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Journal of Chromatography A, 780 (1997) 103–116

JOURNAL OF CHROMATOGRAPHY A

Review

Evaluation of distribution coefficients in micellar liquid chromatography

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Abstract

The possibilities of micellar liquid chromatography for evaluating distribution coefficients are discussed. Determination of solute–micelle association constants and distribution coefficients of solutes between stationary–aqueous, stationary–micellar and aqueous–micellar phases is described. Application of the calculation of distribution coefficients to the study of the retention mechanism of solutes in the chromatographic system and prediction of separation selectivity is also presented.

Keywords: Micellar liquid chromatography; Distribution coefficients; Reviews; Association constants; Retention mechanism

Contents

1. Introduction

Fig. 1 shows the different equilibria existing in micellar liquid chromatography (MLC) [1]. First, a solute can partition between the aqueous mobile phase and the micellar mobile pseudophase, this equilibrium being controlled by a distribution coefficient P_{mw}. Secondly, this solute can also originate a distribution equilibrium between the stationary phase and the micellar pseudophase which is characterized by a distribution equilibrium P_{sm}, and finally, a third equilibrium can be established for the solute distribution between stationary and aqueous mobile phases (P_{sw}). From these equilibria, several equations have been developed relating a solute chromatographic retention to the micellized surfactant concentration in the mobile phase.

Armstrong and Nome [1] have provided an equation relating a solute elution volume in MLC to the

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0021-9673/97/$17.00
PII S0021-9673(97)00329-4

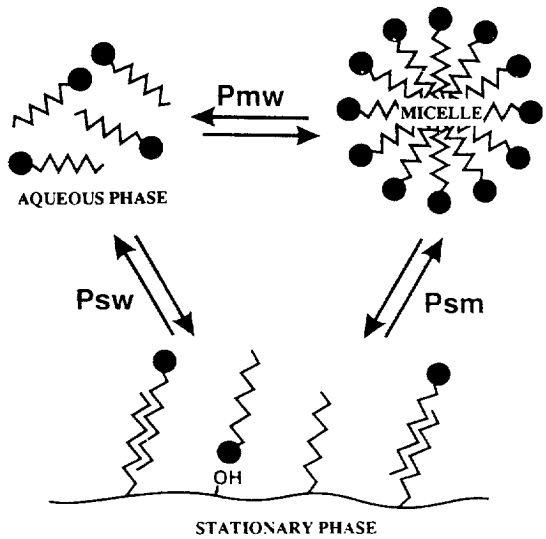

Fig. 1. Distribution equilibria of a solute in micellar liquid chromatography.

concentration of micellized surfactant in the mobile phase:

$$V_s/(V_e - V_m) = \{v(P_{mw} - 1)/P_{sw}\}C_M + 1/P_{sw} \quad (1)$$

where V_s, V_e and V_m are the stationary phase volume, solute elution volume and volume of mobile phase, respectively, v is the molar volume of the surfactant and C_M is the micellized surfactant concentration in the mobile phase which is given by the difference between total surfactant concentration (C) and critical micelle concentration (CMC) ($C_M = C - \mathrm{CMC}$).

Arunyanart and Cline Love [2] produced a similar equation relating the reciprocal of a solute capacity factor with the micellized surfactant concentration in the mobile phase, through the solute–micelle association constant, K_2:

$$1/k' = \{K_2/\Phi[L_S]K_1\}C_M + 1/\Phi[L_S]K_1 \quad (2)$$

where k' is the solute capacity factor, Φ is the phase ratio (the quotient between the stationary and mobile phase volumes, V_s/V_m), $[L_S]$ is the stationary phase concentration and K_1 is the association constant between the stationary and the aqueous mobile phases.

Eqs. (1) and (2) show that a solute retention in MLC decreases when the micelle concentration in the mobile phase is increased. This behavior is opposed to that found in ion-pair chromatography where micelles do not exist. In this case, the addition of an ionic surfactant (at a concentration below the CMC) to the mobile phase increases the compounds retention that electrostatically interacts with it [3,4].

On the other hand, Borgerding et al. [5] have proposed a limit theory to explain the retention in a MLC system of compounds with great affinity to the micellar pseudophase and experiencing a direct transfer from the micellar to the stationary phase. The capacity factor for such highly hydrophobic solutes is related to the micellized surfactant concentration in the mobile phase through the following equation:

$$k' = (V_s/V_m) \cdot (P_{sm}/vC_M) \quad (3)$$

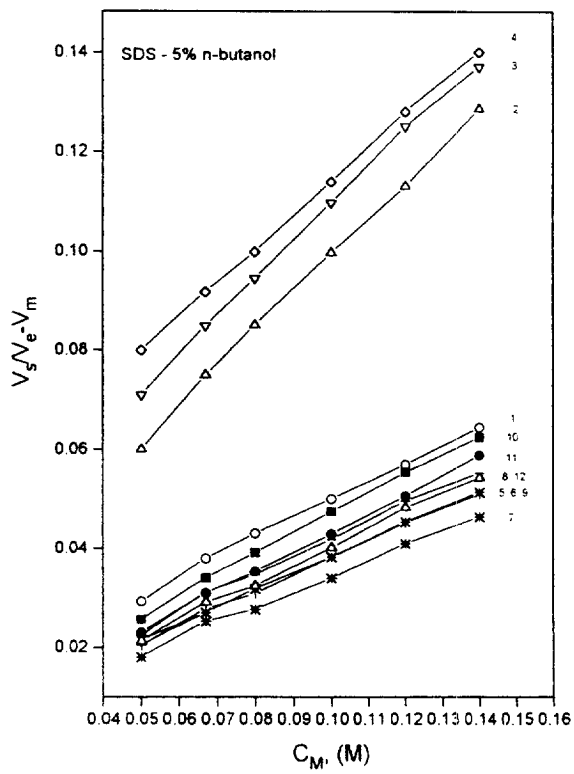

Fig. 2. Variation of the term $V_s/(V_e - V_m)$ as a function of C_M for a group of twelve polycyclic aromatic hydrocarbons in an SDS micellar system modified by 5% n-butanol. (1) Naphthalene, (2) 1-naphthol, (3) 2-naphthol, (4) 1-naphthylamine, (5) pyrene, (6) phenanthrene, (7) 2,3-benzofluorene, (8) fluorene, (9) fluoranthene, (10) acenaphthylene, (11) acenaphthene and (12) anthracene. C_8 column.

2. Evaluation of distribution coefficients in micellar liquid chromatography

From Eq. (1), it can be observed that the plot of the term $V_s/(V_e-V_m)$ versus C_M should provide a straight line from which the term $v(P_{mw}-1)$ can be evaluated as the ratio slope/intercept. From the treatment by Berezin et al. [6], the value of this term coincides with the solute–micelle association constant K_2 which is the parameter most often used to describe solute–micelle interactions. Once K_2 is calculated, the value of the solute distribution coefficient between the aqueous phase and the micellar pseudophase P_{mw} can be obtained if the molar volume of the surfactant is known. The distribution coefficient P_{sw} of the solute can be directly obtained from the value of the intercept of the straight line $V_s/(V_e-V_m)$ versus C_M, and P_{sm} can be evaluated from the P_{sw}/P_{mw} ratio.

In a similar way, the solute–micelle association constant K_2 of a solute with a micelle can be obtained from Eq. (2) as the ratio slope/intercept of the straight line obtained from the plot of the reciprocal of the solute capacity factor as a function of C_M. The value of the distribution coefficient P_{mw} can be obtained from the K_2 value as indicated previously.

The solute–micelle association constant obtained from Eqs. (1) and (2) is the association constant per monomer of surfactant. The solute–micelle association constant per micelle is obtained by multiplying the former by the micelle aggregation number.

Eqs. (1) and (2) have been frequently used to calculate solute–micelle association constants or distribution coefficients for a great number of compounds in purely aqueous micellar media [1–3,7–32]. In those cases in which the comparison was possible, a good agreement was observed between the association constants calculated by MLC and the values obtained by other techniques [11,18,33–35]. Furthermore, the validity of Eqs. (1) and (2) when micellar mobile phases modified by alcohols are used has also been shown [8,10,14,16,17,19–21,25,26,36–38]. In these media, solute retention decreases but the variation of the retention term with C_M still accomplishes Eqs. (1) and (2). This has enabled the determination of solute–micelle association constants in media modified by alcohols. The addition of an organic modifier can alter the characteristics of a micellar system (aggregation number and CMC) and this, in turn, can modify solute–micelle interactions [39,40] changing the chromatographic retention. As an example, Fig. 2 shows the good linearity that can be obtained for the variation of the retention term as a function of C_M. This figure shows the variation of the term $V_s/(V_e-V_m)$ as a function of C_M for a group of twelve polycyclic aromatic hydrocarbons in a sodium dodecyl sulphate (SDS) micellar system modified by 5% *n*-butanol. Table 1 lists the slope, intercept and correlation coefficient values for all

Table 1
Slope, intercept and correlation coefficient values for the variation of the retention term as a function of C_M for a group of polycyclic aromatic hydrocarbons (Fig. 2)

Mobile phase	Compounds	Slope	Intercept	Correlation coefficient (r)	P^a_{mw}	Relative error[a] (%)
SDS–5% *n*-butanol	Naphthalene	0.36	0.015	0.999	98.72	9.23
	1-Naphthol	0.73	0.029	0.996	103.78	14.54
	2-Naphthol	0.84	0.029	0.998	120.08	13.98
	1-Naphthylamine	0.76	0.041	0.998	75.73	8.63
	Pyrene	0.34	0.005	0.999	275.87	13.72
	Phenanthrene	0.37	0.005	0.999	306.83	25.23
	2,3-Benzofluorene	0.32	0.003	1.000	380.06	17.70
	Fluorene	0.37	0.006	0.998	252.07	23.63
	Fluoranthene	0.34	0.004	0.999	317.85	17.75
	Acenaphthylene	0.41	0.007	0.999	230.11	16.26
	Acenaphthene	0.39	0.005	0.999	291.24	13.70
	Anthracene	0.37	0.004	0.999	374.00	24.05

Micelle–water distribution coefficients calculated and the relative error obtained in their determination are also included.
[a] Values taken from Ref. [8].

Table 2
Experimental conditions under which the determination of distribution coefficients or solute–micelle association constants in Eqs. (1) and (2) have been achieved

Compounds	Parameter calculated	Column	Micellar system	Modifier	Buffer	T (°C)	No. of compounds	Ref.
Benzene derivatives	K_2	C_{18} (Varian)	SDS	None	None	25	4	[1]
Benzene derivatives	K_2	Cyano (Varian)	SDS	None	None	25	4	[1]
Benzene derivatives and 1-naphthol	P_{mw}, P_{sw}	LC-1 (Supelco)	SDS	None	None	25	7	[3]
Benzene derivatives and 1-naphthol	P_{mw}, P_{sw}	LC-1 (Supelco)	DTAB	None	None	25	7	[3]
Phenols	P_{mw}, P_{sw}, K_2	μBondapak C_{18} (Waters)	SDS	None	None	25	8	[11]
Catechols	P_{mw}, P_{sw}, K_2	μBondapak C_{18} (Waters)	SDS	None	None	25	5	[11]
Quinols	P_{mw}, P_{sw}, K_2	μBondapak C_{18} (Waters)	SDS	None	None	25	5	[11]
Dyhidroxybenzenes	P_{mw}	RP-18 (Waters)	SDS	None	None	Ambient	3	[12]
Aromatic solutes	K_2	μBondapak C_{18} (Waters)	SDS	None	None	25	10	[2]
Inorganic anions	P_{mw}, P_{sw}, P_{sm}	Spherisorb ODS (HPLC Technology)	CTACl	None	None	Ambient	3	[13]
Benzene derivatives	P_{mw}	C_{18} (Waters)	Brij-35	None	None	Ambient	6	[14]
Benzene derivatives	P_{mw}	C_{18} (Waters)	Brij-35	15% Ethanol	None	Ambient	6	[14]
Toluene, caffeine, SOBS, BTAB	P_{mw}, P_{sw}	Silica, CN, C_1, C_8, C_{18}	SDS	None	None	25	4	[15]
Toluene, caffeine, benzoic acid, CPC	P_{mw}, P_{sw}	Silica, CN, C_1, C_8, C_{18}	CTAB	None	None	25	4	[15]
Toluene, caffeine, SOBS, BTAB, benzoic acid, CPC	P_{mw}, P_{sw}	Hypersil C_{18} Hypersil SAS	SDS	None	None	25	6	[16]
Toluene, caffeine, SOBS, BTAB, benzoic acid, CPC	P_{mw}, P_{sw}	Hypersil C_{18} Hypersil SAS	SDS	0.1 *M* NaCl	None	25	6	[16]
Toluene, caffeine, SOBS, BTAB, benzoic acid, CPC	P_{mw}, P_{sw}	Hypersil C_{18} Hypersil SAS	SDS	5% Methanol	None	25	6	[16]
Toluene, caffeine, SOBS, BTAB, benzoic acid, CPC	P_{mw}, P_{sw}	Hypersil C_{18} Hypersil SAS	CTAB	None	None	25	6	[16]
Toluene, caffeine, SOBS, BTAB, benzoic acid, CPC	P_{mw}, P_{sw}	Hypersil C_{18} Hypersil SAS	CTAB	0.1 *M* NaCl	None	25	6	[16]
Toluene, caffeine, SOBS, BTAB, benzoic acid, CPC	P_{mw}, P_{sw}	Hypersil C_{18} Hypersil SAS	CTAB	5% Methanol	None	25	6	[16]
n-Alkylbenzenes and *n*-alkylphenonas	P_{sw}, K_2	Ultrasphere C_8 (Altex)	CTAB	None	None	31	11	[17]
n-Alkylbenzenes and *n*-alkylphenonas	P_{sw}, K_2	Ultrasphere C_8 (Altex)	SDS	None	None	31	11	[17]
n-Alkylbenzenes and *n*-alkylphenonas	P_{sw}, K_2	Ultrasphere C_8 (Altex)	SDS	3% 2-Propanol	None	31	11	[17]
n-Alkylbenzenes and *n*-alkylphenonas	P_{sw}, K_2	Microsorb C_{18} (Rainin)	SDS	None	None	31	11	[17]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	SDS	None	None	25	15	[33]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	CTAB	None	None	25	15	[33]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	Brij-35	None	None	25	15	[33]
Benzene and naphthalene derivatives	K_2	C_{18} (Altex)	SDS	3% 2-Propanol	None	38	16	[10]
Benzene and naphthalene derivatives	K_2	Ultrasphere C_8 (Altex)	CTAB	3% 2-Propanol	None	38	16	[10]
Amino acids and peptides	K_2	Bakerbond C_{18} (J.T. Baker)	SDS	None	Phosphate (pH = 2.5)	40	9	[18]
Aromatic compounds	K_2	Bakerbond C_{18} (J.T. Baker)	SDS	None	Phosphate (pH = 2.5)	40	8	[18]
Chlorophenols	K_2	Bakerbond C_{18} (J.T. Baker)	SDS	None	Phosphate (pH = 7)	40	10	[18]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	SDS	5% *n*-Butanol	None	25	15	[19]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	SDS	10% *n*-Butanol	None	25	15	[19]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	SDS	0.1 *M* NaCl	None	25	15	[19]
Benzene and naphthalene derivatives	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	CTAB	5% *n*-Butanol	None	25	15	[19]
Benzene and naphthalene derivatives	K_2	Spheri-10 RP-18 (Brownlee)	SDS	None	None	25, 35, 45	7	[20]
Benzene and naphthalene derivatives	K_2	Spheri-10 RP-18 (Brownlee)	SDS	3% *n*-Propanol	None	25, 35, 45	7	[20]
Benzene and naphthalene derivatives	K_2	Spheri-10 RP-18 (Brownlee)	SDS	5% *n*-Propanol	None	25, 35, 45	7	[20]
Mono-, di- and trisubstituted benzenes	K_2	Microsorb ODS (Rainin)	SDS	2% *n*-Propanol	None	25	20	[21]
Mono-, di- and trisubstituted benzenes	K_2	Microsorb ODS (Rainin)	CTAB	None	None	35	21	[21]

Diuretics	K_2	Spherisorb ODS-2 (HP)	SDS	None	None	Ambient	6	[22]
PAHs	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	SDS	None	None	25	17	[23]
PAHs	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	CTAB	None	None	40	17	[23]
PAHs	P_{mw}, P_{sw}, K_2	NovaPak C_{18} (Waters)	Brij-35	None	None	25	17	[23]
Benzene and phenol derivatives	P_{mw}, P_{sw}	Inertsil ODS (Gaskro Kogyo)	Brij-35	None	None	25	8	[24]
Substituted toluenes	log P_{mw}	C_{18} HL (Biorad)	SDS	None	None	Ambient	20	[9]
Catecholamines	P_{sw}, K_2	Spherisorb ODS 1,2 (Sharlau)	SDS	None	Citrate (pH = 4.8)	Ambient	4	[25]
Catecholamines	P_{sw}, K_2	Spherisorb ODS 1,2 (Sharlau)	SDS	10% Ethanol	Citrate (pH = 4.8)	Ambient	4	[25]
Catecholamines	P_{sw}, K_2	Spherisorb ODS 1,2 (Sharlau)	SDS	10% Ethanol	Citrate (pH = 2.3)	Ambient	4	[25]
Catecholamines	P_{sw}, K_2	Spherisorb ODS 1,2 (Sharlau)	SDS	10% Ethanol	Citrate (pH = 7)	Ambient	4	[25]
Amino acids and peptides	P_{mw}, P_{sw}	Nucleosil C_{18} (Alltech)	SDS	3% 2-Propanol	Phosphate (pH = 2.5)	40	10	[26]
Dansylated amino acids	P_{mw}, P_{sw}	Nucleosil C_{18} (Alltech)	SDS	3% 2-Propanol	Phosphate (pH = 2.5)	40	11	[26]
Aromatic compounds	P_{mw}, P_{sw}	Nucleosil C_{18} (Alltech)	SDS	3% 2-Propanol	Phosphate (pH = 2.5)	40	9	[26]
Chlorophenols	P_{mw}, P_{sw}	Nucleosil C_{18} (Alltech)	SDS	3% 2-Propanol	Phosphate (pH = 2.5)	40	7	[26]
PAHs	K_2	NovaPak C_{18} (Waters)	SDS	5%, 10%, 15%, 20% Methanol	None	25	16	[37]
PAHs	K_2	NovaPak C_{18} (Waters)	CTAB	5%, 10%, 15% Methanol	None	40	16	[37]
PAHs	K_2	NovaPak C_{18} (Waters)	SDS	5%, 10%, 15%, 20% 2-Propanol	None	25	16	[37]
PAHs	K_2	NovaPak C_{18} (Waters)	CTAB	3%, 5%, 10%, 2-Propanol	None	40	16	[37]
PAHs	K_2	NovaPak C_{18} (Waters)	SDS	5%, 7%, 10%, *n*-Butanol	None	25	16	[37]
PAHs	K_2	NovaPak C_{18} (Waters)	CTAB	5%, 7%, 10%, *n*-Butanol	None	40	16	[37]
Benzene derivatives	K_2	Hypersil ODS (Alltech)	SB-12	None	Phosphate (pH = 6)	Ambient	9	[27]
Benzene derivatives	K_2	Hypersil ODS (Alltech)	MB-14	None	Phosphate (pH = 6)	Ambient	9	[27]
Benzene derivatives	K_2	Hypersil ODS (Alltech)	SDS	None	Phosphate (pH = 6)	Ambient	9	[27]
Dihydropyridines	P_{mw}, P_{sw}, P_{sm}, K_2	Spherisorb ODS-2 (Waters)	SDS	5% *n*-Butanol	Phosphate (pH = 6.7)	30	24	[36]
Dihydropyridines	P_{mw}, P_{sw}, P_{sm}, K_2	Spherisorb ODS-2 (Waters)	CTAB	5% *n*-Butanol	Phosphate (pH = 6.7)	30	24	[36]
Vanillin compounds	K_2	C_{18}, C_8 (Golden, CO)	SDS	None	Hydrochloric acid (pH = 3)	25	6	[7]
Vanillin compounds	K_2	C_{18}, C_8 (Golden, CO)	CTAB	None	Hydrochloric acid (pH = 3)	30	6	[7]
Cephalosporin	P_{mw}, P_{sw}, K_2	Spheri 5 ODS-224 (Brownlee)	SDS	None	Acetate (pH = 4.02)	Ambient	7	[28]
PAHs	P_{sw}, K_2	Hypersil C_{18}	Brij-35	None	None	60	12	[29]
Benzene derivatives	K_2	Spherisorb C_8 (Tecknocroma)	SDS	None	None	25	15	[8]
Benzene derivatives	K_2	Spherisorb C_8 (Tecknocroma)	SDS	10% Methanol	None	25	15	[8]
Benzene derivatives and PAHs	K_2	Spherisorb C_8 (Tecknocroma)	SDS	3%, 5%, 10% *n*-Propanol	None	25	23	[8]
Benzene derivatives and PAHs	K_2	Spherisorb C_8 (Tecknocroma)	SDS	3%, 5%, 10% *n*-Butanol	None	25	23	[8]
Benzene derivatives	K_2	Spherisorb C_8 (Tecknocroma)	CTAB	None	None	25	15	[8]
Benzene derivatives and PAHs	K_2	Spherisorb C_8 (Tecknocroma)	CTAB	3%, 5%, 10% *n*-Propanol	None	25	23	[8]
Benzene derivatives and PAHs	K_2	Spherisorb C_8 (Tecknocroma)	SDS	3%, 5%, 10% *n*-Butanol	None	25	23	[8]
Plant growth	K_2	Lichrospher R-CN (Merck)	SDS	None	Acetate (pH = 4.3 to 3.5)	Ambient	7	[30]
Aromatic compounds	K_2	LC-18 (Supelcosil)	Tween 60	60% Acetonitrile	None	Ambient	18	[38]
Aromatic compounds	K_2	LC-18 (Supelcosil)	Brij 30	60% Acetonitrile	None	Ambient	18	[38]
Aromatic compounds	K_2	LC-18 (Supelcosil)	DOSS	39% Acetonitrile	None	Ambient	18	[38]
Aromatic compounds	K_2	LC-18 (Supelcosil)	THPA	60% Acetonitrile	None	Ambient	18	[38]
Diuretics	P_{mw}	Spherisorb ODS-2 (Scharlau)	SDS	None	Citric acid–NaOH (pH = 3)	Ambient	5	[31]
Different nonionic compounds	K_2	Silasorb SPH C_8 (Lachema)	CTAB	None	None	Ambient	11	[32]
Different nonionic compounds	K_2	Silasorb SPH C_8 (Lachema)	SDS	None	None	Ambient	10	[32]

SDS sodium dodecyl sulphate; DTAB dodecyltrimethylammonium bromide; CTACl hexadecyltrimethylammonium chloride; SOBS sodium octylbenzene sulfonate; BTAB benzyltrimethylammonium bromide; CPC cetylpyridinium chloride; CTAB hexadecyltrimethylammonium bromide; Brij-35 polyoxyethylene (23) lauryl ether; SB-12 sulfobetaine (12); MB-14 myristyl betaine; Tween-60 polyoxyethylene (20) sorbiton monostearate; Brij-30 polyoxyethylene (4) dodecyl ether, DOSS dioctylsulfo succinate; THPA tetraheptylammonium.

lines included in Fig. 2 and the corresponding calculated coefficients for all compounds with the relative error obtained in their determination.

Table 2 groups the experimental conditions where determination of distribution coefficients and solute–micelle association constants has been achieved by MLC. For each group of compounds, the column, micellar system, modifiers (alcohols or salts), temperature and pH (when a buffer is used) in which each parameter was calculated are given. It can be observed that chemically bonded reversed-phase columns are generally employed, with octadecylsilica and octylsilica stationary phases mostly used. However, sometimes cyano, C_1 and silica columns have also been used. The solute–micelle association constants and distribution coefficients have been calculated mainly for SDS (of anionic nature) and cetyltrimethylammonium bromide (CTAB; of cationic nature) as micellar systems. Nonionic and zwitterionic surfactants have also been studied although only to a small extent. Most works were achieved using purely and unbuffered micellar mobile phases at ambient temperature. When a modifier was introduced in the mobile phase, it consisted of a short or medium chain alcohol such as methanol, ethanol, propanol or butanol, or a salt such as sodium chloride at a low concentration. When pH is fixed, phosphate buffer is frequently used. Table 2 shows the great number of distribution coefficients or solute–micelle association constants calculated by MLC under different experimental conditions. This prevents tabulation of all values determined for these parameters and all compounds studied. However, Table 2 indicates the reference in which a given distribution coefficient or solute–micelle association constant can be found for a given compound under the experimental conditions described. Some values of solute–micelle association constants for aromatic compounds with SDS and CTAB are included in Table 3. Values for the constants obtained by MLC for the same compounds by different authors under identical experimental conditions are also compared at this Table. Only the column used may be different (octadecylsilica and octylsilica). In some cases, K_2 values have been calculated from the distribution coefficients values that were the parameters given in referenced article. It is observed that a good agreement exists when different association constant values are available, especially in the case of SDS micelles, even for very hydrophobic compounds for

Table 3
Solute–micelle association constants (K_2) for different neutral solutes with SDS and CTAB micellar systems

Compounds	Reference										
	[3]	[2]	[17]	[33]	[20]	[18]	[23]	[8]	[11]	[15]	[9]
SDS											
Benzene	18.9	25.8	17.1	19.2	20.3			23.5			
Phenol	9.6			9.4	9.5			10.5	10.2		
Nitrobenzene	22.1			23.1		23.2		25.9			
Toluene	52.9	50.0	59.3	52.4	56.5	54.2		76.1		63.3	44.8
Naphthalene		241.9		290.4	353.0	235.0	245.0	217.1			
Benzyl alcohol				8.8		10.4		11.8			
Anthracene		5322.6					5440.0				
Pyrene		8064.5					8362.0				

	[15]	[17]	[21]	[32]	[33]	[8]
CTAB						
Toluene	141.9	129.0	83.3		141.8	203.8
Benzene		23.7	35.9		40.2	47.2
Phenol			38.5		71.4	79.5
Benzyl alcohol			12.8		13.5	17.3
Benzonitrile			17.9	17.5	19.4	27.2
Chlorobenzene			103.9		157.4	547.9
Nitrobenzene			33.3	27.0	36.9	54.7

which the error in the determination of association constants is usually high [8]. According to literature [41], K_2 values were independent of the stationary phase used.

Determination of distribution coefficients by MLC in media modified by alcohols requires knowing the CMC value of the micellar system in the medium considered (Eqs. (1) and (2)). This has caused CMC values for different micellar systems to be calculated prior to distribution coefficient determination [14,19,21,32,37,42].

The use of MLC to ascertain solute–micelle association constants and distribution coefficients has two main advantages: (1) this determination can be made for all compounds experiencing a chromatographic retention in the system which varies when the surfactant concentration in the mobile phase is modified. This is quite common. They do not need to experience a change in their spectroscopic characteristics in micellar media as when spectroscopic methods are used, for example. (2) Distribution coefficients and solute–micelle association constants can simultaneously be determined for numerous compounds since a mixture of them can often be injected in the chromatographic system enabling the simultaneous determination of many capacity factors under the experimental conditions described.

The main drawback of this method is the intrinsic error associated with the determination of a parameter as a quotient [43]. In fact, as K_2 is obtained from the slope/intercept ratio, error propagation of a quotient affects the error in determining this constant.

If K_2 is expressed as:

$$K_2 = \alpha/\beta \tag{4}$$

where α and β are the slope and intercept, respectively of the straight line of variation of the retention term in Eqs. (1) and (2) with C_M, the error in determining this constant being written as:

$$\Delta K_2 = (\beta\Delta\alpha + \alpha\Delta\beta)/\beta^2 \tag{5}$$

where $\Delta\alpha$ and $\Delta\beta$ are the errors of the slope and intercept of the straight line, respectively.

From ΔK_2, the relative error (RE), in percent, for the solute–micelle association constant can be calculated as:

$$\mathrm{RE}\,(\%) = (\Delta K_2/K_2)100 \tag{6}$$

Eq. (5) shows that the K_2 value obtained from Eqs. (1) and (2) will be affected by the errors in the slope and the intercept of the straight line of variation of the retention term with C_M. The same can be said for the distribution coefficient P_{mw}. A minor error will be obtained for P_{sw} (except for very small intercepts) which is only affected by the error in the intercept. The maximum error will correspond to the distribution coefficient P_{sm} which is calculated from the quotient of the other two, P_{mw} and P_{sw}.

It should be noted that the error in determining distribution coefficients or association constants is affected not only by the error values in the slope and intercept but also by the values of these two parameters. Eq. (5) shows that the error in determining solute–micelle association constants inversely varies with the squared of the intercept of the straight line considered. Although the value of the slope also affects this error, it can be said that for compounds for which very low intercept values are obtained, high errors in determining K_2 will be calculated. These compounds are those experiencing a high retention in the MLC system, that is, for which a high value of the capacity factor or elution volume is obtained. In the case of noncharged compounds, this situation corresponds to those with an important hydrophobic character.

MLC techniques also present a drawback for the evaluation of distribution coefficients since they are limited to low hydrophobic compounds. In fact, if compounds are very hydrophobic, their retention is described by Eq. (3), that is, the variation of the reciprocal of the capacity factor as a function of C_M should give a straight line the intercept of which is equal to zero. This explains the results found in literature related to obtaining negative intercepts which are really zero and not negative [14,23,33,44]. If the intercept obtained from the straight line of variation of retention with C_M is zero or negative, distribution coefficients P_{sw} and P_{mw} and solute–micelle association constants cannot be calculated. Only P_{sm} could be evaluated from Eq. (3). If the intercept value is very small although not equal to zero, distribution coefficients can be calculated, but the error obtained (see Eq. (5)) will be very high [5,8]. Anyway, there is no use in calculating P_{mw}

coefficients or solute–micelle association constants in this case since compounds fulfilling Eq. (3) are retained in the MLC system by experiencing a direct transfer from the micellar pseudophase to the stationary phase [5,8,36] and as a result, no partitioning between aqueous phase and micellar pseudophase exists. This, in turn, is related to the low solubility of these compounds in the aqueous phase. Fig. 3 shows the variation of the reciprocal of the capacity factors for five aromatic compounds (benzene, benzamide, 2-phenylethanol, 2-naphthol and naphthalene) as a function of micellized SDS in the mobile phase. Slope, intercept and correlation coefficient values for the straight lines obtained are grouped in Table 4 together with micelle–water distribution coefficients and their corresponding relative errors. It can be observed that the intercept of the straight lines obtained for these variations increases when the compounds hydrophobicity decreases (the logarithm of the octanol–water distribution coefficient, log P_{ow}, decreases), that is, when compounds solubility in the aqueous phase increases. If the solubility of a hydrophobic compound in the aqueous phase is increased by adding an organic modifier such as an alcohol to the mobile phase, a partitioning of the solute between the aqueous phase and the micellar pseudophase may arise enabling the calculation of P_{mw} or K_2 in these media, whereas that calculation is not possible in purely aqueous micellar media [8,14,16,17,19,20,37,46]. Fig. 4 shows the increase in the intercept of the straight line of variation of $1/k'$ versus C_M for a hydrophobic solute (naphthalene) when *n*-butanol at different percentages is added (3, 5 and 10%) to an aqueous SDS micellar

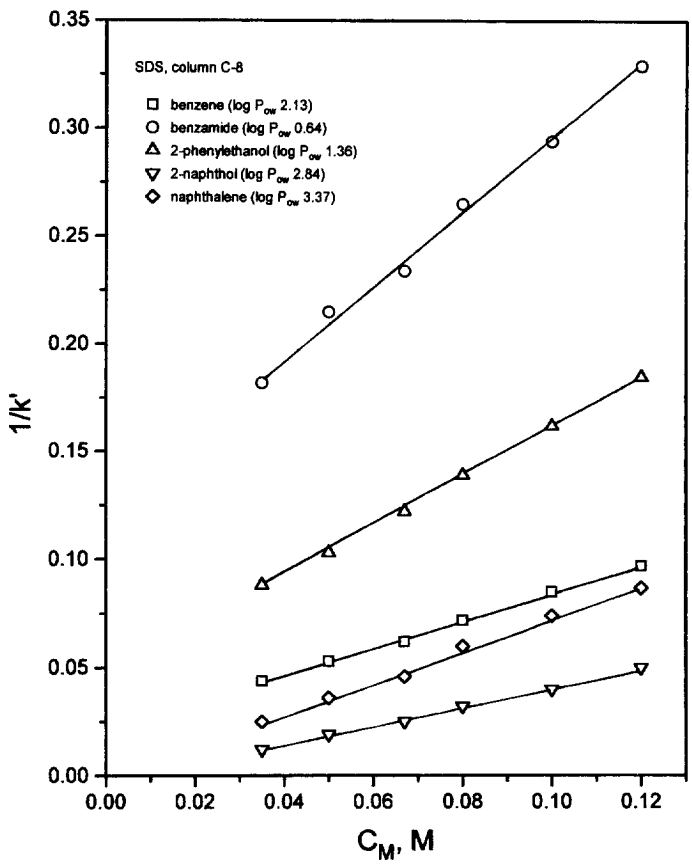

Fig. 3. Variation of $1/k'$ for five aromatic compounds of different hydrophobicity (benzene, benzamide, 2-phenylethanol, 2-naphthol and naphthalene) as a function of C_M in an SDS mobile phase. (Log P_{ow} values taken from Ref. [45]).

Table 4
Slope, intercept and correlation coefficient values for the variation of $1/k'$ as a function of C_M for a group of aromatic compounds (Figs. 3 and 4)

	Mobile phase	Compounds	Slope	Intercept	Correlation coefficient (r)	P^a_{mw}	Relative error[a] (%)
Fig. 3	SDS	Benzene	0.49	0.019	0.999	96.60	5.34
		Benzamide	1.23	0.100	0.998	50.92	6.37
		2-Phenylethanol	0.83	0.040	1.000	85.49	3.17
		2-Naphthol	0.39	0.003	0.998	683.81	40.11
		Naphthalene	0.30	0.001	0.996	883.53	79.77
Fig. 4	SDS–3% n-butanol		0.49	0.005	0.999	394.77	16.27
	SDS–5% n-butanol	Naphthalene	0.36	0.015	0.999	98.72	9.23
	SDS–10% n-butanol		0.78	0.036	0.998	88.52	9.62

Micelle–water distribution coefficients calculated and the relative error obtained in their determination are also included.
[a] Values taken from Ref. [8].

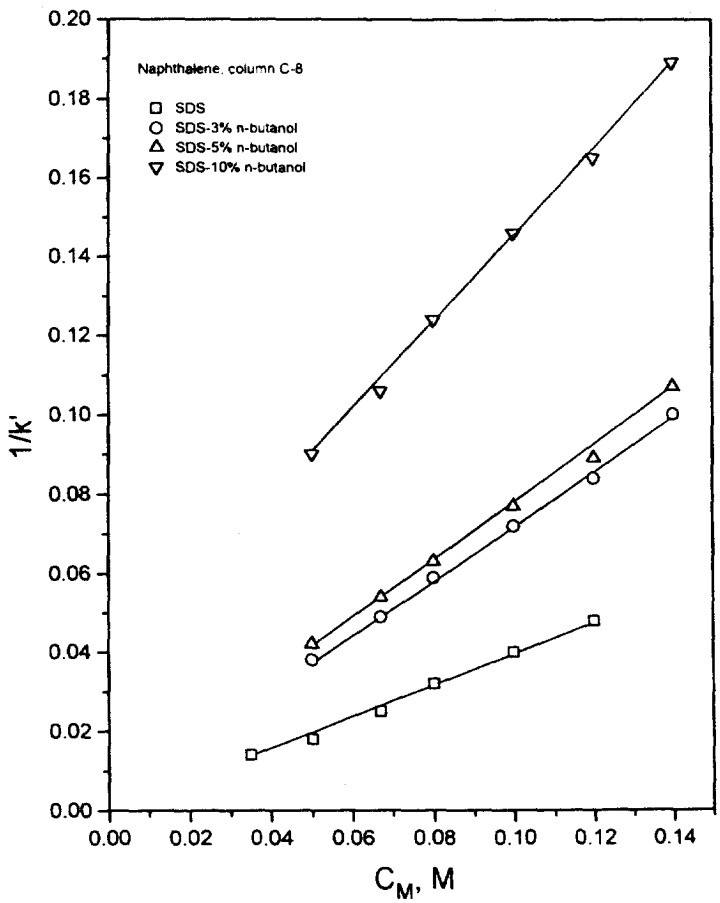

Fig. 4. Variation of $1/k'$ as a function of C_M for a hydrophobic solute (naphthalene) in an SDS mobile phase in absence of additives and in the presence of n-butanol at different percentages (3, 5 and 10%).

system (see Table 4 for slope, intercept and correlation coefficient values).

The addition of an alcohol of short or medium chain length has shown to decrease the P_{mw} distribution coefficients and K_2 values as well as the error in determining these parameters [8] as shown in Table 4 for naphthalene. This decrease is more important when increasing the length of the alcohol chain, that is, when decreasing its polarity (increasing its interaction with micelles) [8,47] as shown in Fig. 5 which shows a comparison between K_2 values for a group of twenty-three aromatic compounds with SDS in media modified by methanol (10%), *n*-propanol (10%) and *n*-butanol (3, 5 and 10%). As can be observed in Fig. 5, K_2 also decreases when increasing the percentage of the alcohol in the mobile phase; the decrease in K_2 values being higher for the most hydrophobic compounds (polycyclic aromatic hydrocarbons).

Fig. 6 shows a considerable decrease in the error obtained in determining K_2 for five aromatic compounds with SDS when increasing the length of the alcohol chain (5% *n*-propanol and 5% *n*-butanol) or its percentage in mobile phase (aqueous media and with 5 and 10% *n*-butanol). Again, the decrease observed in the error is more important for highly hydrophobic solutes.

From the above points, it can be stated that the addition of an alcohol to the mobile phase is an effective way to decrease the error associated to the determination of distribution coefficients. In literature, it is also proposed that the stationary phase be changed for a less apolar one [46]. This should decrease the distribution coefficient of a hydrophobic solute between the stationary and aqueous phases (P_{sw}) increasing the intercept of the straight line of variation of the retention as a function of C_M (see Eq. (1)). Accordingly, the error in determining K_2 or P_{mw} should decrease. However, at least from the results obtained by our research team [47] concerning K_2 values obtained for a group of benzene and naphthalene derivatives in octylsilica and octadecylsilica columns, it was observed that the modification of the stationary phase is not as effective as the addition of an alcohol to the mobile phase in order to decrease the error for K_2 determination.

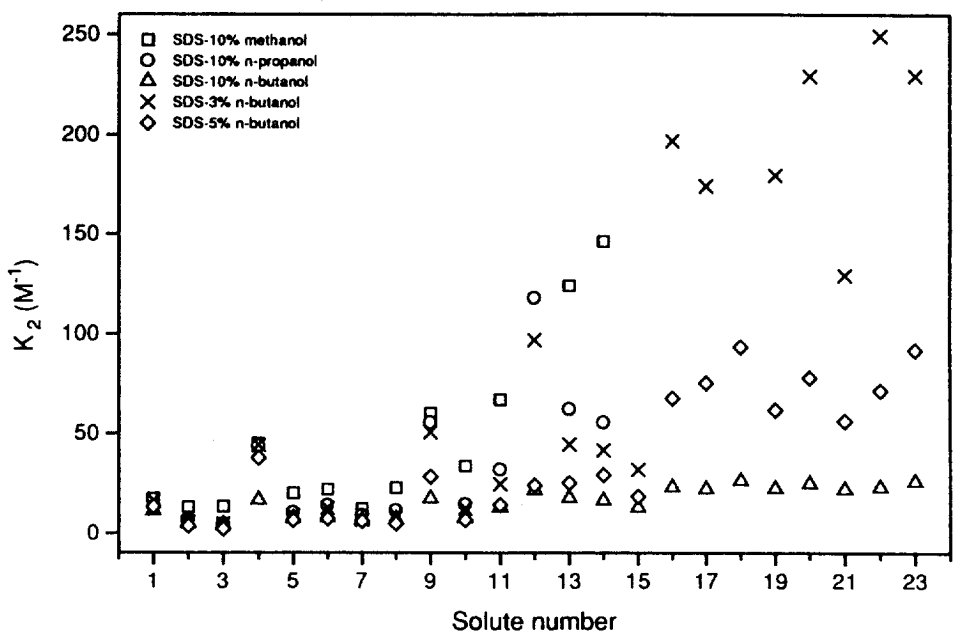

Fig. 5. Solute–micelle association constants for a group of twenty-three aromatic compounds with SDS micelles modified by methanol (10%), *n*-propanol (10%) and *n*-butanol (3, 5, 10%). (1) Benzene, (2) benzylic alcohol, (3) benzamide, (4) toluene, (5) benzonitrile, (6) nitrobenzene, (7) phenol, (8) 2-phenylethanol, (9) chlorobenzene, (10) phenylacetonitrile, (11) 3,5-dimethylphenol, (12) naphthalene, (13) 1-naphthol, (14) 2-naphthol, (15) naphthylamine, (16) pyrene, (17) phenanthrene, (18) 2,3-benzofluorene, (19) fluorene, (20) fluoranthene, (21) acenaphthylene, (22) acenaphthene and (23) anthracene.

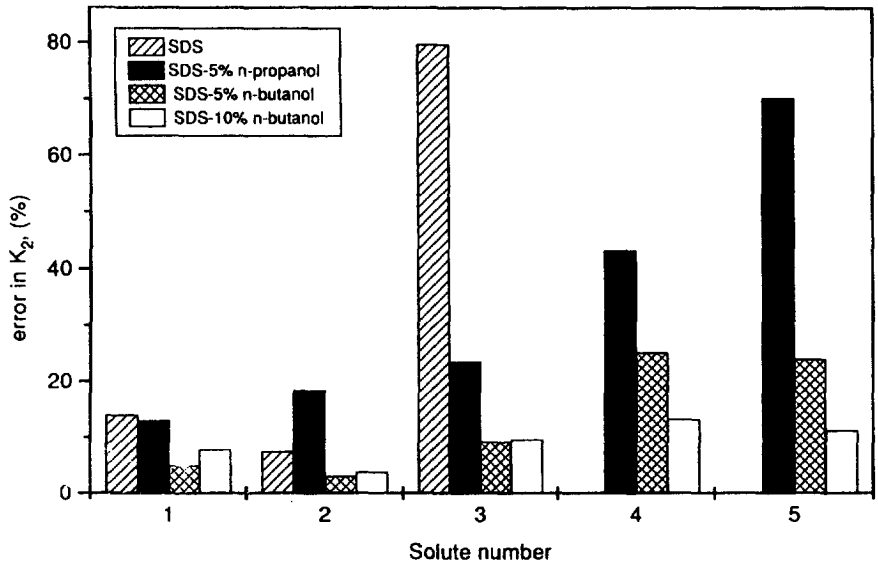

Fig. 6. Relative errors (%) for the determination of solute–micelle association constants for five aromatic compounds with a C_8 column in micellar systems of SDS, SDS–5% *n*-propanol, SDS–5% *n*-butanol, and SDS–10% *n*-butanol. (1) Toluene, (2) phenol, (3) naphthalene, (4) phenanthrene and (5) anthracene.

Errors obtained with the C_8 column were always similar or less than those obtained with the C_{18} column (eight different mobile phases compared), the differences being statistically significant only in three cases (mobile phases of SDS–10% *n*-propanol, CTAB–3% *n*-propanol and CTAB–10% *n*-propanol). Values obtained for K_2 in both columns were statistically similar according to literature [41]. Despite these results, it should be noted that even when the use of less apolar stationary phases decreases the error to a minor extent, they allow the calculation of distribution coefficients for compounds which would experience a very high retention in more apolar columns enabling their elution out of the column or reducing the retention time. Furthermore, calculation of the distribution coefficient is achieved in a given medium while the addition of an alcohol to decrease the error changes the medium where the distribution coefficient is to be calculated.

Error propagation in MLC has been included in this review as it is regarded as an important aspect for the application of this technique to the evaluation of distribution coefficients. However, MLC is not the only technique in which this situation occurs. In fact, this is also the case for other classical techniques used to determine these parameters, such as spectroscopics [34,48,49]. Recently, micellar electrokinetic chromatography (MEKC) has proved to be an interesting alternative to MLC for the calculation of micelle–water distribution coefficients and solute–micelle association constants [18,35,50–53]. A good agreement was found for the values of solute–micelle association constants calculated by MLC and MEKC for different compounds with the latter technique obtaining a considerably smaller error when employed [35]. This decrease is obtained because the K_2 calculation is performed from the slope of the straight line of variation of retention as a function of total surfactant concentration (C) and not from a slope/intercept ratio [18,35].

3. Study of solute retention mechanism in micellar liquid chromatography from distribution coefficient values. Implications for separation selectivity

If the retention of a solute in the chromatographic system takes place through a direct transfer mechanism, its capacity factor can be expressed by Eq. (3) [5]. In this case, and if the surfactant concentration in the mobile phase is high, the separation factor (α) for

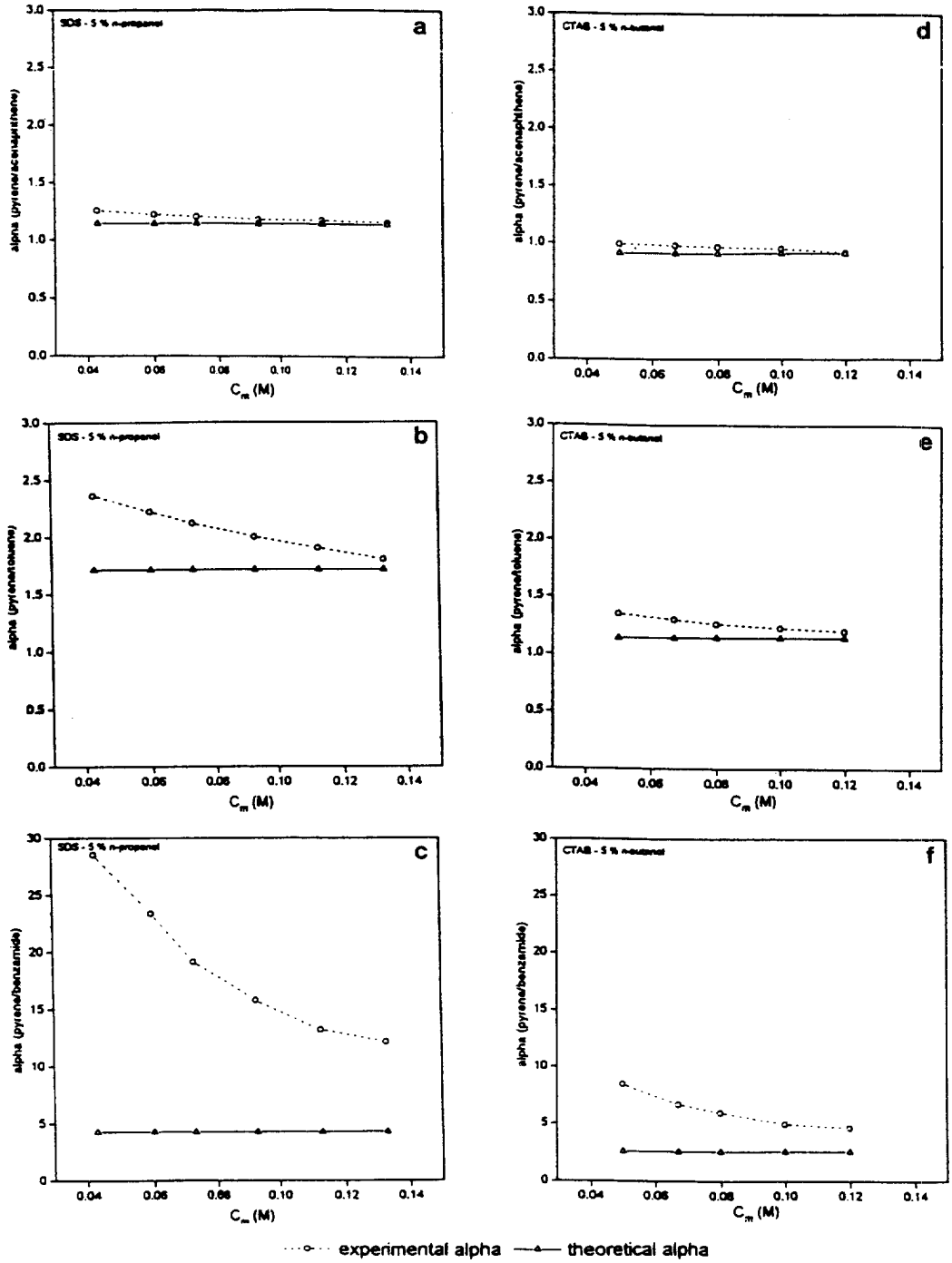

Fig. 7. Variation of the experimental and theoretical separation factors (α) as a function of the micelle surfactant concentration for three pairs of solutes: pyrene–acenaphthene, pyrene–toluene and pyrene–benzamide. (a, b) and (c) SDS–5% *n*-propanol. (d, e) and (f) CTAB–5% *n*-butanol. Reproduced with permission from Ref. [8] by courtesy of Marcel Dekker Inc.

a pair of solutes can be calculated from the ratio of their distribution coefficients between the stationary and micellar phases (P_{sm}) [36]:

$$\alpha = P_{sm1}/P_{sm2} \quad (7)$$

This equation is useful for two reasons: (1) because the knowledge about the retention mechanism of compounds in the chromatographic system can be enhanced. In fact, if the experimental separation factor for a pair of solutes coincides with the ratio of their respective distribution coefficients, P_{sm}, it can then be assumed that retention occurs through a direct transfer from the micellar phase to the stationary phase. (2) Because calculation of the separation factor from Eq. (7) would enable prediction of the separation selectivity of two compounds in the chromatographic system provided the distribution coefficients (P_{sm}) of the solutes are known.

These two interesting possibilities appear as direct applications of the calculation of solutes distribution coefficients between the stationary and micellar phases in MLC.

As an example, Fig. 7 shows the variation of theoretical and experimental separation factors as a function of the micellized surfactant concentration in SDS–5% *n*-propanol (Fig. 7a–c) and in CTAB–5% *n*-butanol mobile phases (Fig. 7d–f) for three pairs of aromatic solutes: pyrene–acenaphthene, which are both highly hydrophobic and for which a direct transfer mechanism can be assumed for any surfactant concentration in these mobile phases, pyrene–toluene in which a direct transfer mechanism can only be assumed for pyrene in all surfactant concentrations, and pyrene–benzamide, where benzamide does not experience a direct transfer mechanism except at very high surfactant concentrations. Fig. 7 shows that, when both solutes experience a direct transfer mechanism, the experimental and theoretical separation factors are very similar for all surfactant concentrations in solution, therefore making it possible to predict the separation factor from the partition coefficients P_{sm} for two solutes. When one of the two solutes does not experience a direct transfer mechanism, the theoretical and experimental selectivities are different decreasing this difference under the same conditions in which the direct transfer mechanism is favored, that is, by increasing solute hydrophobicity, solute–micelle association constants, surfactant concentration in mobile phase and, for mobile phases modified by alcohols when the polarity of the alcohol is increased [8]. Consequently, the separation selectivity for a pair of solutes shows a tendency to match a limit value close to the ratio of stationary–micellar partition coefficients of two solutes. In this case, the separation selectivity cannot be experimentally modified through a change in the surfactant concentration in the mobile phase as when a three partition equilibria mechanism occurs [8,36].

Acknowledgments

The authors gratefully acknowledge the financial support by DGICYT (Spain) (project reference PS90-0026). We also thank C. Marina for linguistic assistance.

References

[1] D.W. Armstrong, F. Nome, Anal. Chem. 53 (1981) 1662.
[2] M. Arunyanart, L.J. Cline Love, Anal. Chem. 56 (1984) 1557.
[3] P. Yarmchuk, R. Weinberger, R.F. Hirsch, L.J. Cline Love, Anal. Chem. 54 (1982) 2233.
[4] A.S. Kord, M.G. Khaledi, Anal. Chem. 64 (1992) 1901.
[5] M.F. Borgerding, F.H. Quina, W.L. Hinze, J. Bowermaster, H.M. McNair, Anal. Chem. 60 (1988) 2520.
[6] I.V. Berezín, K. Martinek, A.K. Yatsimirskii, Russ. Chem. Rev., Eng. Transl. 42 (1973) 787.
[7] B.K. Lavine, S. Hendayana, J. Tetreault, Anal. Chem. 66 (1994) 3458.
[8] M.A. García, M.L. Marina, J. Liq. Chromatogr. Rel. Technol. 19 (1996) 1757.
[9] J.G. Dorsey, M.G. Khaledy, J.S. Landy, J.L. Lin, J. Chromatogr. 316 (1984) 183.
[10] M.G. Khaledi, E.D. Breyer, Anal. Chem. 61 (1989) 1040.
[11] E. Pramauro, E. Pelizzetti, Anal. Chim. Acta 154 (1983) 153.
[12] G.M. Janini, S.A. Atari, Anal. Chem. 55 (1983) 659.
[13] F.G.P. Mullins, G.F. Kirkbright, Analyst 109 (1984) 1217.
[14] M.F. Borgerding, W.L. Hinze, Anal. Chem. 57 (1985) 2183.
[15] A. Berthod, I. Girard, C. Gonnet, Anal. Chem. 58 (1986) 1359.
[16] A. Berthod, I. Girard, C. Gonnet, Anal. Chem. 58 (1986) 1362.
[17] M.G. Khaledi, E. Peuler, J. Ngeh-Ngwainbi, Anal. Chem. 59 (1987) 2738.

[18] A.S. Kord, J.K. Strasters, M.G. Khaledi, Anal. Chim. Acta 246 (1991) 131.
[19] M.A. García, S. Vera, M.L. Marina, Chromatographia 32 (1991) 148.
[20] F.P. Tomasella, J. Fett, L.J. Cline Love, Anal. Chem. 63 (1991) 474.
[21] B.K. Lavine, A.J. White, J.H. Han, J. Chromatogr. 542 (1991) 29.
[22] E. Bonet Domingo, M.J. Medina Hernández, G. Ramis Ramos, M.C. García Alvarez-Coque, Analyst 117 (1992) 843.
[23] V. González, M.A. Rodríguez Delgado, M.J. Sanchez, F. García Montelongo, Chromatographia 34 (1992) 627.
[24] T. Okada, J. Chromatogr. 607 (1992) 135.
[25] J.M. Sanchis Mallols, R.M. Villanueva Camañas, G. Ramis Ramos, Chromatographia 38 (1994) 365.
[26] L.S. Madamba-Tan, J.K. Strasters, M.G. Khaledi, J. Chromatogr. A 683 (1994) 321.
[27] S.A. Zibas, L.J. Cline Love, Anal. Chim. Acta 299 (1994) 17.
[28] C. García Pinto, J.L. Pérez Pavón, B. Moreno Cordero, Analyst 120 (1995) 53.
[29] D. López-López, S. Rubio-Barroso, L.M. Polo-Díez, J. Liq. Chromatogr. 18 (1995) 2397.
[30] F. García Sanchez, A. Navas Díaz, A. García Pareja, J. Chromatogr. A 723 (1996) 227.
[31] J.R. Torres-Lapasió, J.J. Baeza-Baeza, M.C. García Alvarez-Coque, J. Liq. Chromatogr. Rel. Technol. 19 (1996) 1205.
[32] P. Jandera, J. Fischer, J. Chromatogr. A 788 (1996) 279.
[33] M.L. Marina, S. Vera, A.R. Rodríguez, Chromatographia 28 (1989) 379.
[34] C. Hirosi, L. Sepúlveda, J. Phys. Chem. 85 (1981) 3689.
[35] M.A. García, M.L. Marina, J.C. Díez-Masa, J. Chromatogr. A 732 (1996) 345.
[36] J.M. Saz, M.L. Marina, J. Chromatogr. A 687 (1994) 1.
[37] M.A. Rodríguez Delgado, M.J. Sanchez, V. González, F. García Montelongo, Chromatographia 38 (1994) 342.
[38] X. Li, J.S. Fritz, J. Chromatogr. A 728 (1996) 235.
[39] K.L. Mittal and B. Lindman (Editors), Surfactants in Solution, Plenum Press, New York, 1984.
[40] A. Berthod, J. Georges, Nouv. J. Chim. 9 (1985) 101.
[41] A. Berthod, I. Girard, C. Gonnet, Anal. Chem. 58 (1986) 1359.
[42] I. Benito, M.A. García, C. Monge, J.M. Saz, M.L. Marina, Colloids Surfaces, in press.
[43] J.C. Miller and J.N. Miller, Statistics for Analytical Chemistry, Wiley, New York, 1988.
[44] J.P. Foley, Anal. Chim. Acta 231 (1990) 237.
[45] C. Hansch and A. Leo, Substituent Constants for Correlation Analysis in Chemistry and Biology, Wiley-Interscience, New York, 1979.
[46] M.J. Medina Hernández, M.C. García Alvarez-Coque, Analyst 117 (1992) 831.
[47] M.A. García, Doctoral Thesis, Universidad de Alcalá (Madrid), Spain, January, 1996.
[48] E. Pramauro, G. Saini, E. Pelizzetti, Anal. Chim. Acta 166 (1984) 233.
[49] C.A. Bunton, L. Sepúlveda, J. Phys. Chem. 83 (1979) 680.
[50] S. Terabe, K. Otsuka, K. Ichikawa, A. Tsuchiya, T. Ando, Anal. Chem. 56 (1984) 111.
[51] S. Terabe, K. Otsuka, T. Ando, Anal. Chem. 57 (1985) 834.
[52] N. Chem, Y. Zhang, S. Terabe, T. Nakagawa, J. Chromatogr. A 678 (1994) 327.
[53] S. Terabe, T. Katsura, Y. Okada, I. Ishihama, K. Otsuka, J. Microcol. Sep. 5 (1993) 23.