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Solute–solvent interactions in micellar electrokinetic chromatography
Characterization of sodium dodecyl sulfate–Brij 35 micellar systems for quantitative structure–activity relationship modelling

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Abstract

The solvation parameter model has been applied to the characterization of micellar electrokinetic chromatographic (MEKC) systems with mixtures of sodium dodecyl sulfate and Brij 35 as surfactant. The variation in MEKC surfactant composition results in changes in the coefficients of the correlation equation, which in turns leads to information on solute–solvent and solute–micelle interactions. Since the same solvation model can be used to describe many biological processes, particular MEKC surfactant compositions can be selected that model the solute–solvent interactions of some of these processes. Two different MEKC systems have been selected to model the solute–solvent interactions of two processes of biological interest (octanol–water partition and tadpole narcosis).

Keywords: Quantitative structure–activity relationships; Micelles; Solvation parameter model; Micellar electrokinetic chromatography; Solute descriptors; Pseudo-stationary phases; Brij 3; Sodium dodecyl sulfate

1. Introduction

In quantitative structure–activity relationships (QSARs), biological activities of solutes are related to their physicochemical and/or structural descriptors [1–3]. Once the relationship has been established, it is straightforward to estimate the biological activity of a solute of interest from its descriptors. Many QSAR models have been tested that relate biological properties to a host of different solute descriptors. Most QSAR models are based on linear free energy relationships (LFERs), where the biological property is linearly related to independent solute descriptors that measure the different interactions between the solute and the environment (free energy changes). Amongst the host of LFERs established, the solvation parameter model [3–5] has been demonstrated to provide very good descriptions, not only of many processes of biological interest (e.g. octanol–water partition, P_{ow}, [6], blood–brain distribution, BB, [7], tadpole narcosis, C_{nar}, [8], skin permeation, k_p, [9]), but also of many physicochemical processes, such as partition between two immiscible solvents [6,10], reversed-phase liquid

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chromatography (RPLC) [11–18], and micellar electrokinetic chromatography (MEKC) [19–22].

The solvation parameter model [3–5] can be set out as

$$\log SP = c + v\,V_X + r\,R_2 + s\,\pi_2^{H} + a\,\Sigma\alpha_2^{H} + b\,\Sigma\beta_2^{H} \quad (1)$$

where log SP is the dependent solute property (e.g. the logarithm of a partition coefficient) and the solute descriptors are the McGowan's characteristic volume V_X (in $cm^3\ mol^{-1}/100$), an excess molar refraction R_2 (in $cm^3/10$), the solute dipolarity/polarizability π_2^H, and the solute's effective hydrogen-bond acidity and hydrogen-bond basicity $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$, respectively. The solute descriptors V_X and R_2 are easily calculated by addition of fragments while the other descriptors are obtained experimentally from liquid–liquid distribution and gas and liquid chromatographic systems [3–5,10]. Nowadays, the solute descriptors are available for more than 2000 compounds and can be estimated for many more.

The coefficients in Eq. (1) are calculated by the method of multiple linear regression and are characteristic of the system. Since many properties are related to partition of the solute between two phases (octanol and water, blood and brain, mobile and stationary phases, etc.), the *r* constant determines the difference in capacity of the two solvent phases to interact with solute π- and n-electrons; the *s* constant is a measure of the difference in dipolarity/polarizability between the two phases; the *a* and *b* constants measure the difference in the phase's hydrogen-bond basicity and acidity, respectively, because an acidic solute will interact with a basic solvent, and vice versa. The *v* constant is related to two different effects, (i) the endoergic creation of a cavity for the solute, and (ii) the exoergic London dispersion forces between the solute and solvent. If the *v* constant is positive for transfer from water to a solvent, then either the cavity term is less endoergic in the solvent or the dispersion term is more exothermic in the solvent, or both. Invariably, a positive *v* constant will largely be the result of the cavity effects.

Because the same Eq. (1) can be applied to biological and physicochemical processes, it should be possible to set out physicochemical processes (e.g. liquid chromatographic systems) that match the interactions of the solute in a biological system (e.g. blood–brain distribution). If the coefficients *v, r, s, a,* and *b* of Eq. (1) for the biological process are proportional to the same coefficients for the physicochemical process, the latter will model the biological process, and a linear relationship should be obtained between the biological and the physicochemical properties.

In principle, RPLC seems to be a fast and convenient method to model biological and physicochemical processes, because for a given stationary phase, the properties of the mobile phase can be easily changed by changing its composition. In fact, many liquid chromatographic systems have been devised to estimate octanol–water partition coefficients (P_{ow}) from retention parameters. Although octanol–water partition is not a biological process itself, log P_{ow} is a parameter of fundamental biological interest [2,3,5,6]. However, it has been demonstrated for C_{18} stationary phases and methanol–water and acetonitrile–water mobile phases (by far the most used liquid chromatographic systems) that although the coefficients of Eq. (1) change with the composition of the mobile phase, the ratio of the coefficients practically does not alter with the change in mobile phase composition [15]. The reason is probably that the solvation of the stationary phase by the mobile phase changes with the mobile phase composition. Therefore, the properties of both phases change in a similar way with the mobile phase composition, and the difference in properties remains rather constant. This fact makes RPLC inappropriate to model many biological processes. It has been demonstrated that the limited variation in the relative coefficients of Eq. (1) for RPLC does not result in a good match with the coefficients obtained for octanol–water partition [11] and therefore correlations between log P_{ow} and HPLC retention parameters in a given system are valid only within a similar set of solutes [11].

In addition to the same features for physicochemical measurements as RPLC (i.e. no sample purity requirement, small sample size, automation, etc.), MEKC has one main advantage to model biological processes. It is possible to adjust the composition of the micellar pseudo-stationary phase by simply

changing the type of surfactant or surfactants in the system in order to provide better physicochemical models for the interactions in biological systems [1]. In fact a MEKC based system has been already devised that matches almost exactly the octanol–water partition process [19].

Several MEKC systems have been characterized by means of the solvation parameter model (Eq. (1)) [20–22]. The results obtained show that the addition of organic solvent modifiers to the running buffer has even less effect in the correlation coefficients than in RPLC [22]. However, the variation of the surfactant employed leads to large changes in the value of the coefficients of Eq. (1). Specially interesting is the use of mixed micelles, particularly systems containing a mixture of ionic and neutral surfactants [20,21], because the properties of the pseudo-stationary phase, and therefore the coefficients of Eq. (1), can be continuously varied by changing the proportion of the two surfactants in the mixture. By far the most popular of these systems is sodium dodecyl sulfate (SDS) and polyoxyethylene(23) dodecyl ether (Brij 35). The addition of Brij 35 to SDS significantly dampens the hydrogen-bond acidity of the micellar phase, while dipole-type interactions, lone pair electron interactions, and the cohesion of the micelles are only slightly changed [21].

In this study we shall characterize several MEKC systems with SDS and Brij 35 mixtures as surfactant in order to predict their utility to model different biological processes and to establish QSARs between biological activities and solute retention factors (k) in appropriate MEKC systems.

2. Experimental

2.1. Apparatus and conditions

All separations were performed with a Beckman P/ACE System 5500 with a UV diode array detector. The fused-silica separation capillaries were 40 cm of effective length$\times$50 μm I.D. Prior to each separation the capillaries were flushed with water for 2 min followed by the separation buffer for 5 min. Every four injections the capillary was flushed with 1.0 *M* sodium hydroxide for 5 min followed by the normal conditioning cycle. Retention measurements were made at 25°C, +15 kV, and 210 nm. The separation buffers were prepared mixing 20 m*M* sodium dihydrogenphosphate and 20 m*M* sodium tetraborate in the ratio 65:35 (pH 8) or 20 m*M* sodium dihydrogenphosphate and 20 m*M* sodium hydrogenphosphate in the ratio 50:50 (pH 7). The buffers contained 50 m*M* sodium dodecyl sulfate, and various amounts of Brij 35 (0, 5, 10, and 15 m*M*). The buffer of pH 7 was used for the 15 m*M* Brij 35 composition to maintain an acceptable migration window. The buffer of pH 8 was used for all the other Brij 35 compositions. Samples were introduced into the capillary by applying a high pressure during 1 s.

2.2. Reagents and materials

Sodium tetraborate, sodium hydrogenphosphate, sodium dihydrogenphosphate, and sodium dodecyl sulfate were Merck, analytical-reagent grade >99%. Brij 35 was obtained from Aldrich analytical-reagent grade, p.a. Methanol was Fisher for HPLC>99.8%. Water was Culligan ultrapure GS with a resistivity of 18.3 MΩ cm. The test solutes were reagent grade or better and obtained from several makers.

2.3. Calculation

The retention factor, k, was calculated using Eq. (2) with the migration time of methanol used to determine the electroosmotic flow (t_{eo}), and octylbenzene the migration time of the micelles (t_{mc}). t_m is the solute migration time [20–22].

$$k = (t_m - t_{eo})/(1 - t_m/t_{mc})t_{eo} \quad (2)$$

3. Results and Discussion

3.1. Characterization of SDS–Brij 35 mixtures

Separation systems containing 50 m*M* SDS and Brij 35 concentrations of 0, 5, 10, and 15 m*M* have been characterized for the solvation parameter model through Eq. (1) by analysis of the log k data of a series of 30 solutes with known V_X, R_2, π_2^H, $\Sigma\alpha_2^H$, and $\Sigma\beta_2^H$ parameters. Since Eqs. (1) and (2) hold only for neutral solutes, the set selected includes

neutral and moderately acidic and basic compounds in order to assure that they remain in neutral form at working pH values (7 and 8). The studied solutes and their descriptors are given in Table 1. The log k values obtained in the different MEKC systems studied are presented in Table 2.

The system constants and the statistics for the fit of the solvation parameter model to the experimental log k data are summarized in Table 3. Preliminary correlations identified three of the solutes studied (pyrimidine, methyl benzoate and pyridine) as outliers, given in most systems deviations larger than three times the overall standard error of the correlation. These three solutes were excluded from all correlations.

Table 3 shows that the solvation parameter model gives good statistical fits and correlation coefficients and constants which are in good agreement with chemical intuition. For the system with only SDS, we may observe that v and r coefficients are positive, whereas s and b are negative. Coefficient a is practically equally to zero. The largest coefficients in absolute value are v and b. This means that the hydrogen bond basicity of SDS micelles is very similar to the hydrogen bond basicity of water ($a=0$), but that the hydrogen bond acidity of the micelles is much lower than the hydrogen bond acidity of water ($b<<0$). SDS micelles can be polarized more easily than water ($r>0$), but they are less dipolar ($s<0$). It is much easier to create a cavity in the micelle than in the aqueous buffer due to the high cohesive energy of water and since the solute–sol-

Table 1
Solute descriptors used in the solvation parameter model and some biological properties of solutes

Solute	V_x	R_2	π_2^H	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$	log P_{ow} [a]	log $(1/C_{nar})$ [b]
Pyrrole	0.5774	0.613	0.730	0.410	0.290	0.75	
Phenol	0.7751	0.805	0.890	0.600	0.300	1.46	2.28
Nitrobenzene	0.8906	0.871	1.110	0.000	0.280	1.85	
2-Nitroanisole	1.0902	0.968	1.340	0.000	0.380		
Ethylbenzene	0.9982	0.613	0.510	0.000	0.150	3.15	
Furan	0.5363	0.369	0.530	0.000	0.130	1.34	
4-Nitroaniline	0.9904	1.220	1.910	0.420	0.380	1.39	
2,3-Benzofuran	0.9053	0.888	0.830	0.000	0.150	2.67	
2-Naphthol	1.1441	1.520	1.080	0.610	0.400	2.70	
Benzaldehyde	0.8730	0.820	1.000	0.000	0.390	1.48	
Chlorobenzene	0.8388	0.718	0.650	0.000	0.070	2.89	
Resorcinol	0.8338	0.980	1.000	1.100	0.580	0.80	1.64
3-Nitroaniline	0.9904	1.200	1.710	0.400	0.350	1.37	
2-Nitroaniline	0.9904	1.180	1.370	0.300	0.360	1.85	
4-Chlorophenol	0.8975	0.915	1.080	0.670	0.200	2.40	
p-Xylene	0.9982	0.613	0.520	0.000	0.160	3.15	
Aniline	0.8162	0.955	0.960	0.260	0.410		1.96
Acetanilide	1.1137	0.870	1.400	0.500	0.670	1.16	2.31
Benzonitrile	0.8711	0.742	1.110	0.000	0.330	1.56	
Methyl phenyl ether	0.9160	0.708	0.750	0.000	0.290	2.11	2.82
Toluene	0.8573	0.601	0.520	0.000	0.140	2.73	
Benzophenone	1.4808	1.447	1.500	0.000	0.500	3.18	
Benzene	0.7164	0.610	0.520	0.000	0.140	2.13	2.68
Naphthalene	1.0854	1.340	0.920	0.000	0.200	3.30	4.19
3-Methylphenol	0.9160	0.822	0.880	0.570	0.340	1.98	2.75
Bromobenzene	0.8914	0.882	0.730	0.000	0.090	2.99	
Propylbenzene	1.1391	0.604	0.500	0.000	0.150	3.72	
Pyrimidine	0.6342	0.606	1.000	0.000	0.650		
Methyl benzoate	1.0726	0.733	0.850	0.000	0.460		
Pyridine	0.6753	0.631	0.840	0.000	0.520		

[a] Octanol water partition coefficient from Ref. [6].
[b] Tadpole narcosis from Ref. [8].

Table 2
Retention factor (log k) in the mixed-micelle separation system. Sodium dodecyl sulfate concentration 50 mM and sodium phosphate–sodium tetraborate buffer pH 8 for Brij 35 concentrations 0–10 mM and sodium phosphate buffer pH 7 for Brij 35 concentration 15 mM

Solute	Brij 35 concentration (mM)			
	0	5	10	15
Pyrrole	−0.726	−0.541	−0.386	−0.262
Phenol	−0.254	−0.083	0.093	0.212
Nitrobenzene	0.146	0.202	0.331	0.430
2-Nitroanisole	0.330	0.326	0.452	0.550
Ethylbenzene	0.873	0.989	1.115	1.202
Furan	−0.533	−0.441	−0.319	−0.190
4-Nitroaniline	0.089	0.276	0.462	0.605
2,3-Benzofuran	0.597	0.768	0.915	1.024
2-Naphthol	0.907	1.197	1.400	1.540
Benzaldehyde	0.069	−0.061	0.026	0.121
Chlorobenzene	0.596	0.795	0.941	1.043
Resorcinol	−0.523	−0.345	−0.107	0.025
3-Nitroaniline	0.070	0.237	0.411	0.534
2-Nitroaniline	0.326	0.425	0.499	0.575
4-Chlorophenol	0.413	0.678	0.588	0.707
p-Xylene	0.931	1.047	1.180	1.261
Aniline	−0.335	−0.292	−0.167	−0.049
Acetanilide	−0.057	−0.093	0.018	0.120
Benzonitrile	0.074	−0.015	0.080	0.173
Methyl phenyl ether	0.258	0.305	0.424	0.515
Toluene	0.478	0.597	0.721	0.811
Benzophenone	1.475	1.280	1.378	1.468
Benzene	0.030	0.160	0.280	0.389
Naphthalene	1.196	1.395	1.566	1.695
3-Methylphenol	0.138	0.284	0.454	0.577
Bromobenzene	0.746	0.958	1.111	1.218
Propylbenzene	1.364	1.457	1.611	1.699
Pyrimidine	−0.940	−0.990	−0.874	−0.681
Methyl benzoate	0.570	1.047	0.973	1.120
Pyridine	−0.502	−0.656	−0.606	−0.526

vent dispersion terms are probably quite similar the v-coefficient is very positive.

The addition of Brij 35 to the system changes the properties of the micelles and therefore the values of the coefficients (Table 3 and Fig. 1). Addition of Brij 35 up to 5 mM significantly decreases the hydrogen bond acidity of the micelles, but this practically does not change with a further addition of Brij 35 (b coefficient). The variation of the other properties is smaller, but there is a moderate increase in the polarizability (r coefficient) and in the hydrogen bond basicity (a coefficient) of the micelles. In fact, hydrogen bond basicity of SDS–Brij 35 mixed micelles is larger than hydrogen bond basicity of water ($a>0$), in contrast with SDS pure micelles which have the same hydrogen bond basicity as water ($a=0$). The dipolarity (s coefficient) and cohesive energy density (v coefficient) of the micelles practically does not change with the addition of Brij 35. It is also remarkable that the constant of the correlation (c) increases with the addition of Brij 35 to SDS because the amount of pseudo-stationary phase increases and so does solute retention. The coefficients of Table 3 are in good agreement with those reported by Poole and Poole [21], except for the a coefficient for which we have obtained values about 0.3 units larger than those reported in reference [21]. However, the trend in the variation of this coefficient with the addition of Brij 35 is exactly the same.

3.2. Modelling of biological processes

The application of the same QSAR model to both biological and MEKC systems, and the fact that the coefficients of the model for the MEKC systems can be varied by simply changing the composition of the mixed surfactant (SDS–Brij 35 mixtures) enables us to model biological systems by MEKC systems of appropriate surfactant composition.

Table 3
System constants for the mixed-micellar phases at 25°C and strength 15 kV. Sodium dodecyl sulfate concentration 50 mM. The retention factors used to fit the model and buffer system are given in Table 2

Conc. Brij 35 (mM)	pH	System constants						Statistics			
		c	v	r	s	a	b	R	n	s.d	F
0	8	−1.759	2.982	0.348	−0.427	−0.021	−2.024	0.9929	27	0.075	291
5	8	−1.559	2.905	0.518	−0.444	0.311	−2.815	0.9918	27	0.082	252
10	8	−1.412	2.829	0.622	−0.516	0.308	−2.699	0.9866	27	0.105	154
15	7	−1.285	2.767	0.667	−0.515	0.335	−2.723	0.9853	27	0.109	140

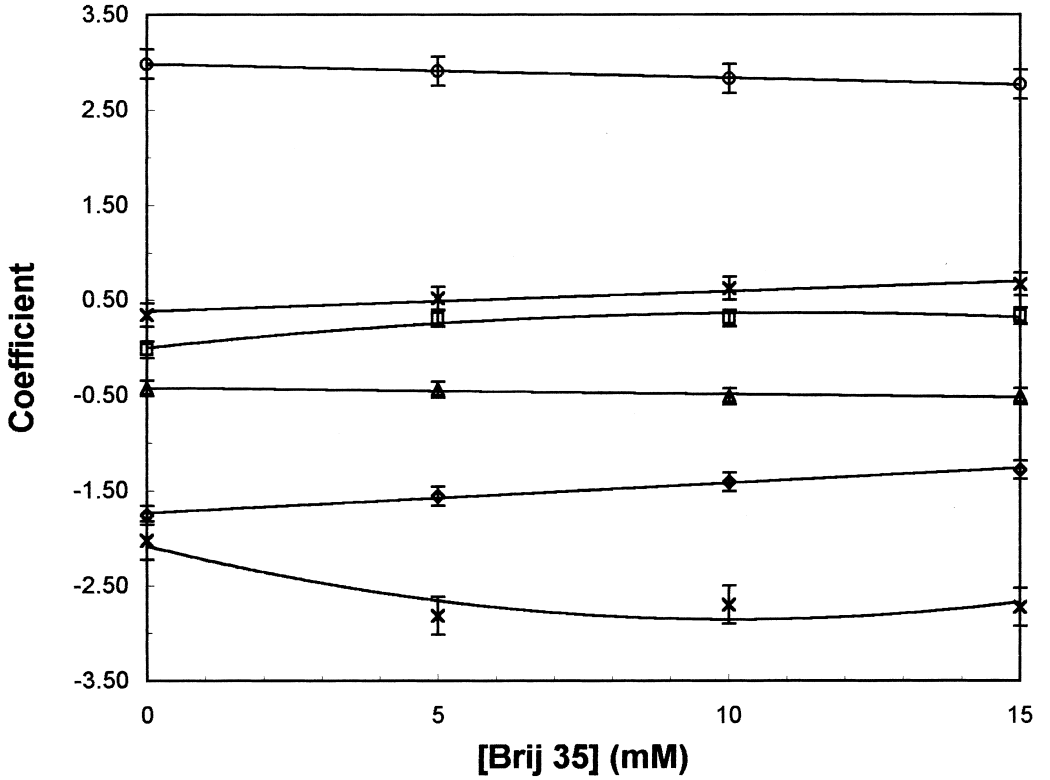

Fig. 1. Plot of the system constants of the solvation parameter model for 50 m*M* sodium dodecyl sulfate and 5–15 m*M* Brij 35 in mixed-micellar systems in reference to 50 m*M* sodium dodecyl sulfate micellar system. (◊): *c*; (*): *r*; (△): *s*; (□): *a*; (×): *b*; (○): *v*. Standard deviations are included.

If we assume that Eq. (1) represents a biological process with log SP a parameter of biological interest, and that a similar equation (Eq. (3)) can be applied to the retention factor, *k*, in a particular MEKC system,

$$\log k = c' + v' V_X + r' R_2 + s' \pi_2^H + a' \Sigma\alpha_2^H + b' \Sigma\beta_2^H \quad (3)$$

it is evident that if the *v*, *r*, *s*, *a*, and *b* coefficients in Eq. (1) are close to the respective *v′*, *r′*, *s′*, *a′*, and *b′* coefficients in Eq. (3), a linear relationship between the biological, log SP, and the MEKC, log *k*, properties must be observed. In fact, it is only required that the coefficients of Eq. (1) be proportional to the coefficients of Eq. (3). This can be checked by dividing the coefficients of the equation by one of them. The largest coefficients in MEKC and in most biological systems are *v* and *b*. Because in many instances a volume correction term (vV_X) is needed, we shall choose *b* coefficient and Eqs. (1) and (3) can be written as

$$\log \mathrm{SP} = c + b\,(v\,V_X/b + r\,R_2/b + s\,\pi_2^H/b + a\,\Sigma\alpha_2^H/b + b\,\Sigma\beta_2^H/b) \quad (4)$$

$$\log k = c' + b'\,(v'\,V_X/b' + r'\,R_2/b' + s'\,\pi_2^H/b' + a'\,\Sigma\alpha_2^H/b' + b'\,\Sigma\beta_2^H/b') \quad (5)$$

If the ratios v/b, r/b, s/b, and a/b are similar to the ratios v'/b', r'/b', s'/b', and a'/b', respectively, the following linear relationship is obtained

$$\log \mathrm{SP} = (c - b\,c'/b') + (b/b')\log k \quad (6)$$

Table 4
Ratios of coefficients of the solvation parameter model for several biological systems

Biological system	v/b	r/b	s/b	a/b	b	c
log P_{ow}	−1.10	−0.16	0.30	−0.01	−3.46	0.09
log BB	−1.43	−0.29	0.99	1.01	−0.70	−0.44
log $(1/C_{nar})$	−1.30	−0.30	0.27	−0.09	−2.59	0.58
log k_p	−0.52	0.00	0.17	0.18	−3.41	1.79

Therefore, one easy way to find out MEKC systems that could model biological processes is to compare the ratios of the coefficients of both systems. Table 4 presents the ratios of the coefficients of the solvation parameter model for several properties of biological interest: octanol–water partition, P_{ow}, [6], blood–brain distribution, BB, [7], tadpole narcosis, C_{nar}, [8], and skin permeation, k_p, [9]). Table 5 presents the ratios of the coefficients for the MEKC systems studied.

Comparison of the ratios of the coefficients for log P_{ow} with those of Table 5 shows that ratios of the coefficients for the MEKC system with 0 m*M* of Brij 35 are quite similar, except for the v/b ratio which is significantly higher than the v'/b' ratio. This prevents modelling of the vV_x term. However, this is not a problem because the V_x parameter is an additive property that can be easily calculated from the molecular formula of the compound. In this instance, Eq. (6) can be modified to

$$\log SP = (c - b\,c'/b') + (b/b')\,[\log k + (b'\,v/b - v')\,V_x] \quad (7)$$

Application of this equation to the log P_{ow} and MEKC with 0 m*M* of Brij 35 coefficients gives

$$\log P_{ow} = 3.10 + 1.71\,(\log k - 0.75\,V_X) \quad (8)$$

That is to say, a linear relationship must be obtained between log P_{ow} and the log k of the solute in the MEKC system with SDS as surfactant corrected by the volume of the solute (log $k - 0.75\,V_X$). The plot obtained for 25 of the solutes studied with known log P_{ow} (Table 1) obtained from Ref. [6] is presented in Fig. 2. The correlation obtained is

$$\log P_{ow} = 2.77 + 1.74\,(\log k - 0.75\,V_x)$$
$$n = 25 \quad R = 0.981 \quad \text{sd} = 0.17 \quad (9)$$

which is not very different from the equation predicted (Eq. (8)).

Tadpole narcosis $(1/C_{nar})$ can be also modelled by the MEKC systems with 10 or 15 m*M* Brij 35, provided that a volume correction is done. We have chosen the system with 10 m*M* Brij 35 because it has a larger migration window. The equation predicted is

$$\log (1/C_{nar}) = 1.92 + 0.96\,(\log k + 0.65\,V_x) \quad (10)$$

There are only 8 of the test solutes of Table 1 with known log $(1/C_{nar})$ values, but we have completed the set with 5 additional solutes of known log $(1/C_{nar})$. The log k values in the MEKC system with 10 m*M* Brij 35 were measured and they are presented in Table 6 together with the volume of the solutes (V_x) and their log $(1/C_{nar})$ values. The plot of the log $(1/C_{nar})$ against the log k value corrected by the volume (log $k + 0.65\,V_x$) is presented in Fig. 3. The correlation obtained is

Table 5
Ratios of coefficients of the solvation parameter model for the MEKC systems of Table 3

Conc. Brij 35 (m*M*)	v'/b'	r'/b'	s'/b'	a'/b'	b'	c'
0	−1.47	−0.17	0.21	0.01	−2.02	−1.76
5	−1.03	−0.18	0.16	−0.11	−2.81	−1.56
10	−1.05	−0.23	0.19	−0.11	−2.70	−1.41
15	−1.02	−0.24	0.19	−0.12	−2.72	−1.28

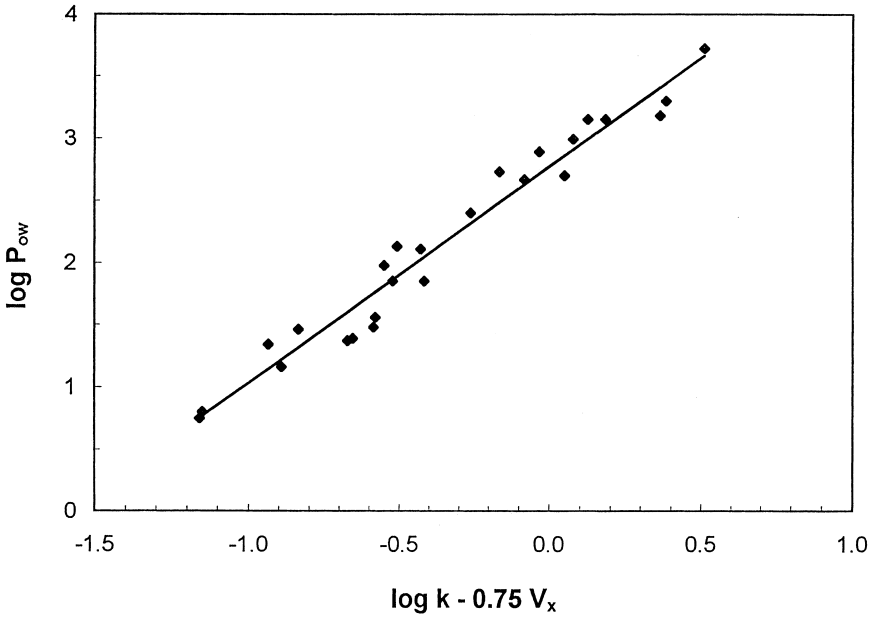

Fig. 2. Plot of the logarithm of the octanol–water partition coefficient against the logarithm of the retention factor of the solutes in the 50 m*M* sodium dodecyl sulfate micellar system corrected by the solute volume.

$$\log (1/C_{nar}) = 1.44 + 1.21 (\log k + 0.65 V_x)$$
$$n = 13 \quad R = 0.973 \quad \text{sd} = 0.17 \qquad (11)$$

The agreement between this equation and the predicted one (Eq. (10)) is not as good as for the log P_{ow}, probably because the MEKC system does not match the biological system as well as for octanol–water, and also because the number of solutes tested is lower. Anyway, the equation is better than the traditional QSAR correlations of log $(1/C_{nar})$ with log P_{ow}, even if a volume correction is done [8] and allows an accurate estimation of narcosis concentration from MEKC retention.

Table 6
Tadpole narcosis concentration [8], log $(1/C_{nar})$, volume descriptor, V_x, and retention factor, log k, in the 50 m*M* SDS + 10 m*M* Brij 35 MEKC system for additional test solutes

Substance	Log $(1/C_{nar})$	V_x	Log k
Quinoline	2.72	1.0443	0.450
m-Xylene	3.42	0.9982	1.134
Acetophenone	3.04	1.0139	0.550
Phenylthiourea	2.18	1.1774	−0.165
Paraldehyde	1.60	1.0215	−0.471

Table 4 reports two other biological systems which cannot be modelled by the MEKC systems studied. We may observe that the r/b and a/b ratios for the rate of skin permeation from water, log k_p, are higher than the corresponding ratios of any studied MEKC system. Also, the s/b and a/b ratios for blood–brain distribution, log BB, are much higher than the s/b and a/b ratios of the SDS–Brij 35 MEKC systems. In fact, surfactants with a hydrogen bond basicity lower than that of water ($a<0$) would be required to model both biological systems.

4. Conclusions

MECK is a fast and convenient method to estimate parameters of biological interest, such as log P_{ow}. The solute–solvent interactions in processes of biological interest can be simulated by MECK by simply changing the surfactant composition. In this sense, mixed surfactants are particularly useful.

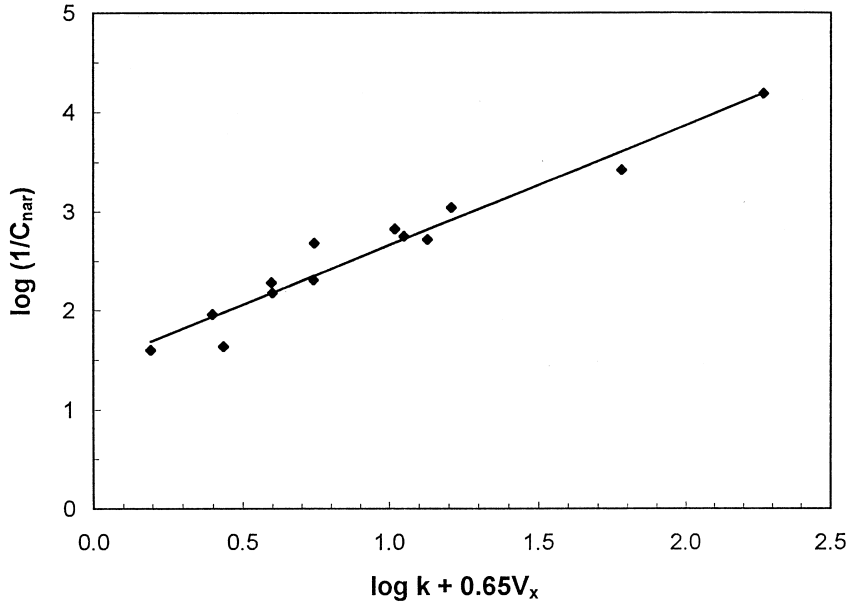

Fig. 3. Plot of the logarithm of the reverse of the narcosis concentration against the logarithm of the retention factor of the solutes in the 50 m*M* sodium dodecyl sulfate and 10 m*M* Brij 35 mixed-micellar system corrected by the solute volume.

SDS–Brij 35 mixtures can model some biological processes, such as tadpole narcosis, although the characterization of surfactants with complementary properties would be desirable to model other processes as blood–brain distribution or skin permeation.

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