

Polymer–water partition coefficients of extended range measured by using organic modifiers in the aqueous phase

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Received 1 June 2007; received in revised form 19 October 2007; accepted 26 October 2007

Available online 4 November 2007

Abstract

A procedure for estimating equilibrium polymer–water partition coefficients over a broad range of solute hydrophobicity is presented and evaluated. The coefficients were calculated from the concentration change in the liquid phase and hydro-organic mixtures of varying proportions were used to extend the range. Three hydrophobic polymers (PP, PE, and EBA), two types of solvent (acetonitrile and alcohols) and 12 model solutes were used. The estimated polymer–water partition coefficients, $\log K_{pw}$, ranged from -0.5 to 8.5 . The coefficients correlated to other partitioning systems such as the calculated $\log P_{\text{octanol-water}}$ up to ~ 14 and the retention factor ($\log k_w$) in reversed-phase liquid chromatography.

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Keywords: Polymer–water partition; Sorption; Lipophilicity

1. Introduction

For a polymer in direct contact with a solution, the distribution of low molar mass solutes between the phases is a fundamental interaction process. The equilibrium distribution of a compound between a solid and a liquid phase is determined by its differential solubility in the two phases. The corresponding polymer–solution partition coefficient is therefore an important basic measure that is used in numerous studies, for example, interactions and sorption kinetics in polymer–solvent systems [1]. Depending on the value of the partition coefficient for each species in the system, the interaction upon equilibration will range from leaching of components from the polymeric material (desorption) to binding of components from the solution by the material (sorption). Low molar mass additives, such as plasticizers or antioxidants, are known to leach into the environment, causing health issues or

shortening of the expected lifetime of the polymer, at a rate that depends on the partitioning to the surrounding material. Moreover, in the packaging of pharmaceuticals and foods, these processes could impair the quality and safety of the product. In a review article Tehrani and Desobry [2] summarized the theories and factors influencing polymer partitioning, focusing on food packaging systems. They discussed the influence of temperature, the chemical structure and size of the migrant, and the pH and other characteristics of the liquid phase.

The sorption–desorption balance may also be utilized in many ways. Polymers can be used to release a controlled amount in drug delivery systems [3]. Another example is in studies of complex systems such as the gastrointestinal absorption of drugs, where silicone sheets acted as a partitioning receptor phase [4]. Polymer sorbents are also used as stationary phases in chromatography and in analytical sample preparation to extract and concentrate hydrophobic analytes from a liquid phase. In a recent example, phthalate esters released into water by leaching from food contact polymers were analyzed after enrichment by microdialysis on a polysulfone hollow fiber [5]. Meluch and Lloyd [6] compared partition

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coefficients obtained by liquid chromatography (LC) to those from equilibrium partition experiments for various alcohols in a water–cellulose acetate system. They used cellulose acetate powder as the stationary phase and injected the alcohols in water as the mobile phase. Equilibrium was, however, not attained in LC due to the kinetics of diffusion into the core of the cellulose particles, although the data were qualitatively useful.

Polymer–solution systems are being used as models for other partitioning systems and *vice versa*. Mostly $\log P$, the distribution coefficient of neutral compounds between two immiscible liquids, is applicable. A novel way of estimating $\log P_{ow}$ (octanol–water) for highly lipophilic solutes from the binding into PDMS discs has been proposed [7]. The fiber–water distribution in SPME is also correlated to $\log P_{ow}$ [8]. Likewise, the partitioning of solutes from an aqueous solution to polypropylene (PP) and polyethylene (PE) has been found to correlate closely to their hexane–water partition coefficients [9], while the octanol–water partition coefficient has been used in other studies and polymers [10,11]. The $\log P_{ow}$ was found to be applicable to plasticized polyvinylchloride (PVC), for example, although for PE or PP, with no or very low hydrogen bonding activity, a combination of several $\log P_s$, such as $\log P_{ow}$ and $\log P_{hw}$ (hexane–water), was found to be more applicable [12]. Liquid chromatography, using different types of stationary phases, is often used for an automated estimation $\log P$. Jenke et al. [13] used a reversed-phase LC silica C_8 -system for the determination of $\log P_{ow}$ in a study of container interactions. In a comparison between a silanol-deactivated amide C_{16} and a polymer-based octadecylpolyvinyl (ODP) stationary phase, the silica-based column showed the best correlation to $\log P_{ow}$ [14]. For $\log P_{aw}$ (alkane–water), a polymer-based column has been shown to provide quite a good estimation [15]. A polymethacrylate gel based column with octadecyl groups, used to extend the pH range, has proven useful for lipophilicity determinations [16]. $\log P_{ow}$ may be experimentally determined or calculated from the structure of the solute by using suitable software. Although the calculated value is an approximation, it is convenient to use and is applicable to highly hydrophobic solutes, for which an experimental measurement is very difficult or practically impossible.

The equilibrium polymer–solution partition coefficient depends on all three parts in the system – the solute, the polymer, and the composition of the liquid phase – and is defined as the ratio of the concentration of the solute in the polymer to that in the solution:

$$K = c_{\text{polymer}}/c_{\text{solution}} = c_p/c_s \quad (1)$$

Gavara et al. [17] determined the partitioning of organic compounds in polystyrene–water systems and compared three experimental techniques. They used size exclusion chromatography and dynamic thermal stripping thermal desorption (DTS-TD) to determine the equilibrium concentration in the polymer, and gas chromatography was used for determination of the solute concentration in the water phase. The solution was pre-concentrated by an extraction step to accurately

quantify the solute concentration since the high affinity for the polymer resulted in a very low equilibrium concentration in the solution. This example illustrates some of the practical obstacles associated with high partition coefficients. A solute's partition coefficient can be determined from its concentration in only one of the phases, provided the total amount of solute available in the system and the volume/mass of the two phases are known. Due to the unavoidable extraction step when quantifying the amount of solute in the polymer it is more convenient to use its concentration in the liquid phase, but the sensitivity of the analytical procedure becomes the limiting factor for high partition coefficients. For polymer–water systems, the use of binary hydro-organic solvent mixtures over water alone makes it possible to control and moderate the partition ratio in order to facilitate the quantitation. A series of water solutions containing 0–100% of ethanol was used in a study of flavor desorption from low density PE and polyethylene terephthalate (PET) packaging films [18]. Jenke [19] showed that there is a linear correlation between the polarity of the solvent and the equilibrium binding constant for a series of solutes in contact with PVC and a multicomponent polyolefin film. In subsequent studies by the same author, binary mixtures of ethanol–water were used to model the polarity of pharmaceutical formulations in the assessment of container/content interactions [20,21].

This principle is used when regulating the retention in reversed-phase liquid chromatography (RP-LC) by the admixture of an organic modifier to the aqueous mobile phase. The chromatographic retention is due to the partitioning of the analyte between the stationary and mobile phases. The logarithm of an analyte's retention factor, $\log k$, is ideally linearly related to the fraction of organic modifier in the mobile phase (φ):

$$\log k = \log k_w + S\varphi \quad (2)$$

The intercept, $\log k_w$, corresponds to the retention when pure water is used as the mobile phase and is determined indirectly at $\varphi \neq 0$, since most compounds will be completely retarded using 100% water as mobile phase. The S -value depends on the identity of the organic modifier and is an approximate descriptor of solvent strength [22]. Since, the stationary phase is affected by changes in the composition of the binary mobile phase there are limitations to this linear model unless the composition range (φ) is restricted. Another drawback is that the $\log k_w$ is usually not independent on the identity of the organic modifier due to interactions with the stationary phase. However, in a partitioning system where the solid phase is less affected by the identity and composition of the liquid phase, then Eq. (2) becomes applicable. Thus, provided this prerequisite is met, it would be possible to use this model to measure the polymer–water partition coefficient over an extended range in solute hydrophobicity.

Here, the aim is to develop a fast and convenient procedure for estimating the polymer–water partition coefficient that works over a broad range of solute lipophilicity. Hydro-organic mixtures are used over pure water in order to increase

the solubility of hydrophobic compounds. In this way the partition ratio is moderated facilitating the quantitation of the equilibrium solute concentration in the liquid phase. $\log K_{ps}$ (polymer–solution) is expected to be a linear function of the fraction of organic modifier, ϕ , where the intercept corresponds to the polymer–water partition coefficient. To verify the suggested methodology, model compounds are equilibrated in different hydro-organic mixtures in contact with polyolefins. The polymer–water partitioning data obtained are evaluated for solvent dependency and compared to other partitioning systems such as reversed-phase LC and calculated $\log P_{ow}$.

2. Experimental

2.1. Materials

The test compounds were selected to represent a very wide range of lipophilicity and are structurally related: substituted monoaromatic compounds including acids, aromatic and aliphatic alcohols, and esters. This class of compounds' represents, for example, antioxidants and degradation products thereof. They are all easy to quantify using RP-LC with UV detection. The test compounds are listed in Table 1, together with their calculated $\log P_{ow}$, in the order of elution in the gradient LC system used for quantitation. All compounds are commercially available.

The organic solvents used in the partitioning experiments were acetonitrile (ACN), ethanol (EtOH), and 2-propanol (IPA) of chromatographic grade. These solvents are not likely to interact with the selected polymers in any appreciable extent and represent two different classes of solvents with regard to their hydrogen bonding strengths. In addition, methanol (MeOH) was used in the chromatography.

Three commercial materials were used as model polymers: a polypropylene (PP) that is a random co-polymer with about 2 w/w% ethylene, a low density polyethylene (PE), and a polyethylene-*co*-butyl acrylate (EBA) with about 17 w/w% of butyl acrylate.

Table 1
Test compounds and their calculated $\log P_{ow}$

No	Chemical name	$\log P_{ow}$ ^a
1	4-Hydroxybenzoic acid	1.42
2	Methyl-4-hydroxybenzoate	1.86
3	4-Methylbenzyl alcohol	1.49
4	2-Methylbenzoic acid	2.35
5	Propyl-4-hydroxybenzoate	2.93
6	Diethyl phthalate	2.70
7	Toluene	2.68
8	3,5-Di- <i>tert</i> -butyl-4-hydroxyphenyl propanoic acid	4.48
9	2,4-Di- <i>tert</i> -butyl phenol	4.86
10	2,6-Di- <i>tert</i> -butyl-4-methyl phenol	5.32
11	Bis(2-ethylhexyl) phthalate	8.71
12	Octadecyl-3-(3',5'-di- <i>tert</i> -butyl-4'-hydroxyphenyl) propionate	13.9

The solutes are numbered in the order of elution in the gradient RP-LC system.

^a Calculated using the Advanced Chemistry Development (ACD) Software V8.14 for Solaris.

2.2. Procedures

2.2.1. Sample preparation

A series of solutions containing approximately 20 $\mu\text{g/ml}$ of the test substances was prepared in mixtures 1–100% of solvent in 5–50 mM phosphate buffer $\text{pH} \leq 3$. A less concentrated buffer was used for mixtures with the highest fractions of organic solvent. In most of the experiments the proportion of polymer to test solutions was about 1 g/10 ml. Up to 2 g of polymer per 10 ml test solution was used when the partitioning of the polymer was very low. To speed up the equilibrium process, the polymer granules were cryoground in a 6750 Freezer Mill (SPEX CertiPrep, USA) to give particles typically less than 0.5 mm (80%). The samples were equilibrated at 40 °C for ≥ 5 days. Reference solutions were prepared in the same manner without the polymer. Glass wool was used to keep the otherwise floating polymer submerged. The solutions were filtered before analysis.

2.2.2. Liquid chromatography

The quantitation of the test solutes in the polymer partitioning experiments was carried out by gradient RP-LC using a Waters Symmetry C₁₈ column, 3.9 × 159 mm, 5- μm particles, and detection by UV at 210 nm. Eluent A was 5 mM formic acid in water and eluent B a 50/50% mixture by volume of ACN and IPA, run in a linear gradient of 2–100% for 30 min at 1 ml/min, 20–40 μl was injected and the column temperature was set at 50 °C.

The RP-LC partitioning data were collected in the isocratic mode using the same column and settings. Here, 100% ACN, 50/50% ACN/IPA, 75/25% MeOH/IPA, and 100% IPA were used as organic modifiers in combination with the formic acid buffer. The liquid chromatography was performed on an Agilent 1100 instrument.

2.2.3. Calculations

The equilibrium polymer–solution partition coefficient, $\log K_{ps}$, was calculated using Eq. (1), on the assumption that the loss from the solution following equilibration between the phases reflected the amount in the polymer:

$$c_{p,eq}w_p = (c_{init} - c_{eq})V_s \quad (3)$$

$c_{p,eq}$ = concentration of solute in polymer at equilibrium, w_p = mass of polymer and V_s = volume of solution, c_{init} and c_{eq} = concentrations of solute in solution initially and at equilibrium, respectively.

$$\log K_{ps} = \log \left[\left(\frac{c_{init} - c_{eq}}{c_{eq}} \right) \frac{V_s}{w_p} \right] \quad (4)$$

The retention factor in LC was calculated from the retention time of the solute, t_r , compared to the solvent front (i.e., no retention), t_0 :

$$\log k = \log \left(\frac{t_r - t_0}{t_0} \right) \quad (5)$$

3. Results and discussion

3.1. Generation of polymer partitioning data

3.1.1. Verification of the equilibration conditions

The conditions of the equilibration procedure were verified by monitoring the partition process over time using a solution of 50% ACN in water and substances #10 and #11 (Table 1). Three different polymer particle size distributions from very finely ground, i.e., the cryogrinding process representing ≤ 0.5 mm, up to half to whole size polymer granules were used. Coarsely ground polymer, approximately 0.5–1 mm, was used as an intermediate. The results, which are shown in Table 2, are reported in percent of the value obtained on the 5th day of equilibration for the finest particles, since the partition reached a constant level under those conditions for all three polymers. The results show that the equilibrium partition coefficient is independent of the size of the polymer particles; although the time needed to reach equilibrium varies from days to considerably longer periods, depending on the polymer, the solute, and the size of the particles. For polypropylene, the very fine particle size distribution obtained by the cryogrinding process was proven to be necessary in order to reach equilibrium within a reasonable time, see Fig. 1. Thus, the polymer partition measurements were carried out using the cryogrinding procedure followed by equilibration for 5–7 days at 40 °C.

3.1.2. Polymer partition measurements

A series of solutions of the 12 model compounds (Table 1) were prepared at low concentrations in hydro-organic mixtures with increasing fractions of organic modifiers, and then allowed to equilibrate in contact with the polymers at the

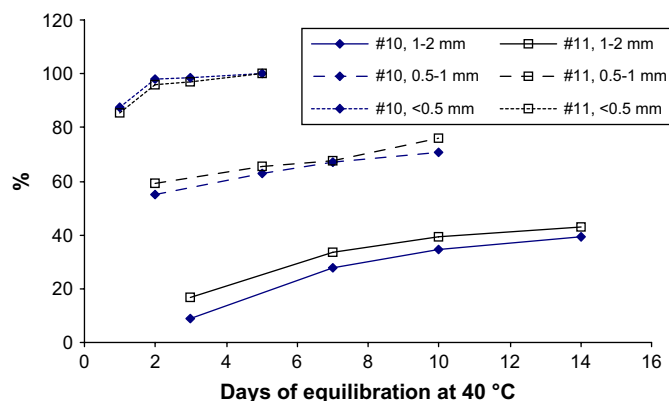


Fig. 1. Time to equilibrate the partitioning of solutes #10 and #11 to PP, depending on particle size. The partitioning data are presented in percent of the result obtained after 5 days using the finest particle size.

conditions outlined above. Gradient LC with UV detection was used for the analysis of the solutions. By assuming that the concentration is proportional to the area of the peak, Eq. (4) can be rearranged and the partition coefficient calculated for each solute from the ratio of the peak area before and after equilibration:

$$\log K_{ps} = \log \left[\left(\frac{\text{area}_{\text{init}}}{\text{area}_{\text{eq}}} - 1 \right) \frac{V_s}{w_p} \right] \quad (6)$$

In this way $\log K_{ps}$ was determined for the polymers PP, PE, and EBA at varying proportions of the organic modifiers in the aqueous phase. Using Eq. (7), in analogy with Eq. (2), the polymer–water coefficient $\log K_{pw}$, was calculated by linear regression of the $\log K_{ps}$ data versus the fraction of organic modifier, ϕ .

$$\log K_{ps} = \log K_{pw} + s\phi \quad (7)$$

In Table 3, the resulting polymer–water partition coefficients, $\log K_{pw}$, are shown for three polymers using different organic modifiers. Fig. 2, illustrates the partitioning data and the results from linear curve fitting according to Eq. (7) for PE with ACN in the aqueous phase. The range of ϕ , within which the partition ratio was measured, varied with the characteristics of each solute. Due to the large difference in solute hydrophobicity, the whole scale up to 100% organic modifier was used.

$\log K_{ps}$ was calculated from the ratio of two areas according to Eq. (6) measured in the same analytical sequence to eliminate the need for calibration standards. Even so, a small difference in areas, $\leq 2\%$, corresponding to low binding, was difficult to distinguish from the experimental error of analytical procedure. At the other end of the scale, when there was a significant binding, the very small area after equilibration approached the determination limit of the method. Each solute was therefore measured within a fraction range where $\log K_{ps}$ was approximately ranges from -0.5 to 2. The accuracy and precision of the intercept $\log K_{pw}$ depend on the degree of extrapolation to zero fraction of organic modifier. Single

Table 2
Time needed for equilibration depending on polymer particle size

Solute	Polymer	Approximate particle size (mm)	Days							
			1	2	3	5	7	10	14	
#10	PP	≤ 0.5	88	98	98	100				
		$\sim 0.5-1$		55		63	67	71		
		$\sim 1-2$			9		28	34	39	
	PE	≤ 0.5	—	—	101	100				
		$\sim 0.5-1$		—			99	101		
		$\sim 1-2$			—		—	94	95	
	EBA	≤ 0.5	95	103	101	100				
		$\sim 0.5-1$		102		100	100	100		
		$\sim 1-2$			101		100	99	97	
#11	PP	≤ 0.5	85	96	97	100				
		$\sim 0.5-1$		59		66	68	76		
		$\sim 1-2$			17		34	39	43	
	PE	≤ 0.5	—	—	100	100				
		$\sim 0.5-1$		—			94	98		
		$\sim 1-2$			—		—	83	94	
	EBA	≤ 0.5	95	102	102	100				
		$\sim 0.5-1$		99		99	99	99		
		$\sim 1-2$			99		99	100	98	

Partitioning data presented in percent of the result obtained after 5 days using the finest particle size.

Table 3

Partitioning data for the model solutes to PE, PP and EBA using different organic modifiers in the liquid phase

No	PE–ACN		PP–ACN		PP–IPA		EBA–ACN		EBA–EtOH	
	$\log K_{pw}$	r^2	$\log K_{pw}$	r^2	$\log K_{pw}$	r^2	$\log K_{pw}$	r^2	$\log K_{pw}$	r^2
1	–0.80						–0.41	0.916		
2	–0.68						0.44	0.984		
3	–0.71		–0.56	0.948	–0.59	0.966	0.30	0.986	0.31	0.980
4	–0.09	0.992	0.35	0.995	0.46	0.895	0.76	0.989	0.87	0.975
5	0.12	0.996	0.05	0.984	0.10	0.999	1.41	0.995	1.33	0.975
6	0.84	0.998	1.01	0.992	1.02	0.979	1.63	0.999	1.61	0.995
7	1.61	0.973	1.83	0.960	2.34	0.993	2.11	0.978	2.84	0.996
8	1.46	0.975	1.47	0.992	2.88	0.992	2.15	0.993	3.16	0.999
9	2.51	0.975	2.53	0.990	2.63	0.991	3.89	0.992	3.72	0.998
10	3.25	0.990	3.67	0.980	4.03	0.982	4.35	0.977	4.19	0.999
11	5.26	0.997	4.62	0.999	4.46	0.989	4.21	0.994	5.14	0.988
12	8.23	0.992	8.03	0.995	5.52	0.995	8.55	0.997	8.32	0.991

The polymer–water partition ($\log K_{pw}$) and r^2 were obtained by linear regression of partition data versus fraction of organic modifier according to Eq. (7).

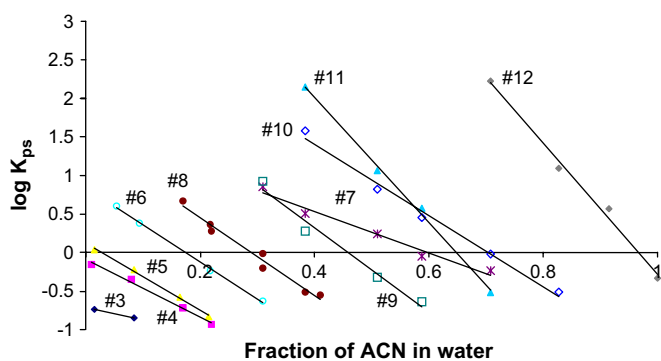


Fig. 2. Linear curve fits to PE partition versus fraction of ACN in water for model substances 3–12.

samples at several values of ϕ were used in order to increase the number of data points and the chance of matching the measuring range in $\log K_{ps}$. Thus, replicate measurements far apart and at as low modifier fractions as possible will increase the precision significantly, especially for the most hydrophobic substances.

3.2. Solvent dependency

As the conditions for linearity and the value of the intercept in Eq. (7) are associated with interactions due to the identity of the organic modifier, the data were compared for solvent dependency. The alcohols and acetonitrile represent two different types of solvent, e.g., strong and weak hydrogen bonding characteristics. Since acetonitrile and isopropanol were used in the eluent of the gradient LC system, these solvents were originally also selected for the polymer partitioning experiments, although ethanol was also used. For substance #8, which is an acid, the results using the alcohol were significantly higher than for acetonitrile. Since only the neutral acid will show affinity for the polymer, the partitioning is pH-dependent, and the difference between the solvents was probably due to the enhanced buffer effect in the alcohol. Excluding #8, the results agreed well for most of the test

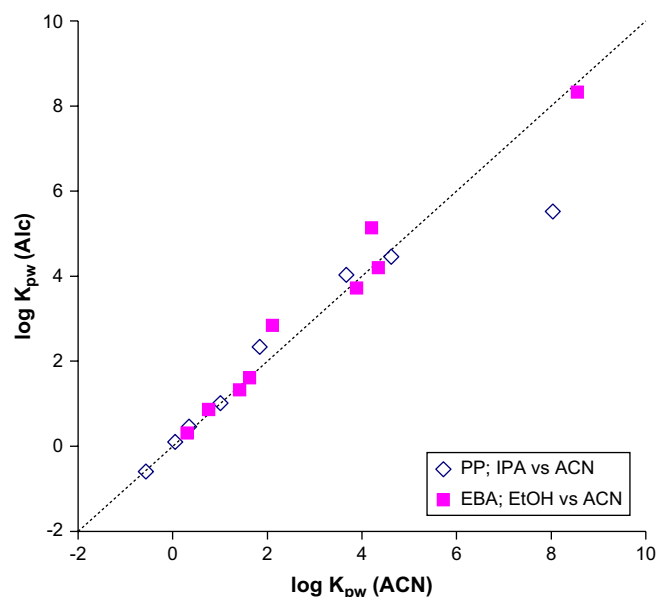


Fig. 3. Effects of different organic modifiers on the polymer–water partition ($\log K_{pw}$) for PP and EBA. The alcohols IPA and EtOH are compared to ACN for PP and EBA, respectively.

substances, as shown graphically in Fig. 3. This independence of the solvent indicates that there was little or no interaction between the polymer and the solvent. PP was, however, most likely affected at higher fractions of IPA since there was a tendency for curved lines when exceeding approximately 50% in the solution, which explains the low result for the most lipophilic solute, #12. In addition, this substance has an alkyl chain that might show conformational changes depending on the solvent. IPA was used for PP, but was considered to be too lipophilic to be used for EBA. It was therefore replaced by ethanol and the results for EBA did not show any solvent interaction. This effect needs to be considered when choosing the organic modifier, since the fraction of ethanol is likely to affect the solubility and diffusivity when more polar polymers are used [23,24]. Altogether, estimation of the polymer–water partition according to this principle seemed

feasible and the resulting $\log K_{pw}$ was highly independent of the identity of the organic solvent used.

3.3. Polymers

Most of the model solutes exhibited measurable binding to these polymers, Table 3. The exceptions are at the hydrophilic end of the scale, where the two most hydrophilic solutes did not bind to any appreciable extent to PE and PP, and $\log K_{ps}$ was below -0.5 at low values of φ . Fig. 4 shows the polymer–water partition for PP and EBA versus that of PE. As expected, PP and PE exhibit similar characteristics. For EBA, all compounds except the most hydrophilic one show a positive $\log K_{pw}$ and the values are higher than for the other polymers. In EBA the presence of butyl acrylate units (17w/w%) incorporates a polar feature and consequently the binding of moderately polar solutes is more pronounced to EBA than it is to PP and PE.

3.4. Correlations to other partitioning systems

Since liquid chromatography is a quick and automated process, it is interesting to compare retention data from standard reversed-phase C_{18} columns to polymer partition data. These two systems are comparable since a C_{18} column resembles a polyalkene surface but it displays some very fundamental differences. In all, four different mobile phase compositions were tested in the isocratic mode: hydro-organic mixtures with ACN 100%, ACN/IPA 50/50%, MeOH/IPA 75/25%, and IPA 100% as the organic modifiers. By using up to 98% of solvents in water, all model solutes eluted within a reasonable time. For each solute, the LC retention factor was calculated using Eq. (5) and, as an example, the retention data obtained using MeOH/IPA as organic modifier are shown in Fig. 5. Linear regression of the retention data for all four

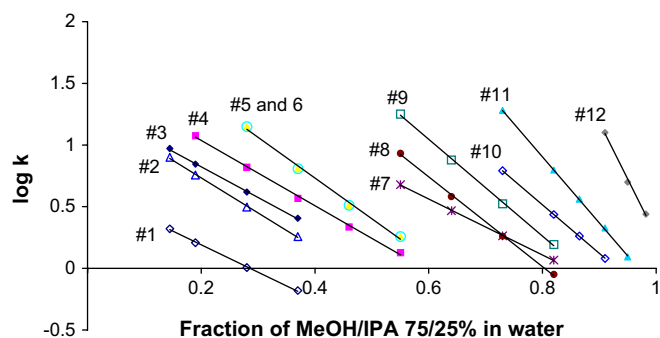


Fig. 5. The retention factor measured in isocratic RP-LC using 75/25% MeOH/IPA as organic modifier.

eluent, Eq. (2), is shown in Table 4. The linearity was quite good for systems with ternary mixtures, i.e., ACN/IPA and MeOH/IPA in water, and not as good for the binary mixtures with ACN and IPA, respectively. In contrast to the polymer systems, there were pronounced effects of the organic modifier on the value of $\log k_w$, although the latter should ideally be independent of the modifier and represent pure water. In Fig. 6 the different values of $\log k_w$ are plotted using the data obtained with MeOH/IPA as reference, and the retention properties varied significantly with the identity of the organic modifiers. IPA as organic modifier had a very strong effect on the retention factor. As discussed in a review by Poole and Poole [22], it has been extensively shown that the linear model for the correlation of the retention to the fraction of organic modifier, Eq. (2), is an approximation and a second-order polynomial model often provides a better fit to data. Furthermore, the intercept is dependent on the identity of the organic modifier and the range within which it is determined. The stationary phase has been found to be much more polar than would be expected compared to a bulk alkane phase [25]. Tan et al. [26,27] used the linear solvation energy relationship (LSER) to evaluate the two phases. They verified that the stationary phase is strongly influenced by the mobile phase and is very dynamic in its characteristics. It is at all times a mixture of the bonded phase, which itself includes defects such as free

Table 4

Retention data in LC using different organic modifiers in the mobile phase

No	ACN		ACN/IPA		MeOH/IPA		IPA	
	$\log k_w$	r^2	$\log k_w$	r^2	$\log k_w$	r^2	$\log k_w$	r^2
1	0.64	0.985	0.50	0.996	0.63	0.999	0.43	0.998
2	1.39	0.987	1.16	0.996	1.30	0.999	0.86	0.998
3	1.38	0.973	1.22	0.997	1.33	0.999	0.89	0.999
4	1.31	0.984	1.36	0.989	1.56	0.998	1.00	0.982
5	1.81	0.984	1.68	0.991	2.05	0.996	1.08	0.978
6	1.94	0.989	1.48	0.994	2.05	0.996	1.12	0.968
7	1.72	0.995	1.67	0.994	1.92	1.000	0.63	0.999
8	2.27	0.994	2.23	0.996	2.92	0.999	1.48	0.968
9	2.58	0.998	2.66	0.995	3.40	0.999	1.42	0.984
10	2.86	1.000	2.77	1.000	3.67	1.000	1.56	0.996
11	4.49	1.000	3.96	1.000	5.19	1.000	2.08	0.998
12	8.08	1.000	7.05	1.000	9.46	0.996	3.12	1.000

The retention factor for water ($\log k_w$) and r^2 were obtained by linear regression according to Eq. (2).

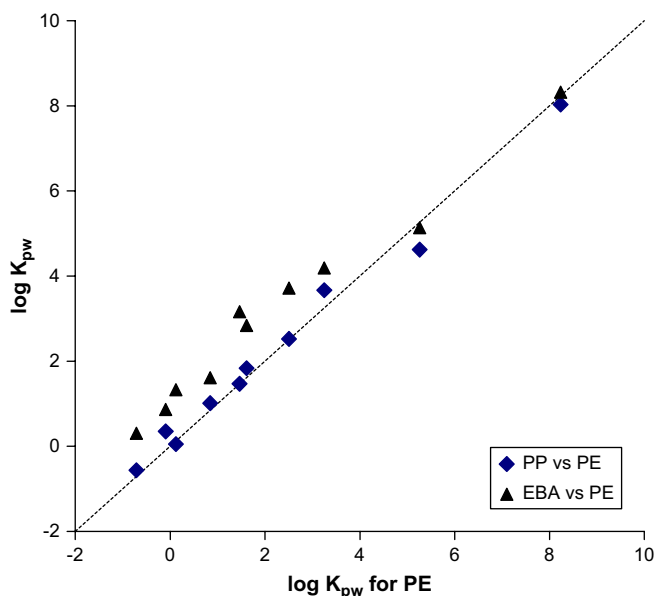


Fig. 4. Polymer–water partition ($\log K_{pw}$) for PP and EBA compared to PE.

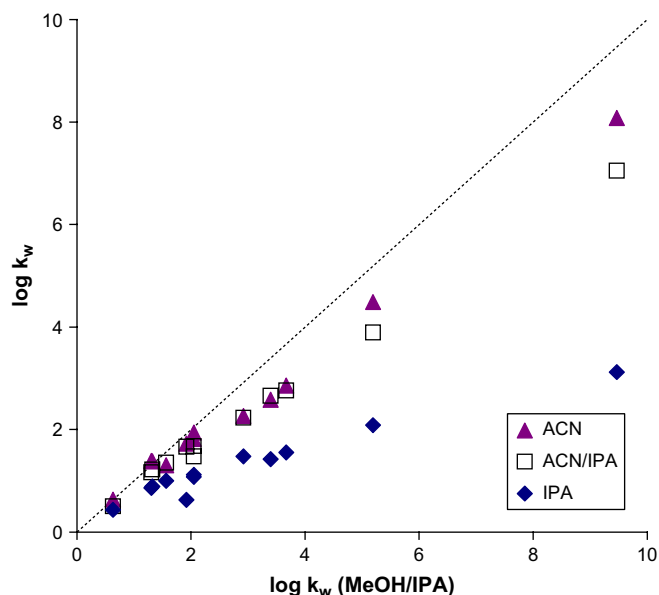


Fig. 6. Effects of varying the organic modifier on the retention factor ($\log k_w$) in RP-LC.

silanol groups, and of sorbed mobile phase constituents. Due to these effects, that enables other types of interaction not present in a liquid–liquid partitioning, Poole and Poole [28] concluded in a review paper that the RP-LC parameter $\log k_w$ is not perfect in estimations of $\log P_{ow}$, and that there are other

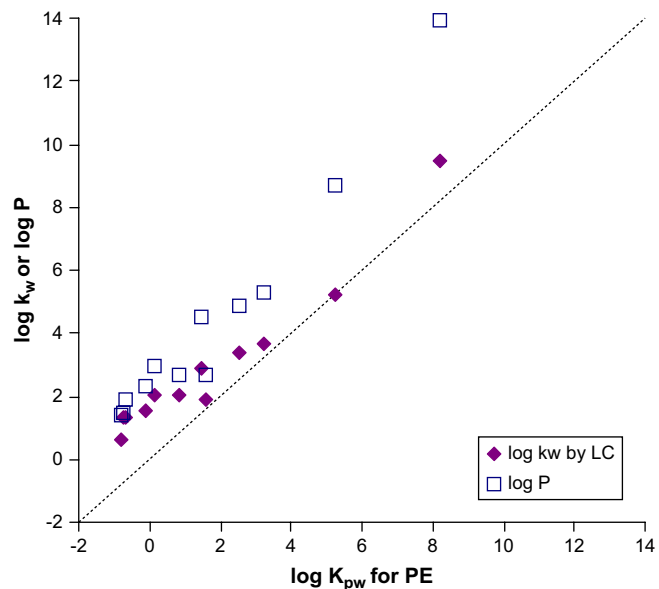


Fig. 7. Retention factor in LC (MeOH/IPA) and $\log P$ compared with PE–water partition data.

more applicable techniques such as microemulsion electrokinetic chromatography (MEEKC).

A comparison of the polymer–solution partition results for PE (Fig. 2) and the retention factor in RP-LC (Fig. 5) illustrates the analogy and the differences between these two systems. The polymer–solution partition ratio, $\log K_{ps}$, and $\log k$ from LC showed a similar pattern, although for the more polar solutes there was a much stronger partitioning to the column than to the tested polymers. This effect is also seen from Fig. 7, where the retention in LC ($\log k_w$) using MeOH/IPA as organic modifier is compared to the partition coefficient representing PE–water ($\log K_{pw}$). The PE–water partition correlation to the calculated $\log P_{ow}$ is also shown in Fig. 7. Correlation data for all three systems are summarized in Table 5. Since the polymers in this study are very hydrophobic by nature, an LC system that shows hydrophobic rather than polar selectivity would be the better model. For the same stationary phase acetonitrile provides higher polar selectivity than methanol, since the use of methanol leads to a selectivity based on mainly hydrophobic interaction [29]. Likewise, in $\log P_{ow}$ determinations using LC, methanol has shown the best results [28]. In line with this, the LC system with MeOH/IPA as organic modifier showed the best linear correlation to the polymer systems and a slope close to one. The octanol–water partitioning, as the calculated $\log P_{ow}$, was an equally good descriptor for polymer partitioning. These results are in close agreement with data presented by Jenke et al. [21] for a multi-layer polyolefin laminate, where solutes up to a calculated $\log P_{ow}$ of 8.2 were included.

4. Conclusions

With the proposed procedure, equilibrium polymer–water partition coefficients of low molar mass compounds can conveniently be measured. Partitioning coefficients were calculated from the change in solute concentration in the liquid phase following equilibration, without the more laborious quantitation in the polymer phase, by using hydro-organic mixtures to control the distribution between the phases. The polymer–water partition coefficients were obtained by linear regression and independent of the solvent identity. The coefficients are in line with previous research, in which other experimental concepts were used, and shown to correlate to their corresponding calculated $\log P_{ow}$ (octanol–water) and to their retention factors in reversed-phase LC. All in all, this procedure is applicable for substances of a large hydrophobic range and the equilibrium polymer–solution partition coefficient can be estimated over at least nine orders of magnitude, $\log K = -0.5$ to 8.5.

Table 5

Correlations of $\log P_{ow}$, $\log K_{pw}$, (PE) and $\log K_{pw}$, (EBA) to LC retention data and calculated $\log P_{ow}$

LC retention (MeOH/IPA)		Calculated $\log P_{ow}$	
$\log P_{ow} = \log k_w \cdot 1.51 - 0.07$	$r^2 = 0.989$	–	
$\log K_{pw} \text{ (PE)} = \log k_w \cdot 1.11 - 1.53$	$r^2 = 0.945$	$\log K_{pw} \text{ (PE)} = \log P_{ow} \cdot 0.73 - 1.48$	$r^2 = 0.955$
$\log K_{pw} \text{ (EBA)} = \log k_w \cdot 1.00 - 0.51$	$r^2 = 0.939$	$\log K_{pw} \text{ (EBA)} = \log P_{ow} \cdot 0.65 - 0.40$	$r^2 = 0.910$

References

- [1] Bertoldo M, Ciardelli F. *Polymer* 2004;45(26):8751–9.
- [2] Tehrany EA, Desobry S. *Food Addit Contam* 2004;21(12):1186–202.
- [3] Prabhu S, Hossainy S. *J Biomed Mater Res Part A* 2006;80A(3):732–41.
- [4] Boyd BJ, Porter CJH, Charman WN. *J Pharm Sci* 2003;92(6):1262–71.
- [5] Jen J-F, Liu T-C. *J Chromatogr A* 2006;1130(1–2):28–33.
- [6] Meluch TB, Lloyd DR. *Polymer* 1993;34(9):1984–7.
- [7] Kong XQ, Shea D, Gebreyes WA, Xia X-R. *Anal Chem* 2005;77(5):1275–81.
- [8] Paschke A, Popp R. *J Chromatogr A* 2003;999(1–2):35–42.
- [9] Polack AE, Nunez LJ, Autian J. *Int J Pharm* 1979;3:157–75.
- [10] Illum L, Bundgaard H. *Int J Pharm* 1982;10(4):339–51.
- [11] Pitt CG, Bao YT, Andrady AL, Samuel PNK. *Int J Pharm* 1988;45(1–2):1–11.
- [12] Hayward DS, Jenke DR. *Int J Pharm* 1990;66(1–3):87–96.
- [13] Jenke DR, Hayward DS, Kenley RA. *J Chrom Sci* 1990;28:609–12.
- [14] Liu XL, Tanaka H, Yamauchi A, Testa B, Chuman H. *Helvetica Chim Acta* 2004;87(11):2866–76.
- [15] Abraham MH, Chadha HS, Leitao ARE, Mitchell RC, Lambert WJ, Kaliszan R, et al. *J Chromatogr A* 1997;766(1–2):35–47.
- [16] Pehourcq F, Matoga M, Jarry C, Bannwarth B. *J Liq Chromatogr Related Technol* 2001;24(14):2177–86.
- [17] Gavara R, Hernandez RJ, Giacin J. *J Food Sci* 1996;61(5):947–52.
- [18] Hwang Y-H, Matsui T, Hanada T, Shimoda M, Matsumoto K, Osajima Y. *J Agric Food Chem* 2000;48(9):4310–3.
- [19] Jenke DR. *Int J Pharm* 2001;224(1–2):51–60.
- [20] Jenke DR, Brennan J, Doty M, Poss M. *J Appl Polym Sci* 2003;89(4):1049–57.
- [21] Jenke DR, Odufu O, Poss M. *Eur J Pharm Sci* 2006;27(2–3):133–42.
- [22] Poole CF, Poole SK. *J Chromatogr A* 2002;965(1–2):263–99.
- [23] Wang DM, Chu CY, Wu ST, Lai JY. *J Chin Inst Chem Eng* 2002;33(6):555–63.
- [24] Chuang W-Y, Young T-H, Wang D-M, Luo R-L, Sun Y-M. *Polymer* 2000;41(23):8339–47.
- [25] Cheong WJ, Carr PW. *J Chromatogr* 1990;499:373–93.
- [26] Tan LC, Carr PW, Abraham MH. *J Chromatogr A* 1996;752(1–2):1–18.
- [27] Tan LC, Carr PW. *J Chromatogr A* 1998;799(1–2):1–19.
- [28] Poole SK, Poole CF. *J Chromatogr B* 2003;797(1–2):3–19.
- [29] Sándi Á, Nagy M, Szepeszy L. *J Chromatogr A* 2000;893(2):215–34.