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Effect of physico-chemical properties and molecular structure on the micelle–water partition coefficient in micellar electrokinetic chromatography

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Abstract

Quantitative structure–migration relationship (QSMR) analyses for neutral compounds were carried out in micellar electrokinetic chromatography (MEKC) with sodium dodecyl sulfate solution. Linear log–log relationships were found between both the micelle–water partition coefficient ($\log P_{mc}$) and the capacity factor and the octanol–water partition coefficient ($\log P_{oct}$). The quantitative relationship between $\log P_{mc}$ for neutral compounds and the solvatochromic parameters is described. The relationships developed from this work were used to predict micelle–water partition coefficients in MEKC.

1. Introduction

Micellar electrokinetic chromatography (MEKC) is a branch of high-performance capillary electrophoresis (HPCE) that allows electrically neutral substances that cannot be separated in principle by conventional free-solution capillary electrophoresis to be effectively separated. MEKC is a relatively recent and important modification of capillary zone electrophoresis (CZE) [1–5].

Resolution in MEKC can be enhanced through careful manipulation of the micelle–water partition coefficient, which is directly re-

lated to the capacity factor, and through extending the migration time window (i.e., reducing the ratio of the migration time of the aqueous phase to the micellar phase). The selectivity for neutral solutes in MEKC is determined almost exclusively by micelle–water partition coefficients, which gives useful information about the partition mechanism of the analyte between the micellar phase and the aqueous buffer. MEKC allows the calculation of the partition coefficient between the micelle and the surrounding aqueous phase, and is more suitable than micellar liquid chromatography for calculation of the micelle–water partition coefficient [4,5].

The micelle–water partition coefficient gives very interesting characteristics of selectivity to MEKC with regard to the separation of many neutral solutes. An accurate knowledge of mi-

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celle–water partition coefficients is essential for a better understanding of the separation mechanisms and in designing optimization strategies [3,4]. Accurate prediction of this value from physico-chemical parameters and molecular structures of the solute is useful in elucidating the migration mechanism in MEKC, which will be especially advantageous for studies of quantitative structure migration–relationships (QSMR).

QSMRs result from applying the methodology used for quantitative structure–biological activity relationships (QSAR) to the analysis of capillary electrophoretic data [6–9]. To obtain valuable QSARs, reliable input data must be provided and a stringent statistical analysis should be carried out. Quantitative retention–biological activity relationship studies by micellar liquid chromatography have been reported [7–10]. Capillary electrophoresis (CE) is now able readily to yield a great amount of unequivocally precise and reproducible data. In the CE process, all electrophoretic conditions can be kept constant, so structural parameters of the solutes such as the charge and molecular size become the single independent variable in the system [11,12]. QSMRs can be utilized for testing the applicability of individual structural parameters for property description, which may be applicable to biological or biomedical QSARs. In MEKC, the migration parameter can be well represented by the capacity factor or the micelle–water partition coefficient. In this study, QSMR analyses for neutral compounds in MEKC were carried out and the thermodynamic equation for the correlation between the micelle–water partition coefficient ($\log P_{mc}$) and the octanol–water partition coefficient ($\log P_{oct}$) was established. A quantitative relationship between the micelle–water partition coefficient and solvatochromic parameters of the solutes was established by utilizing the linear solvation energy relationship (LSER). The relationships developed from this work were used for the prediction of micelle–water partition coefficients and also capacity factors in MEKC. All the MEKC capacity factors and $\log P_{mc}$ values were taken from published data [4,5,13,14].

2. Results and discussion

2.1. Linear relationship between micelle–water and octanol–water partition coefficients

According to the well known equation in chromatography in which the capacity factor is related to the partition coefficient (P_{mc}), the capacity factor in MEKC can be expressed by

$$k' = P_{mc} V_{mc} / V_{aq} \quad (1)$$

where k' is the capacity factor, V_{mc} and V_{aq} are the volumes of the micelle and the remaining aqueous phase, respectively, and P_{mc} is the micelle–water partition coefficient.

According to an extrathermodynamic relationship [8,9], a linear relationship between the partitioning behaviour in micelle–water and octanol–water is generally observed, hence an approximately linear relationship between $\log P_{mc}$ and $\log P_{oct}$ is obtained and can be expressed by the Collander equation:

$$\log P_{mc} = a_1 \log P_{oct} + a_0 \quad (2)$$

where P_{mc} and P_{oct} are micelle–water and octanol–water partition coefficients, respectively, and a_0 and a_1 are constants.

In addition, an approximately linear relationship between $\log k'$ and $\log P_{oct}$ can also be obtained:

$$\log k' = a_0 + \log V_{mc} / V_{aq} + a_1 \log P_{oct} \quad (3)$$

Logarithmic plots of the sodium dodecyl sulfate (SDS)–water partition coefficients vs. octanol–water partition coefficients for six and nine neutral compounds are shown in Figs. 1 and 2.

The effect of temperature (T) on the micelle–water partition coefficient follows the Van 't Hoff equation:

$$\log P_{mc} = -\Delta H^0 / RT + \Delta S^0 / R \quad (4)$$

where ΔH^0 is the standard enthalpy change of transfer between the micelle and water and ΔS^0 is the corresponding standard entropy change.

The observed parallel linear relationships between $\log P_{mc}$ and $1/T$ [5] implies that the micelle–water partition process is mainly gov-

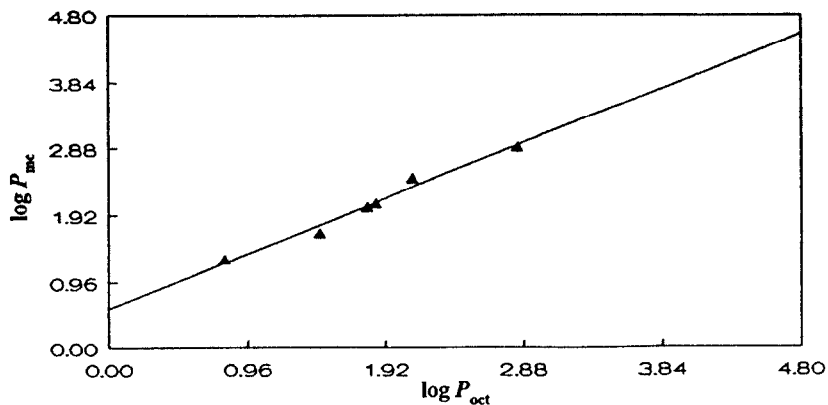


Fig. 1. Linear relationship between $\log P_{mc}$ and $\log P_{oct}$ for six neutral compounds in SDS–buffer system. Log P_{mc} values from Ref. [5], $\log P_{oct}$ from Ref. [15]. 100 mM borate–50 mM phosphate buffer (pH 7.0), 25°C. The linear regression is $\log P_{mc} = 0.579 + 0.825 \log P_{oct}$ ($n = 6$, $r = 0.989$).

erned by the contribution of the entropy term, and the MEKC selectivity factors are independent of the temperature applied, which is different from that in RP-HPLC [16]. Better linear relationships between $\log P_{mc}$ and $\log P_{oct}$ at different temperature were obtained. The following are the results of linear regression analyses between $\log P_{mc}$ and $\log P_{oct}$ for resorcinol, phenol, *p*-nitroaniline, nitrobenzene, toluene and 2-naphthol at five different column temperatures:

$$30^{\circ}\text{C}: \log P_{mc} = 0.816 \log P_{oct} + 0.553, \\ n = 6, r = 0.987 ;$$

$$35^{\circ}\text{C}: \log P_{mc} = 0.801 \log P_{oct} + 0.533, \\ n = 6, r = 0.983 ;$$

$$40^{\circ}\text{C}: \log P_{mc} = 0.784 \log P_{oct} + 0.539, \\ n = 6, r = 0.981 ;$$

$$45^{\circ}\text{C}: \log P_{mc} = 0.785 \log P_{oct} + 0.498, \\ n = 6, r = 0.977 .$$

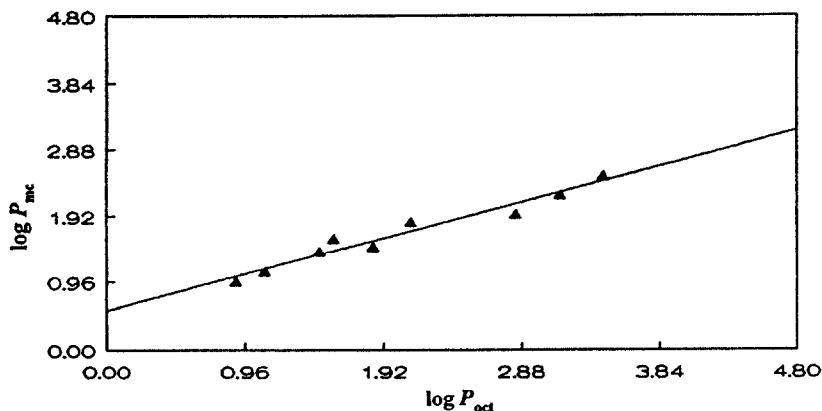


Fig. 2. Linear relationship between $\log P_{mc}$ and $\log P_{oct}$ for nine neutral compounds in SDS–buffer system. The regression equation is $\log P_{mc} = 0.555 + 0.541 \log P_{oct}$ ($n = 9$, $r = 0.977$). See Table 1 for details.

It was shown by Nielsen and Foley [14] that a buffer solution containing magnesium dodecyl sulfate $[\text{Mg}(\text{DS})_2]$ exhibited electroosmotic velocities one third to half that of an SDS solution, and the migration time window for $\text{Mg}(\text{DS})_2$ was independent of the percentage of organic modifier in the buffer solution while the migration time window for SDS increased as the percentage of organic modifier increased. Fig. 3 shows linear log–log plots between $\log k'$ and $\log P_{\text{oct}}$ for seven neutral compounds in two surfactant systems. The parallel linear relationships between $\log k'$ and $\log P_{\text{oct}}$ in the two surfactant systems implies that the retention mechanisms are similar and the selectivities are the same. From the linear relationships between $\log k'$ and $\log P_{\text{oct}}$ in both surfactant systems, it is interesting to note that the $\text{Mg}(\text{DS})_2$ micelle is more hydrophobic than the SDS micelle, which agrees well with the results of hydrophobic selectivity found by Nielsen and Foley [14].

2.2. Quantitative relationship between the micelle–water partition coefficient in MEKC and the solvatochromic parameters

The effect of molecular parameters on $\log P_{\text{mc}}$ can be studied based on the LSERs, where for neutral compounds the solvent-dependent prop-

erties depend on four types of terms and the general LSER for solutes takes the form [17–21]

$$SP = SP_0 + m\nu + d\pi + b\beta + a\alpha \quad (5)$$

where SP represents solvent-dependent properties and here it refers to $\log P_{\text{mc}}$, ν is the molar volume or Van der Waals volume ($\nu_w/100$), π is a measure of the solute dipolarity/polarizability, β is the hydrogen bond donor ability, α is the hydrogen acceptor ability and m , d , b and a are constants. Therefore, $\log P_{\text{mc}}$ can be given by the following equation:

$$\log P_{\text{mc}} = SP_0 + m\nu + d\pi + b\beta + a\alpha \quad (6)$$

For structurally related compounds whose solvatochromic parameters π , β and α are almost the same, a linear relationship between $\log P_{\text{mc}}$ and ν can be derived. Fig. 4 shows the linear relationship between $\log P_{\text{mc}}$ and ν for six structurally related alkylphenols in an SDS–buffer system.

The sign of the coefficients in Eq. 6 is determined by whether the term represents an exoergic or endoergic situation in the micelle–water partitioning process. The hydrophobic volume of a neutral solute makes a positive contribution to $\log P_{\text{mc}}$. Therefore, there is general trend that as the solute becomes increas-

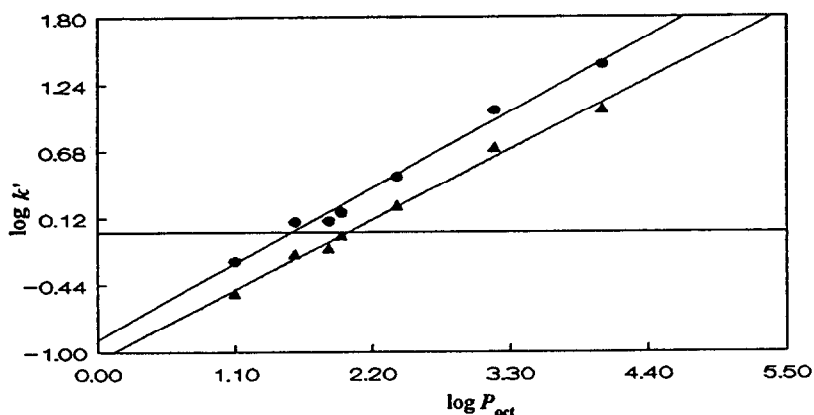


Fig. 3. Linear relationships between $\log k'$ and $\log P_{\text{oct}}$ for seven neutral compounds (benzyl alcohol, acetophenone, nitrobenzene, nitrophenyl acetate, *m*-nitrotoluene, benzophenone and biphenyl) in (\blacktriangle) SDS and (\bullet) $\text{Mg}(\text{DS})_2$ systems. $\log P_{\text{mc}}$ values from Ref. [14], $\log P_{\text{oct}}$ from Ref. [15]; Buffer: 50 mM surfactant–10% acetonitrile–5 mM phosphate–4 mM EDTA at pH 7.2. The regression equations in SDS and $\text{Mg}(\text{DS})_2$ buffer systems are $\log k' = -1.067 + 0.533 \log P_{\text{oct}}$ ($n = 7$, $r = 0.996$) and $\log k' = -0.899 + 0.576 \log P_{\text{oct}}$ ($n = 7$, $r = 0.994$), respectively.

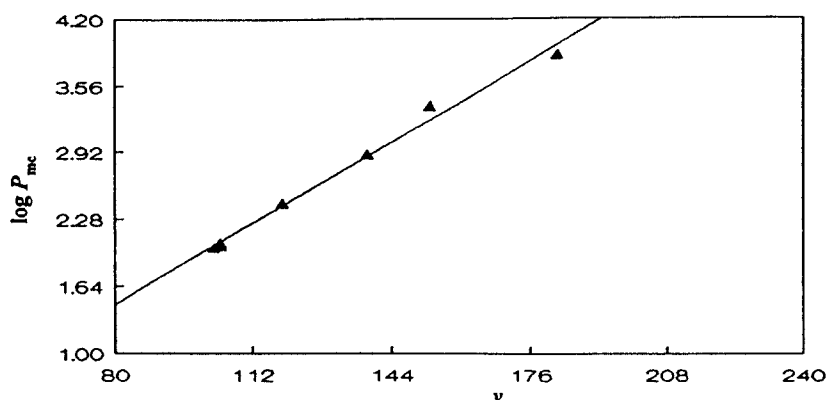


Fig. 4. Linear relationship between $\log P_{mc}$ and molar volume for seven structurally related alkylphenols (*o*-cresol, *m*-cresol, *p*-cresol, 2,4-xyleneol, *p*-propylphenol, *p*-butylphenol and *p*-amylphenol) in SDS–buffer system (100 mM borate–50 mM phosphate buffer, pH 7.0) at 30°C. Log P_{mc} values from Ref. [5]. The regression equation is $\log P_{mc} = 0.0242v - 0.475$ ($n = 7$, $r = 0.995$).

ingly hydrophobic, $\log P_{mc}$ will become increasingly positive, which is consistent with the practical observations in MEKC. For complex compounds with different functional groups, a quantitative relationship between the micelle–water partition coefficient and the solvatochromic parameters was found. Table 1 shows the solvatochromic parameters for eleven compounds and a comparison of the experimentally mea-

sured $\log P_{mc}$ and the values calculated from the solvatochromic parameters. The resulting equation obtained by least-squares regression is

$$\log P_{mc} = -0.0033 + 4.057\nu_w/100 - 0.542\pi - 1.534\beta - 0.397\alpha \quad (7)$$

$n = 11, r = 0.991$

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Table 1

Values of solvatochromic parameters and comparison of the experimental $\log P_{mc}$ and the predicted values for eleven neutral compounds in SDS–buffer system

Compound ^a	$\nu_w/100$	π	β	α	Log P_{mc}		Difference
					Exptl.	Calc.	
1	0.562	0.73	0.50	0.26	0.96	1.01	0.05
2	0.536	0.72	0.33	0.61	1.04	1.03	-0.01
3	0.634	0.99	0.52	0.39	1.10	1.08	-0.02
4	0.606	0.92	0.44	0.00	1.39	1.28	-0.11
5	0.631	1.01	0.30	0.00	1.47	1.55	0.08
6	0.788	1.30	0.58	0.00	1.55	1.60	0.05
7	0.690	0.90	0.49	0.04	1.58	1.54	-0.04
8	0.592	0.55	0.11	0.00	1.83	1.93	0.10
9	0.581	0.71	0.07	0.00	1.94	1.86	-0.08
10	0.668	0.53	0.12	0.00	2.22	2.24	0.02
11	0.753	0.70	0.15	0.00	2.49	2.44	-0.05

Solvatochromic parameters taken from Ref. [17]. Data recalculated from Ref. [13], $\log P_{oc}$ from Ref. [15]. 25 mM borate buffer at pH 8.5 with SDS concentrations of 30, 70, 110 and 150 mM; fused-silica capillary (57 cm \times 75 μ m I.D.); 25°C.

^aNos. 1–11 denote aniline, phenol, benzyl alcohol, benzaldehyde, nitrobenzene, phenylacetone, acetophenone, toluene, chlorobenzene, ethylbenzene, naphthalene, respectively.

paper, n is the number of data points in the regression, r is the regression coefficient and ν_w is the Van der Waals volume.

The calculated $\log P_{mc}$ values are consistent with the experimental values. The contribution of the ν_w term is very significant; the ν_w term makes a positive contribution to $\log P_{mc}$, whereas the π , β and α terms make negative contributions, indicating that there is a general trend that as the solute becomes increasing hydrophobic, $\log P_{mc}$ will become increasingly positive. In contrast, as the solute becomes more polar or stronger to accept or donor the hydrogen bonding, $\log P_{mc}$ will decrease when other conditions remain the same, which is similar to the effects observed in RP-HPLC [17,18,20].

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