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Comparison of the models describing the retention in micellar liquid chromatography with hybrid eluents for a group of benzene derivatives and polycyclic aromatic hydrocarbons

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Abstract

Some models for predicting capacity factors of benzene derivatives and some polycyclic aromatic hydrocarbons as a function of surfactant and organic modifier concentrations in micellar liquid chromatography with hybrid eluents have been tested. The surfactants used in this study were hexadecyltrimethylammonium bromide and sodium dodecyl sulphate and as organic modifiers *n*-propanol and *n*-butanol were employed both on C_8 and C_{18} columns.

The equation that best explains the experimental results is $1/k' = A\mu + B\varphi^2 + C\varphi + D\mu\varphi + E$ so we propose the use of this model in conjunction with the appropriate factorial design to predict the solute retention behaviour in micellar liquid chromatography with hybrid eluents.

1. Introduction

Micellar liquid chromatography (MLC) was first described by Armstrong and co-workers in 1979 [1,2]; since then, many reports have been published on the retention dependence of micellar concentrations [3–7], selectivity [4,8–13], and efficiency [14–18].

The primary advantages of this type of liquid chromatography compared to conventional reversed-phase liquid chromatography (RPLC) are low cost and non-toxicity of surfactants *versus* expensive and flammable solvents of chromatographic grade [3,4,19,20], unique selectivity [14,17,18,20–22], compatibility of mobile phases with salts and water-insoluble compounds [18], and shorter equilibration times for gradient elution. Perhaps the main drawback of this separation technique is its reduced efficiency compared to conventional reversed-phase systems [14,17,18,20,23,24], which is probably due to a poor wetting of the stationary phase [14] and restricted mass transfer [14,15].

In MLC, solutes may interact with both the stationary and mobile phases and thus partition equilibria are established between water and stationary phase, between water and micelles, and between micelles and stationary phase [25,26]. If the solute is water-insoluble partition occurs directly between the micelle solute species and the surfactant-coated stationary phase [26–28].

The addition of propanol and more generally short-chain alcohols to the mobile phase improves the chromatographic efficiency but the mechanism of solute retention in such hybrid

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eluents is very complex because alcohol modifiers alter the characteristics of surfactant [7,11,13,27,29,30] and the nature of the surfactant-modified stationary phase [27].

Although the use of hybrid eluents in MLC is a separation technique of widespread application there is a lack of knowledge about the solute retention mechanism. It seems clear that solute retention depends mainly on micelle and organic modifier concentrations and nature, on the nature of the solute, on pH and ionic strength, etc, but more work is needed to establish an equation that permits to predict the retention behaviour of solutes in such complicated systems and thus enable us to exploit the full potential advantages of this separation technique in a more judicious way.

Some authors have explored the possibilities of predicting the solute retention in MLC with hybrid eluents with varying concentrations of surfactant and organic modifier. Thus, Strasters *et al.* [6] using a dimensional space design determined the capacity factors of five mobile phases (four at the corners and the last one at the centre). Then, an equation of the type

$$\log k' = A\mu + B\varphi + C \quad (1)$$

is fitted in each of the four triangle subspaces with three measurements, two at the corners and the central point (μ being the total surfactant concentration and φ the volume fraction of organic modifier).

Torres-Lapasió *et al.* [7] also used the capacity factor of five mobile phases (with different experimental designs) to achieve the constants calculation for different equations and then with all the capacity factors measurements (thirteen mobile phases and five solutes) the prediction errors were calculated. The equations that they checked consisted in linear and quadratic expressions in which the reciprocal or the logarithm of the capacity factor were related to μ and φ. As an example of such expressions we can cite three of them with which the least errors were obtained

$$1/k' = A\mu + B\varphi + C\mu\varphi + D \quad (2)$$

$$1/k' = A\mu + B\varphi^2 + C\varphi + D\mu\varphi + E \quad (3)$$

$$\log k' = A\mu + B\varphi + C\mu\varphi + D \quad (4)$$

The best results were obtained with Eq. 2. It was also indicated that for the catecholamines studied by them and for several aromatic compounds the retention did not follow a linear model ln k' *versus* (μ,φ). However, they only tested the models with an anionic surfactant (sodium dodecyl sulphate, SDS).

The objective of this report is to provide more data for a better understanding of the solute retention mechanism in MLC with hybrid eluents and to find, if possible, an equation to describe it which should allow an easy way to predict the retention of a solute in any mobile phase with a minimum effort.

To study the influence of the nature and concentration of the surfactant and the alcohol on the retention of the solute, we have used the retention data of fifteen benzene and naphthalene derivatives and eight polycyclic aromatic hydrocarbons in micellar mobile phases with different concentrations of hexadecyltrimethylammonium bromide (CTAB) and SDS modified with different percentages of *n*-propanol and *n*-butanol. This study has been made for two columns, octadecylsilica and octylsilica.

2. Experimental

2.1. Apparatus

The Chromatograph consisted of a 1050 pump, a 1050 automatic injector, a 1050 spectrophotometric detector of variable wavelength, and a HP 3394 integrator (all from Hewlett-Packard).

Retention data were obtained with a Spherisorb C_8, 15 cm × 4.0 mm I.D. column ($d_p = 5$ μm) (Teknokroma).

A 0.45-μm filter and filtration system (Millipore) were used.

2.2. Reagents

SDS, CTAB, *n*-propanol and *n*-butanol (all from Merck) were used as received. Water

purified with a Milli-Q system (Millipore) was used.

Benzene derivatives and polycyclic aromatic hydrocarbons were as follows: (1) benzene, (2) benzylic alcohol, (3) benzamide, (4) toluene, (5) benzonitrile, (6) nitrobenzene, (7) phenol, (8) 2-phenylethanol, (9) chlorobenzene, (10) phenylacetonitrile, (11) 3,5-dimethylphenol, (12) naphthalene, (13) 1-naphtol, (14) 2-naphtol, (15) 1-naphthylamine, (16) pyrene, (17) phenanthrene, (18) 2,3-benzofluorene, (19) fluorene, (20) fluoranthene, (21) acenaphtylene, (22) acenaphthene and (23) anthracene.

2.3. Procedure

Micellar mobile phases (with a surfactant concentration from 0.035 to 0.12 *M*) were prepared by dissolving the appropriate amount of surfactants and *n*-propanol or *n*-butanol in water in a ultrasonic bath followed by filtration. Stock solutions of test solutes were prepared in the mobile phase itself and their concentrations were adjusted to permit their detection from the injection of a 20-μl volume of sample. The void volume of the column for SDS micelles was determined from the retention time of the peak originating from the injection of the nitrate anion into the chromatographic system. For CTAB mobile phases, the first deviation of the baseline was employed.

The column and the mobile phase were water jacketed and thermostated at 25 ± 1°C with a circulating water bath.

2.4. Data manipulation

Multiple regression analysis and Box plots were carried out using a SOLO Statistical System [31].

3. Results and discussion

The capacity factors of eight polycyclic aromatic hydrocarbons in a MLC system in the presence of *n*-propanol and *n*-butanol were determined by using SDS and CTAB as surfactants in the mobile phase and a C_8 column. The results of these experiments have been used in this article in conjunction with the results obtained previously for a group of benzene and naphthalene derivatives on C_{18} and C_8 columns with mobile phases of SDS and CTAB without and in the presence of *n*-propanol and *n*-butanol. Table 1 groups all experimental data used in this work. All these data allowed conclusions to be drawn regarding the models which better fit the experimental retention data.

In order to compare models 1 and 2 (Eqs. 2 and 4 in the Introduction section of this article), several factorial designs were employed depend-

Table 1
Summary of experimental data used in this study

Experiment	Compounds	Surfactant and concentration range (*M*)	Alcohol and concentration range (%, v/v)	Column	n^a	Ref.
1	1–23	CTAB (0.035–0.1)	Propanol (0.03–0.1)	C_{18}	345	13, this work
2	1–15	SDS (0.035–0.08)	Butanol (0–0.1)	C_{18}	180	25,32
3	1–15	CTAB (0.05–0.12)	Propanol (0–0.1)	C_8	299	33
4	1–15	CTAB (0.05–0.12)	Butanol (0–0.1)	C_8	292	33
5	1–15	SDS (0.05–0.12)	Propanol (0–0.1)	C_8	300	33
6	1–15	SDS (0.05–0.12)	Butanol (0–0.1)	C_8	300	33
7	16–23	CTAB (0.05–0.12)	Propanol (0.03–0.1)	C_8	112	This work
8	16–23	CTAB (0.05–0.12)	Butanol (0.03–0.1)	C_8	120	This work
9	16–23	SDS (0.05–0.12)	Propanol (0.03–0.1)	C_8	118	This work
10	16–23	SDS (0.05–0.12)	Butanol (0.03–0.1)	C_8	120	This work

[a] *n* = Number of experimental data per experiment (number of mobile phases multiplied by number of compounds).

ing on the hybrid system considered (Fig. 1). As shown in Fig. 1 capacity factors for compounds 16 to 23 were not obtained in the absence of alcohol due to the great retention times of these solutes in such media. With the capacity factors for these five mobile phases (Fig. 1) a multiple regression analysis [31] was achieved for each solute and then capacity factors for all mobile phases were calculated. With both, experimental and predicted capacity factors for models 1 and 2, the relative errors were calculated.

Our results, globally, show that the mean relative errors obtained for Eq. 4 are greater than those for Eq. 2, both for C_8 and C_{18} columns (Fig. 2), which is in agreement with the work reported by Torres-Lapasió *et al.* [7]. This is true in all the systems studied with only one exception that we will discuss later. As shown in Fig. 2 the mean relative errors are low, lesser than 5 and 10% for Eqs. 2 and 4, respectively.

With the aim of studying the influence of the surfactant nature on the errors obtained with

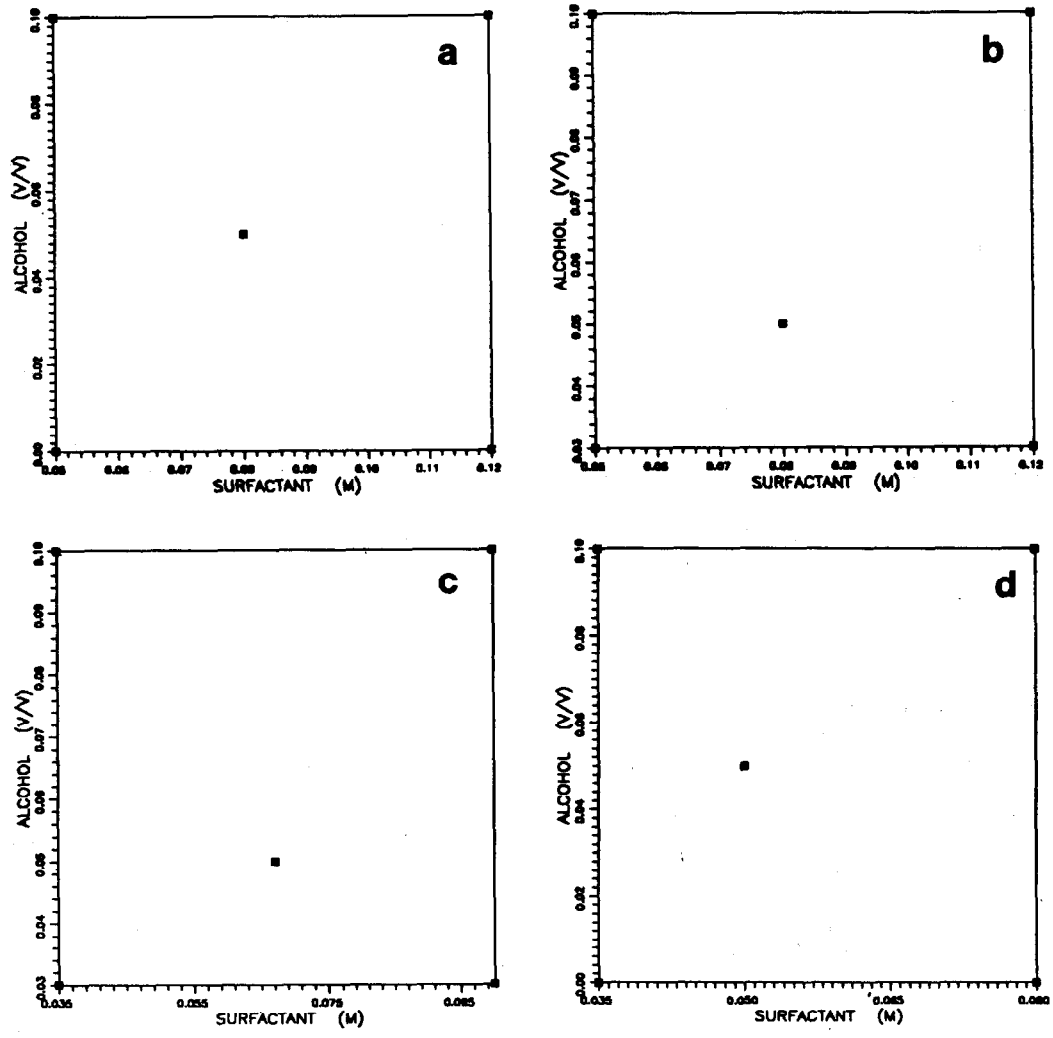

Fig. 1. Factorial designs used in the modellization study for systems (a) CTAB–*n*-propanol, CTAB–*n*-butanol, SDS–*n*-propanol and SDS–*n*-butanol (compounds 1–15 and C_8 column), (b) CTAB–*n*-propanol, CTAB–*n*-butanol, SDS–*n*-propanol and SDS–*n*-butanol (compounds 16–23 and C_8 column), (c) CTAB–*n*-propanol (compounds 1–23 and C_{18} column) and (d) SDS–*n*-butanol (compounds 1–15 and C_{18} column).

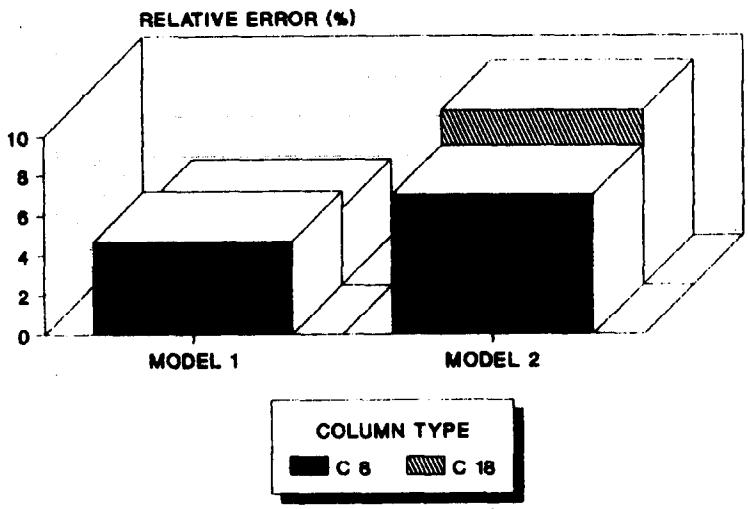

Fig. 2. Mean relative errors (%) for models 1 (Eq. 2) and 2 (Eq. 4) for C_8 and C_{18} columns.

Eqs. 2 and 4, the mean relative errors in hybrid phases of SDS and CTAB modified with the same alcohol were compared. Thus, in Fig. 3a and b the mean relative errors for the fifteen benzene and naphthalene derivatives (1–15) *versus* the type of equation for two different systems (CTAB–butanol and SDS–butanol) are shown. We can observe that in both cases the equation that best explains the experimental results is Eq. 2. Further, the mean relative errors for both equations are lesser when CTAB is used as surfactant. Although the results are not shown, the same conclusions have been found for the systems CTAB–propanol *versus* SDS–propanol with compounds 1–23.

CTAB and SDS are positively and negatively charged surfactants, respectively, so the solutes can interact in a different way with both surfactants. The solutes studied in this work have aromatic rings, so favourable electrostatic interactions between the positively charged CTAB head groups and the unlocated charge of the aromatic ring(s) of the solutes can be expected [25]. Thus, it seems that Eq. 2 better explains the results than Eq. 4 when, both, favourable electrostatic and hydrophobic interactions with micelles are responsible for the solute retention behaviour.

Although it has not been possible to compare the relative errors with both equations when the surfactant nature is modified using a C_{18} column, at least in the systems studied the results show, again, that Eq. 4 grants the poorest prediction of the solute retention behaviour.

In Fig. 3 the relative error of capacity factor prediction with Eqs. 2 and 4 when the hybrid eluents are SDS–propanol (Fig. 3c) and SDS–butanol (Fig. 3b) are shown in order to study the organic modifier nature. As we can observe for both alcohols, the equation that best explains, the experimental results is Eq. 2 being the mean relative errors greater when butanol is used as the organic modifier. Although the results obtained when CTAB is used as surfactant in the hybrid eluent and propanol as organic modifier have not been included in the figure the same conclusions can be drawn. In these systems, CTAB–propanol and CTAB–butanol, the mean relative errors of capacity factors prediction are 2.02 and 3.60% with Eq. 2 and 3.38 and 9.86% with Eq. 4, respectively.

Consequently, the equation that best explains the experimental results for compounds 1–15 is Eq. 2. This is also valid with the polycyclic aromatic compounds 16–23 with a C_{18} column (results not shown). With a C_8 column, as shown in Fig. 4, the relative errors obtained with Eq. 4 are lesser than those obtained with Eq. 2 only when SDS is used as the surfactant and butanol is employed as organic modifier (Fig. 4d), and

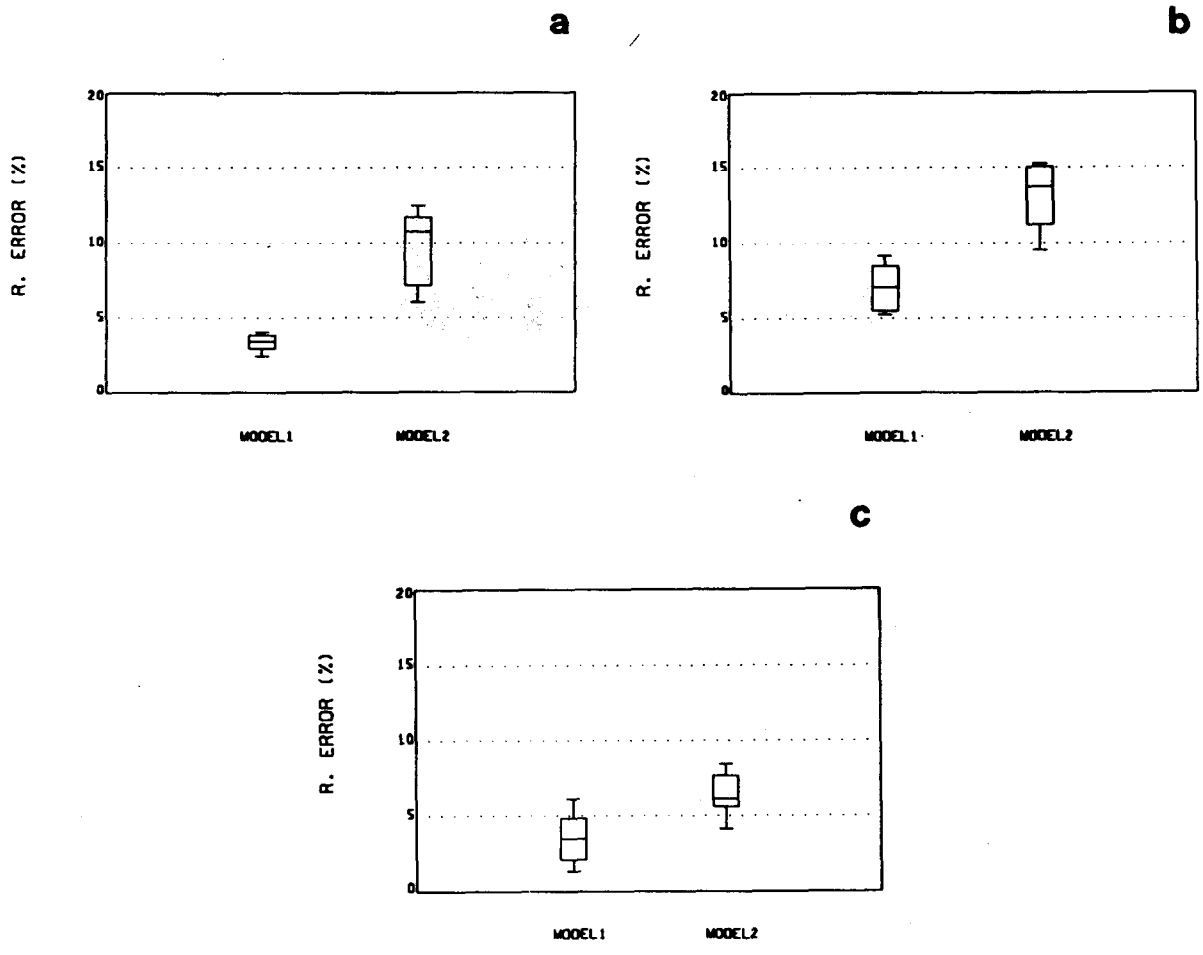

Fig. 3. Box plots for relative (R.) errors *versus* models of capacity factor prediction 1 and 2 for compounds 1–15 and a C_8 column with hybrid systems (a) CTAB–*n*-butanol, (b) SDS–*n*-butanol and (c) SDS–*n*-propanol.

not in the other cases (Fig. 4a–c). In Fig. 4a–c the relative errors *versus* models 1 and 2 are plotted for the hybrid eluents CTAB–propanol, CTAB–butanol and SDS–propanol, respectively. It can be concluded from these figures that changes in surfactant nature and alcohol influence the relative errors obtained for both models. The relative errors are low when CTAB is used as surfactant and they enhance when systems containing SDS are considered. These facts together seem to indicate that both models fail in taking into account some interactions of solutes, and that they are more important in very hydrophobic systems and when solute–micelle interactions are diminished.

Borgerding *et al.* [27] have reported that the amount of sorbed surfactant in the stationary phase decreases with the addition of alcohol modifiers compared to that possible in their absence and that the amount of surfactant desorbed by such additives is proportional to the additive concentration and increases as the hydrophobicity of the additive increases. Thus, one can expect that the amount of surfactant desorbed by butanol is greater than that by propanol. One can also expect that butanol can compete in a greater extent than propanol with the micelle for the interaction of the solutes.

In order to clarify the anomalous behaviour observed in Fig. 4d, another equation (Eq. 3 or model 3 in this discussion) has been included in the retention prediction study with all the com-

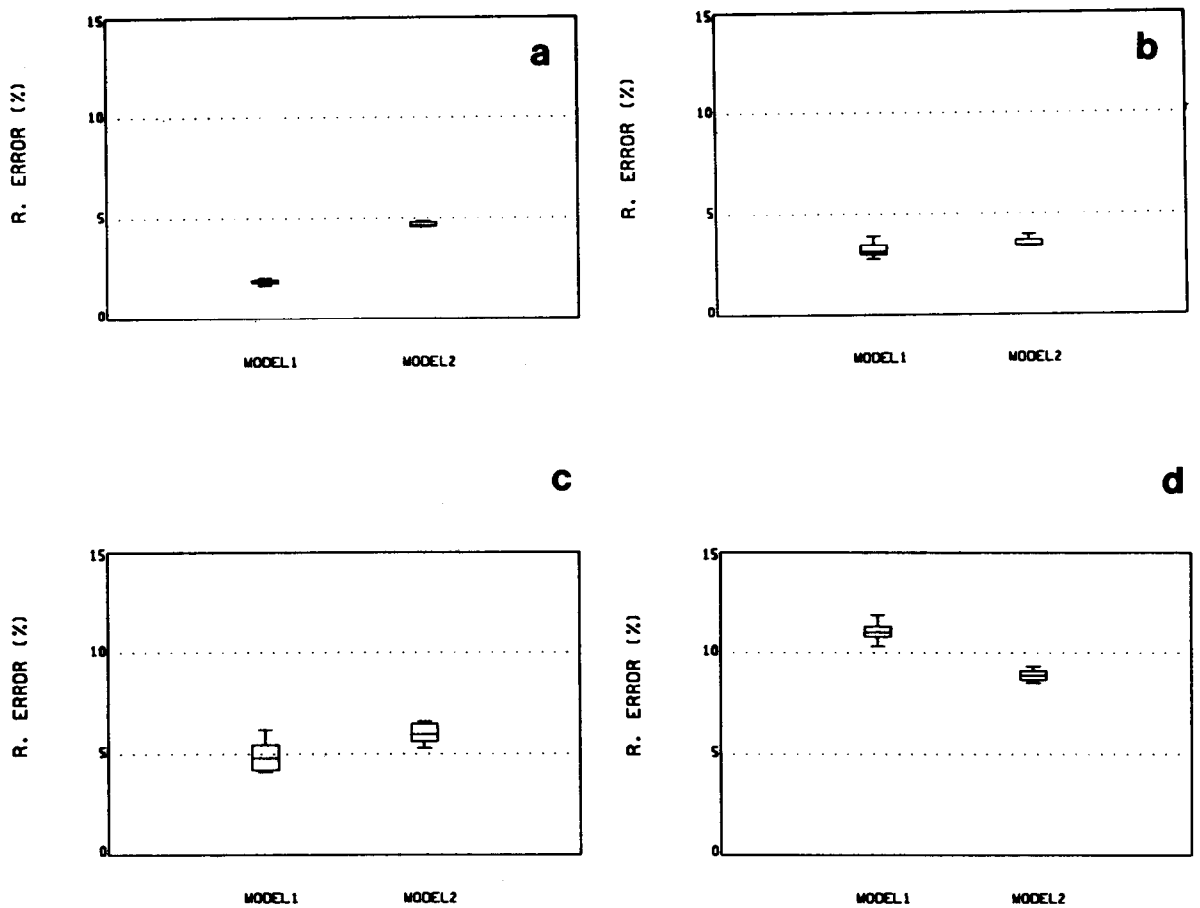

Fig. 4. Box plots for relative errors *versus* models of capacity factor prediction 1 and 2 for compounds 16–23 and a C_8 column with hybrid eluents (a) CTAB–*n*-propanol, (b) CTAB–*n*-butanol, (c) SDS–*n*-propanol and (d) SDS–*n*-butanol.

pounds (1–23) since the dependence of the capacity factor on the concentration of micelles seems to be different from the dependence of the concentration of the modifier [7]. Torres-Lapasió *et al.* [7] have reported that equivalent coefficients (A–E) in both Eqs. 2 and 3 have been obtained for catecholamines and the φ^2 term was negligible compared to the $\mu\varphi$ term. In the case of compounds 16–23 the coefficients (A–E) for Eq. 3 have been calculated and for the system SDS–butanol (with a C_8 column) they are given in Table 2. These results show that for these compounds the term φ^2 is not negligible compared to the $\mu\varphi$ or the μ term. This behaviour is clearly shown in Fig. 5 in which the inverse of the capacity factor for pyrene (compound 16) *versus* φ is plotted for different concentrations of surfactant. It is evident that the relation between $1/k'$ and φ is quadratic and the effect is more pronounced as the surfactant concentration is increased.

Once the necessity of including a term in φ^2 is explained for the most hydrophobic compounds the validity of this equation has been checked with all the compounds in the different systems. The mean relative errors obtained with Eq. 3 are equal or clearly better as compared with those obtained with Eqs. 2 or 4. For instance, in Fig. 6, the relative errors with Eqs. 2, 3 and 4 for the different solutes in two systems (CTAB–propanol and SDS–butanol for a C_8 column) are shown. These two systems represent the best and the worst results for the prediction of solutes capacity factors. In Fig. 6a (CTAB–propanol) it

Table 2
Parameter values for Eq. 3 with the system SDS–*n*-butanol and a C_8 column

Compound	*A*	*B*	*C*	*D*	*E*
16	0.2092	10.1449	−1.2521	8.6939	0.0296
17	0.2653	11.2225	−1.3491	8.3469	0.0320
18	0.1647	12.0061	−1.4949	8.9388	0.0340
19	0.2955	13.0041	−1.5542	8.2449	0.0365
20	0.2184	12.1469	−1.4885	8.6735	0.0344
21	0.3498	13.6612	−1.6768	8.6735	0.0409
22	0.3449	13.3878	−1.5551	7.6939	0.0346
23	0.2600	13.1000	−1.6044	8.5714	0.0371

can be observed that the relative errors are low (individual values below 5%) for all the equations checked but significant differences can be detected among them, for example, for compound 2 the relative error by using model 2 is more than 5-fold higher than that obtained with model 3 and more than 2-fold higher if we compare models 1 and 3. In Fig. 6b the mean relative errors for all the compounds under study and with the three models checked (mobile phases containing SDS and butanol) have been plotted. These values are below 20, 13 and 12% for models 2, 1 and 3, respectively. It is interesting to note that great differences between models 1 or 2 with respect to model 3 are obtained for compounds 16–23 (mean relative errors below 6% for model 3), so apparently the inclusion of the term φ^2 (model 3), previously mentioned, clearly improves the prediction of capacity factors for these compounds.

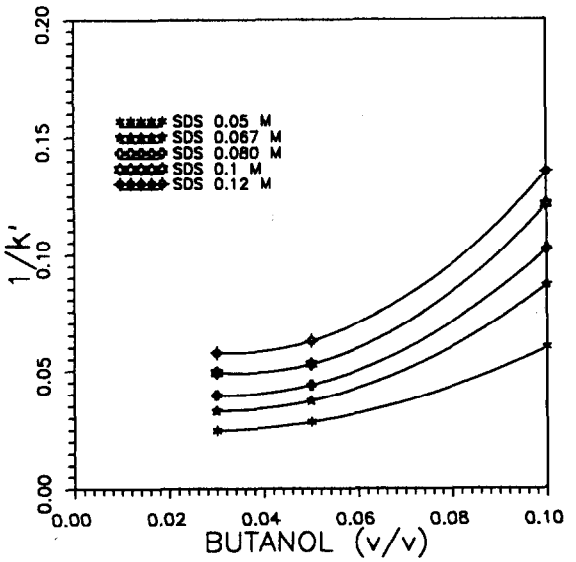

Fig. 5. Variation of the inverse of capacity factor for pyrene as a function of alcohol concentration for some fixed total surfactant concentrations (0.05, 0.067, 0.080, 0.100 and 0.120 *M*). Hybrid eluent containing SDS and butanol.

In Fig. 7 the calculated k' values according to Eq. 3 were plotted against the experimental values for compounds 1–15 (Fig. 7a) and 16–23 (Fig. 7b) both in mobile phases containing CTAB as surfactant and *n*-propanol as organic modifier (C_8 column). The straight lines obtained have slopes values very near to unity and intercepts near zero.

As a consequence of the results obtained in this article, we propose the use of Eq. 3 to describe the retention of a solute in MLC with hybrid eluents due to the fact that this equation is generally more valid than the others proposed.

4. Conclusions

From the results obtained in this work it can be concluded that at least for the group of compounds studied the following statements can be established:

First, the equation $1/k' = A\mu + B\varphi^2 + C\varphi + D\mu\varphi + E$ allows to obtain lower errors in the prediction of the capacity factors for all com-

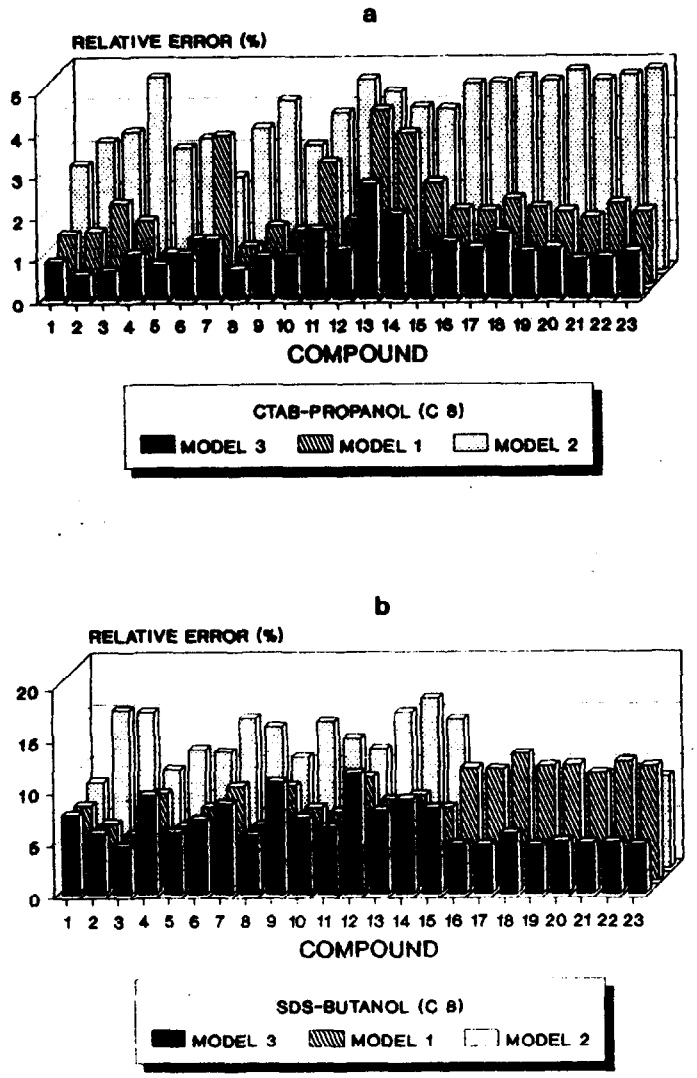

Fig. 6. Relative errors (%) obtained for the capacity factor prediction of compounds 1–23 with models 1, 2 and 3, the hybrid eluents being (a) CTAB–*n*-propanol and (b) SDS–*n*-butanol.

pounds, especially for the more hydrophobic ones. In fact the φ^2 term can be negligible for some compounds but not for these strongly hydrophobic ones. For these compounds, a clearly non-linear variation for $1/k'$ with φ can be obtained.

On the other hand, the nature of surfactant and alcohol used in the mobile phase seem to have an influence on the error obtained in the prediction of the capacity factor; CTAB and *n*-propanol being the surfactant and modifier that allow to decrease the relative errors.

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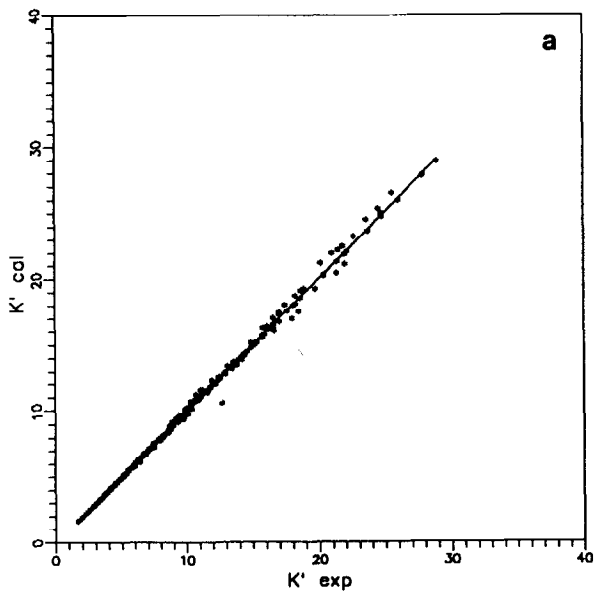

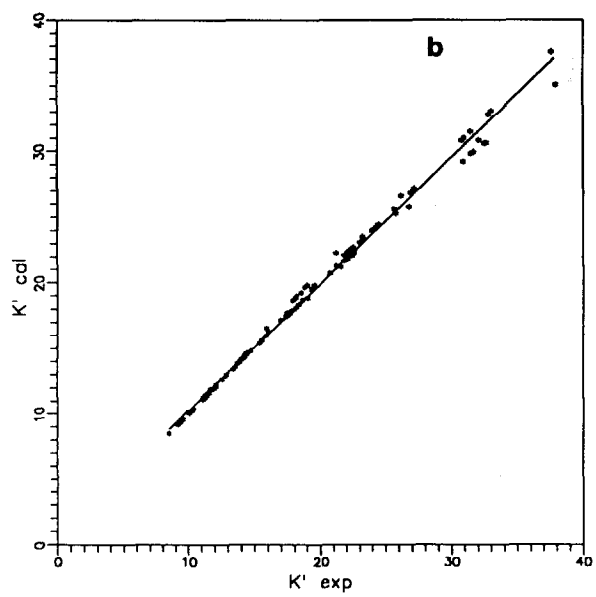

Fig. 7. Variation of calculated k' (K' cal) with model 3 as a function of experimental k' (K' exp) for (a) compounds 1–15 and (b) compounds 16–23 in systems containing CTAB as surfactant and n-propanol as organic modifier. (a) $y = 1.008x - 0.068$, $n = 299$; (b) $y = 0.963x + 0.659$, $n = 112$.

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