-11,4-Dioxane-1.39-1.590.20-1.38-0.015110613764-18-61,4,6,7-tetramethylnaphthalene4.784.740.044.460.325257132-65-0Dibenzothiophene4.024.10-0.083.860.1653Na1620-98-03-ter-butyl-4-hydroxybenzaldehyde2.81?-2.780.03	42	123	33284-52-5	3,3',5,5'-Tetrachlorbiphenyl	6.31	5.89	0.42	5.88	0.43
442140-88-5Ethyl acrylate -0.10 0.08 -0.18 -0.23 0.13 451563380-34-5Triclosan 3.30 2.02 1.28 2.70 0.60 4661109-74-0Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 4775118-79-6 $2,4,6$ -Tribronophenol 2.30 1.87 0.43 2.59 -0.05 48139100-41-4Ethylbenzene 2.48 2.54 -0.06 2.53 -0.05 4912141464-43-1 $2,3,3',4'$ -Tertachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 5029123-91-1 $1,4$ -Dioxane -1.39 -1.59 0.20 -1.38 -0.01 5110613764-18-6 $1,4,6,7$ -tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 5257132-65-0Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53Na1620-98-03-ter-butyl-4-hydroxybenzaldehyde 2.81 ? $ 2.78$ 0.03	43	53	100-06-1	Acetanisole	0.27	0.29	-0.02	0.36	-0.09
45 156 3380-34-5 Triclosan 3.30 2.02 1.28 2.70 0.60 46 61 109-74-0 Butynoitrile -0.90 -0.70 -0.20 0.11 -1.01 47 75 118-79-6 2,4,6-Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48 139 100-41-4 Ethylbenzene 2.48 2.54 -0.06 2.53 -0.05 49 121 41464-43-1 2,3,3',4'-Tetrachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 50 29 123-91-1 1,4-Dioxane -1.39 -1.59 0.20 -1.38 -0.01 51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-ter-butyl-4-hydroxybenzaldehyde 2.81 ? 2.78 0.03	44	2	140-88-5	Ethyl acrylate	-0.10	0.08	-0.18	-0.23	0.13
46 61 109-74-0 Butyronitrile -0.90 -0.70 -0.20 0.11 -1.01 47 75 118-79-6 2,4,6-Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48 139 100-41-4 Ethylbenzene 2.48 2.54 -0.06 2.53 -0.05 49 121 41464-43-1 2,3,3',4'-Tetrachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 50 29 123-91-1 1,4-Dioxane -1.39 -1.59 0.20 -1.38 -0.01 51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? 2.78 0.03	45	156	3380-34-5	Triclosan	3.30	2.02	1.28	2.70	0.60
47 75 118-79-6 2,4,6-Tribromophenol 2.30 1.87 0.43 2.59 -0.29 48 139 100-41-4 Ethylbenzene 2.48 2.54 -0.06 2.53 -0.05 49 121 41464-43-1 2,3,3',4'-Tetrachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 50 29 123-01-1 1,4-bioxane -1.39 -1.59 0.20 -1.38 -0.01 51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? 2.78 0.03	46	61	109-74-0	Butyronitrile	-0.90	-0.70	-0.20	0.11	-1.01
48 139 100-41-4 Ethylenzene 2.48 2.54 -0.06 2.53 -0.05 49 121 41464-43-1 2,33'4'-Tetrachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 50 29 123-91-1 1,4-Dioxane -1.39 -1.59 0.20 -1.38 -0.01 51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? 2.78	47	75	118-79-6	2,4,6-Tribromophenol	2.30	1.87	0.43	2.59	-0.29
49 121 41464-43-1 2,3,3',4'-Tetrachlorbiphenyl 5.86 5.72 0.14 5.61 0.25 50 29 123-91-1 1,4-Dioxane -1.39 -1.59 0.20 -1.38 -0.01 51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? — 2.78 0.03	48	139	100-41-4	Ethylbenzene	2.48	2.54	-0.06	2.53	-0.05
50 29 123-91-1 1,4-Dioxane -1.39 -1.59 0.20 -1.38 -0.01 51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? — 2.78 0.03	49	121	41464-43-1	2,3,3',4'-Tetrachlorbiphenyl	5.86	5.72	0.14	5.61	0.25
51 106 13764-18-6 1,4,6,7-tetramethylnaphthalene 4.78 4.74 0.04 4.46 0.32 52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? — 2.78 0.03	50	29	123-91-1	1,4-Dioxane	-1.39	-1.59	0.20	-1.38	-0.01
52 57 132-65-0 Dibenzothiophene 4.02 4.10 -0.08 3.86 0.16 53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? - 2.78 0.03	51	106	13764-18-6	1,4,6,7-tetramethylnaphthalene	4.78	4.74	0.04	4.46	0.32
53 Na 1620-98-0 3-tert-butyl-4-hydroxybenzaldehyde 2.81 ? — 2.78 0.03	52	57	132-65-0	Dibenzothiophene	4.02	4.10	-0.08	3.86	0.16
	53	Na	1620-98-0	3-tert-butyl-4-hydroxybenzaldehyde	2.81	?	_	2.78	0.03

^a Calculated by using Eq. (3).

^b Calculated by using Eq. (3), but employing QSPR-based solute descriptors instead of experimental solute descriptors for test solutes.

104) to construct a LSER(EV)-model:

$$logK_{i,LDPE/W} = -0.499 + 1.111 \text{ E}_i - 1.607 \text{ S}_i - 3.400 \text{ A}_i - 4.517 \text{ B}_i + 3.870 \text{ V}_i$$

n = 104, R²=0.994, RMSE=0.220, F=3287
(3)

Further statistics associated to Eq. (3) is provided in Table SI 1 of the supplemental information (SI).

For the validation set, calculated values were again derived but now based on LSER Eq. (3) for the calibration set and were linearly regressed against the experimentally determined values, resulting in:

 $logK_{i,LDPE/W} exp = 0.98 (0.02) \cdot logK_{i,LDPE/W} LSER / expdesc + 0.16 (0.07)$ n = 52, R² = 0.985, RMSE = 0.352, F = 3218 (4)

(3)

The essentially unit slope and close to zero intercept of the regression line for experimental vs. predicted values for the independent validation set supports excellent accuracy of the calibrated LSER model for $\log K_{i,LDPE/W}.$ With $R^2 = 0.985$ and RMSE = 0.352, a good precision of estimates could be demonstrated.

The universe of chemicals potentially leaching from plastics for medicinal and medical device applications comprises a considerable number of chemical structures with no experimental LSER solute



Fig. 1. LSER-predicted partition coefficients $\log K_{i,LDPE/W}$ for the validation set calculated from (i) experimental solute descriptors and (ii) QSPR-predicted solute descriptors against experimental partition coefficients.

et al., 2019; Ulrich and Ebert, 2022), it appears appropriate stating that the chemical nature of the majority of non-ionic extractable compounds is well within the domain of LSERs.

2.2. Evaluation of a LSER screening model for polyethylene from the literature

For polyethylene (PE), amongst other polymers, Reppas-Chrysovitsinos and coworkers (Reppas-Chrysovitsinos et al., 2016), have compiled an extensive set of literature data (n = 383) on logK_{i,PE/W}. Here, values originated from studies involving various types of polyethylene in combination with predominantly environmental contaminants, rendering the compound set to be of some limited chemical diversity. Based on these data and utilizing QSPR-based solute descriptors (ABSOLV Version 15.01), the authors constructed an LSER ("VL"-type) model by emphasizing that the character of the model is "for screening" due to its generation and purpose:

(6)

Seeking comparison to the data from the study herein, first, in addition to the experimentally based LSER(VL) model according to Eq. (2) and similarly to Eq. (6), an LSER ("VL"-type) screening model was also calibrated based on our full dataset and QSPR-based solute descriptors:

$$\begin{split} \log & K_{i,\text{PE/W}} &= -0.740 - 1.241 S_{i,\text{qspr}} - 3.651 A_{i,\text{qspr}} - 4.680 B_{i,\text{qspr}} + 2.407 V_{i,\text{qspr}} + 0.516 L_{i,\text{qspr}} \\ n &= 156, \text{R}^2 = 0.960, \text{RMSE} = 0.571, \text{F} = 711 \end{split}$$

descriptors available. In such a case, the LSER solute descriptors must be calculated by means of a quantitative structure property relationship (QSPR) algorithm (Jover et al., 2004; Platts et al., 2000, 1999; Ulrich et al., 2017) with an inherently lower quality of the obtained descriptors when compared to thoroughly obtained experimental descriptors (see below).

By now deploying solute descriptors generated by a QSPR as implemented in the publicly available LSER database (Ulrich et al., 2017), predicted values for the validation set (still calculated by Eq. (3)) now gave the correlation:

$$\begin{split} \log & K_{i,LDPE/W} &= 0.98(0.03) \cdot \log K_{i,LDPE/W} LSER / QSARdesc + 0.07(0.11) \\ & n &= 52, R^2 = 0.984, RMSE = 0.511, F = 1500 \end{split}$$

Again, an essentially unit slope and intercept of the regression line indicates high accuracy of the model while R^2 =0.984 and RMSE = 0.511 suggest still acceptable predictions also for a compound set with no experimental solute descriptors available. Both the values predicted by using experimental - and QSPR-derived solute descriptors for the validation set are plotted against experimental partition coefficients in Fig. 1. Note that one has to be cautious with extrapolating this result to compounds exhibiting a higher degree of chemical complexity, for example, multifunctionality in combination with sterical variability. For such structures, QSPR predicted solute descriptors might be distinctly less reliable (Stenzel et al., 2014). With research on the improvement of algorithms to predict LSER solute descriptors ongoing (Niederquell with further statistics associated to Eq. (7) provided in Table SI 2 of the SI.

Comparing Eqs. (6) and (7), an only weak match between the two models was found with strong disparities of the system parameters c, s and v. Reversely, Eq. (6) matched our full dataset with only $R^2 = 0.861$ and RMSE = 1.18 when based on QSPR solute descriptors and $R^2 = 0.858$ and RMSE = 1.25 when based on experimental solute descriptors. Both variabilities are considered inappropriate.

In contrast, Eqs. (7) and (2) along with associated statistics show appreciable similarity. Thus, in conclusion, it appears that discrepancies between Eqs. (6) and (7) mainly result from a high variability in materials and/or inclusion of inaccurate partition coefficients in the literature dataset used in the cited work.

Further, in a very recent work (Zhu et al., 2021), Zhu and coworkers, along with non-linear QSPR-approaches for partitioning low density polyethylene/water, reported a pp-LFER (LSER) model derived from a large set of (n = 120) hydrophobic chemicals of interest to environmental monitoring. Their optimized model reads:

$$\begin{array}{rcl} \log K_{i,PE/W} &=& -0.957 + 1.186B + 3.592V \\ n &=& 96, R^2 = 0.898, RMSE = 0.300, F = 420 \end{array} \tag{8}$$

The model revealed statistically insignificant values for e, s and a and was successfully characterized and validated by means of dedicated statistical tests as recommended by internationally accepted reports and guidelines (Gramatica, 2007, 2013; OECD, 2007). Comparison of the

Table 2		
Overview of LSER and log-linear models for polymer/water and solvent/water systems (log K	data near	25°C)

Model no.	Log K for system ^a	Data set	Model type ^a	LSER system parameters ^a											
				e/l	s	а	b	v	1	c	Ν	\mathbb{R}^2	RMSE	F	Reference
1	PDMS/water	_	LSER	0.601	- 1.416	- 2.523	-4.107	3.637	_	0.268 (0.038)	170	0.993	0.171	4475	(Sprunger et al., 2007)
	(L _{water} /L _{PDMS})		EV	(0.043)	(0.073)	(0.092)	(0.084)	(0.044)							
2	POM/water	_	LSER	+ 0.39	0.28	0.46	-3.98	+ 2.98		- 0.37	116	0.986	0.24	-	(Endo et al., 2011b)
	(L _{water} /kg _{POM})		EV	(0.06)	(0.10)	(0.15)	(0.09)	(0.10)		(0.11)					
3	PA/water	_	LSER	+ 0.50	- 0.16	0.16	-4.00	3.28		- 0.12	79	0.97	0.23	-	(Endo et al., 2011a)
	(L_{water}/L_{PA})		EV	(0.10)	(0.16)	(0.10)	(0.15)	(0.11)		(0.08)					
4	n-hexadecane/water	_	LSER	+ 0.667	- 1.617	- 3.587	-4.869	+ 4.433		0.087	_	_	_	_	(Stephens et al., 2012)
	(Lwater/Lsolvent)		EV	(na)	(na)	(na)	(na)	(na)		(na)					
5	n-hexane/water	—	LVER	0.560	-1.710	-3.578	-4.939	4.463		0.333	201	0.996	0.156	8671	(Stephens et al., 2012)
	(L _{water} /L _{solvent})		EV	(0.014)	(0.053)	(0.051)	(0.065)	(0.037)		(0.032)					
6	1-octanol/w (wet)	—	LSER	0.56	-1.05	0.03	-3.46	3.81		0.09	_	_	_	_	(Abraham and Acree, 2010)
	(L_{water}/L_{PA})		EV	(na)	(na)	(na)	(na)	(na)		(na)					
7	LDPE/water	—	LSER	0.7	-0.9	-2.7	-3.9	+ 0.8	+ 0.3	- 0.9	383	0.79	1.16	_	(Reppas-Chrysovitsinos et al., 2016)
	(L_{water}/L_{PE})		VL (QSAR)	(na)	(na)	(na)	(na)	(na)	(na)	(na)					
8	LDPE/water	full set	LSER	0.516	- 1.241	-3.651	-4.680	2.407	_	-0.740 (0.172	156	0.960	0.571	711	this study
	(L_{water}/L_{LDPE})		VL (QSAR)	(0.063)	(0.201)	(0.270)	(0.283)	(0.266)							
9	LDPE/water	full set	LSER	0.594	- 1.512	-3.396	-5.069	2.115	—	-0.330 (0.103	138	0.988	0.308	2237	this study
	(L_{water}/L_{LDPE})		VL (EXP)	(0.036)	(0.105)	(0.152)	(0.140)	(0.155)							
10	LDPE/w	full set	LSER	1.098	- 1.557	- 2.991	-4.617	3.886	—	-0.529 (0.077)	156	0.991	0.264	3436	this study
	$[L_{water}/L_{LDPE}]$		EV	(0.047)	(0.082)	(0.117)	(0.111)	(0.059)							
11	LDPEamorph/w	full set	LSER	1.099	- 1.553	- 2.979	-4.617	3.889	—	-0.529 (0.077)	156	0.996	0.267	3370	
	$[L_{water}/L_{LDPE}]$		EV	(0.047)	(0.081)	(0.12)	(0.110)	(0.058)							
12	LDPE/w	Calibration	LSER	1.111	- 1.607	- 3.400	-4.516	3.870	—	-0.499 (0.077)	156	0.994	0.220	3287	this study
	$[L_{water}/L_{LDPE}]$	Set	EV	(0.049)	(0.081)	(0.126)	(0.108)	(0.065)							
13	LDPE/w	weak HD/HA only	LL	1.18 (0.01	l 4) log K _{O/V}	_v – 1.33 (0.0)69)				115	0.984	0.313	7046	this study
14	$[L_{water}/L_{LDPE}]$	full set	LL	1.26 (0.02	28) log K _{O/V}	_/ – 1.99 (0.1	125)				156	0.930	0.742	2040	this study

^a For abbreviations and information on model details see text.



Fig. 2. Structural repeat units of polymers.

system parameters with the model from this study given by Eq. (1) reveals a comparable contribution of molecular size (v = 3.592 vs. v = 3.886), however, the remaining system parameters (e, s, a = 0; b = +

1.186 vs. b = -4.167) suggest a notable disparity of predictions obtained from Eqs. (1) and (8) if applied to more polar compounds, especially if they are capable to undergo hydrogen-bonding interactions. Mainly, this is expected to affect the applicability domain of the model which directly corresponds to its underlying training set. As the training set applied to derive Eq. (8) is restricted to widely hydrophobic, weak hydrogen donors / - acceptors, respectively, this accordingly, restricts the application domain of the model.

2.3. Comparison of solute partitioning from water into LDPE, n-hexadecane and selected polymers

Given the structural similarity of the polymer backbone to that of linear hydrocarbons, the partitioning behavior of LDPE was previously supposed to be close to the one of n-hexadecane (Hale et al., 2010). Deploying the full set of test solutes, this can indeed be confirmed by plotting LSER calculated logarithmic partition coefficients for LDPE/water versus those for n-hexadecane/water (Fig. 3A). It is noted that, in general, compounds show stronger sorption to n-hexadecane than to LDPE, with a more pronounced tendency at increasing hydrophobicity and size of molecule. Naturally, this behavior is also expressed by the differences in system parameters c (-0.529 for LDPE/w versus 0.667 for n-hexadecane/w) and as well by the system parameter v accounting for molecular volume and therefore, cavity formation energy (3.886 for



Fig. 3. Comparison of the differential sorption behavior polymer-water of selected polymers based on LSER calculated partition coefficients: $\log K_{i,LDPE/W}$ vs. $\log K_{i,n-hexadecane/W}$ (A) $\log K_{i,LDPE/W}$ vs. $\log K_{i,PDMS/W}$ (B) $\log K_{i,LDPE/W}$ vs. $\log K_{i,PDM/W}$ (C) $\log K_{i,LDPE/W}$ vs. $\log K_{i,POM/W}$ (D).



Fig. 4. Comparison of LSER system parameters for partition systems polymer/water as compared to n-hexadecane/water and 1-octanol/water.

Table 3

Experimental values for logK_{i, PE/W} from the literature along with their logK_{i, O/W} and logK_{i, PE/W} values calculated by the COSMO-RS method and by LSER

ID	CAS no	Compound	$logK_{i,\ O/W} \ ^a$	$logK_{i,\ PE/W} \ ^{b}$			Hydrogen donor/acceptor strength
				Experi- mental. ^c	COSMO- RS ^d	LSER ^e	
1	99-96-7	4-Hydroxybenzoic acid	1.42	-0.84	-3.64	-2.07	strong HD/weak HA
2	99-76-3	Methyl-4-hydroxybenzoate	1.86	-0.72	-1.44	-1.42	strong HD/weak HA
3	589-18-4	4-Methylbenzyl alcohol	1.49	-0.75	-0.04	-0.66	strong HD/HA
4	118-90-1	2-Methylbenzoic acid	2.35	-0.13	-0.34	-0.32	strong HD/weak HA
5	94-13-3	Propyl-4-hydroxybenzoate	2.93	0.08	-0.54	-0.34	strong HD/weak HA
6	84-66-2	Diethyl phthalate	2.70	0.80	1.66	0.68	weak HD/strong HA
7	108-88-3	Toluene	2.68	1.57	1.86	2.00	weak HD/HA
8	20170-32-	3,5-Di-tert-butyl-4-hydroxyphenyl propanoic acid	4.48	1.42	1.96	1.29	strong HD/HA
	5						
9	96-76-4	2,4-Di-tert-butyl phenol	4.86	2.47	2.96	2.72	strong HD/weak HA
10	128-37-0	2,6-Di-tert-butyl-4-methyl phenol	5.32	3.21	4.76	3.99	strong HD/weak HA
11	117-81-7	Bis(2-ethylhexyl) phthalate	8.71	5.22	6.96	6.14	weak HD/strong HA
12	2082-79-3	Octadecyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate	13.9	8.19	13.3	12.1	strong HD/HA

^a Values calculated by Advanced chemistry Development (ACD) Software V8.14 for Solaris as reported in (Gasslander et al., 2007).

^b Data from (Gasslander et al., 2007), measured by cosolvency method.

^c Non-specified type of polyethylene.

^d Calculated by COSMOR-RS (FV) method as reported in (Loschen and Klamt, 2014).

^e Calculated by LSER Eq. (1).

^f See classification in (Egert, 2022).

LDPE/w versus 4.869 for n-hexadecane/w (see Table 2)). While the constant c causes the overall offset from the 1:1 line, a larger system parameter v for n-hexadecane translates to a stronger sorption to n-hexadecane with increasing molecular size/volume.

Sorption to polymers can be loosely divided into two general cases. Firstly, situations involving amorphous ("liquid like") polymers, which exhibit linear sorption isotherms with absorption being the dominating mechanism of sorption into the macromolecular network. Secondly, polymers of significant crystallinity and polymorphic structures often give rise to more complex sorption mechanisms, e. g. surface sorption subject to saturation, nano-scaled capillary effects and, as a result, nonlinearity of sorption isotherms (Fang and Vitrac, 2017; Guo et al., 2012; Uber, 2019). Furtheron, polymer crystallites are deemed inaccessible to a solute which consequently would lead to the effective polymer volume being similar to its amorphous fraction, only. However, in general, published experimental partition coefficients involving a polymer phase have not been calculated in account of the polymer's crystallinity (see Table 2). If the polymer's accessible volume is corrected by crystallinity, this would be expected to affect the constants in both LSER approaches (Goss, 2011; Hale et al., 2011; Loschen and Klamt, 2014; Van Noort,

2012).

Hence, to account for disparities in total-versus accessible polymeric phase volume a related LSER model requires calibration based on partition coefficients calculated from the accessible (amorphous) experimental polymer phase volume to render it comparable to models for (organic) liquid phase systems.

In part I of this study, partition coefficients between LDPE and water, $\log K_{i,LDPE/W}$, were thoroughly obtained from equilibrium concentrations as measured in both phases:

$$\log K_{i,LDPE/W} = \log \left(\frac{C_{i,LDPE}^{eq}}{C_{i,W}^{eq}} \right)$$
(9)

and hence further converted to a partition coefficient related to the amorphous polymer phase, $K_{i,LDPEamorph/W}$ by:

$$logK_{i,LDPEamorph/W} = log\left(\frac{10^{logK_{i,LDPE/W}}}{1 - X_{LDPE}^{C}}\right)$$
(10)

where X^C_{LDPE} is the polymer's crystalline fraction by volume assumed as



Fig. 5. Correlations for partition coefficients polyethylene-water. Experimental $\log K_{i,PE/W}$ from Gasslander et al. (2007) versus $\log K_{i,O/W}$ (A), experimental $\log K_{i,PE/W}$ vs LSER calculated $\log K_{i,LDPE/W}$ (B), experimental $\log K_{i,PE/W}$ vs log $K_{i,PE/W}$ calculated by COSMO-RS (FV) (C), and comparison of values predicted by COSMO-RS (FV-term) and LSER (D). For abbreviations see text.

0.35.

From the amorphous volume – based partition coefficients $\log K_{i,LDPEamorph/W}$ obtained by Eq. (10), another LSER(EV) model was constructed:

$$\begin{split} logK_{i,LDPEamorph/W} &= -0.079 + 1.099E - 1.553S - 2.979A - 4.626B + 3.889V \\ n &= 156, R^2 = 0.996, RMSE = 0.267, F = 3370 \end{split} \label{eq:ki,LDPEamorph/W} \end{split}$$

It is noted that the constant c showed an associated standard error of 0.078 and is therefore de facto insignificant. Further statistics associated to Eq. (11) provided in Table SI 3 of the SI.

As expected, when comparing the models in Eqn 1 and 11, utilizing $\log K_{i,LDPEamorph/W}$ for calibration mainly affected the model's offset, i.e. the constant to change from -0.529 to now -0.079 rendering it more similar to the LSER model for n-hexadecane/water (and hexane/water, see Table 2).

Along these lines, a comparison of the sorption behavior of LDPE to other polymers of pharmaceutical interest can be made, both visually (Fig. 3B–D, and also supported by the differences in LSER system parameters listed in Table 2 and visualized in Fig. 4. Here, polydimethylsiloxane (PDMS), in comparison to LDPE, shows a stronger sorption to (more polar) compounds of the lower log K range and less sorption in the higher log K range, with a center point between a log K of 3 to 4. In contrast, polyacrylate (PA) exhibits overall stronger sorption (up to about 3 log units!) of polar compounds below a log K range of 5 with some scatter around the 1:1 line above a log K of 5. A quite similar behavior can be seen for polyoxymethylene (POM) with stronger sorption of nonpolar compounds into LDPE above a log K of 5 (Fig. 3).

A comparison of the LSER system parameters for the systems polymer/water versus n-hexadecane/water, and finally octanol/water, respectively, is depicted by Fig. 4. Inspecting the parameters for the specific intermolecular interactions, i.e., s, a and b, the trend from nonpolar towards more polar materials becomes readily visible. Similarly, for the non-specific type of interactions (e, v) a similar but opposite trend can be clearly seen.

2.4. Evaluation of literature data on $\log K_{i,PE/W}$ for compounds representative for potential leachables

One of the rare datasets on partition coefficients polyethylene/water for compounds being chemically representative for chemicals potentially leaching from polymers for pharmaceutical and food applications and specifying adequate experimental details was reported by Gasslander et al. (2007). The reported partition coefficients were measured using the cosolvency method (Smedes, 2018; Smedes et al., 2009). Loschen and Klamt (2014), in a previous study, have referenced this dataset for evaluating the performance of the COSMO-RS method (Klamt, 2018) by including a free-volume (FV) term for the estimation of partition coefficients polyethylene/water.

With the compound set and associated partition coefficients provided in Table 3, plots were generated (Fig. 5) to depict correlations between experimental values and $\log K_{i,O/W}$ as well as values predicted by COSMO-RS and the LSER-model from this study (Eq. 1). Some conclusions can be drawn upon inspection of the plots and statistics of linear correlations between the experimental values and their predictors:

Linear regression of $log K_{i,PE/W}$ against $log K_{i,O/W}$ gave:

$$\begin{array}{rcl} logK_{i,PE/W} &=& 0.74(0.05) \cdot logK_{i,O/W} - 1.52(0.28) \\ n &=& 12, R^2 = 0.955, RMSE = 0.607, F = 214 \end{array} \tag{12}$$

A significantly better fit is obtained for the correlation between experimental and LSER predicted values:

$$logK_{i,PE/W} = 0.69(0.03) \cdot logK_{i,LDPE/W}LSER + 0.33(0.12)$$

n = 12, R² = 0.992, RMSE = 0.363, F = 618 (13)

However, the slope of 0.69 is still markedly different from unity. Correlation to estimates calculated by COSMO-RS (FV), although with a somewhat lower fit, resulted in a quite similar slope:

Noted by Loschen and Klamt (2014), this indicates that the experimental partition coefficients, especially for the very hydrophobic compounds, might be somewhat out of range from what is reliably measurable. By regressing values predicted by LSER and COSMO-RS (FV), however, a satisfactory fit was obtained, underpinning the reliability of the estimates from the two methods.

$$\begin{array}{rcl} \log K_{PE/w}COSMO &=& 1.12(0.05) \cdot \log K_{LDPE/w}LSER \pm 0.04(0.20) \\ n &=& 12, R^2 = 0.983, RMSE = 0.605, F = 588 \end{array} \tag{15}$$

This example provides some indication on how high performing models can be of value for plausibility assessment of experimental datasets on partitioning. This is of particular relevance for partition coefficients at the extremes of the log K scale, rendering the measurement of reliable data a significant challenge. In the context of studies on extractables and leachables, this also translates to a toolset, which offers plausibility checks for meaningful correlations between extractables and leachables, as required by several regulatory texts (PQRI, 2006; USP, 2020).

3. Conclusion and Outlook

Abraham-type Linear Solvation Energy Relationships (LSERs) were demonstrated to provide an accurate and robust means for the prediction of partition coefficients between LDPE and water, as proven by a coefficient of determination of 0.985 and a standard deviation of 0.352 for an independent validation set. The availability of reliable experimental partition coefficients for model calibration was found of high importance, as expected. Using solute descriptors obtained from a QSPR prediction tool instead of experimentally derived descriptors yielded a somewhat lower predictivity (R^2 =0.984, RMSE = 0.511, *n* = 52). It is stressed that the both the quality of experimental partition coefficients and the chemical diversity of the applied compound training set is crucial to the quality and application domain of the LSER model obtained, as shown by evaluation and external benchmarking of the model.

Comparison of LSER calculated partition profiles between LDPE, polydimethylsiloxane, polyacrylate and polyoxymethylene revealed, in part, pronounced differences in the sorption characteristics between polymers. As expected, sorption capacities towards a specific solute were observed to strongly depend on the match between the chemical nature (potential for molecular interactions) of the polymer building block to the one of the solute.

As speculated by previous research, n-hexadecane was demonstrated to represent a good surrogate for LDPE. Notably, if partition coefficients LDPE/water are calculated based on the effective volume of the amorphous LDPE fraction only, the inherent offset in the correlation for solute partitioning between systems LDPE/water to n-hexadecane/water becomes less pronounced.

To identify maximum (i.e. worst-case) levels of leaching within chemical safety risk assessments on systems exhibiting partition controlled / equilibrium driven behavior, it appears adequate to utilize LSER calculated partition coefficients (in combination with solubility data) by ignoring any kinetical information, i.e. time to equilibrium. Thus, projection of patient exposure can, in a first step, be facilitated based on reliable quantitative extractables data along with robust estimates of partition coefficients, only. By taking this further, the LSERbased calculation of partition coefficients polymer/water was found of high value for predictive modeling of small molecule mass transport in healthcare applications and also, with no constraints, for the concept of migration modeling as officially recognized for compliance testing of food contact materials. Future research should focus on establishing additional experimental LSER solute descriptors for the chemical space of extractables and as well on enhanced algorithms to derive solute descriptors from structural information, only.

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The authors report no competing financial interest.

CRediT authorship contribution statement

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Supplementary materials

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