A Study on Retention of a Series of Aromatic Compounds in Mixed Micellar Liquid Chromatography Using Linear Solvation Energy Relationship (LSER)

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ABSTRACT: *The effect of SDS (0.03-0.07 M) and Brij-35(0-0.003 M) concentrations and temperature on retention parameters of 30 solutes in micellar reversed- phase liquid chromatography systems were studied using solvation parameter model. The system constants were determined by multiple linear regression analysis from experimental values of the retention factors with known descriptors by computer using the program SPSS/PC. The experimental results showed that the variation in concentration of surfactants (SDS, Brij-35) changes the cavity formation (m) and hydrogen-bond acidity (b). The value of m decreases while the value of b increases as the SDS concentration increases. The value of m and b slightly decrease as the Brij-35 concentration increases. Variation of temperature (25-38°C) showed changes in cavity formation (m) and hydrogen-bond acidity (b). A comparison of the predicted and experimental retention factors indicated a satisfactory agreement between the two. Normalized residual plot showed that the contribution of the systematic modeling errors is approximately minor using the linear solvation energy relationship (LSER) equation. The value of cross-validated r^2 was 0.973.*

INTRUDUCTION

Micellar liquid chromatography (MLC) is a mode of reversed phase liquid chromatography (RPLC), which uses a surfactant solution above its critical micelle concentration (CMC) as the mobile phase [1].

In some situations, the MLC can offer many advantages over conventional RPLC. For instance, cationic, anionic and neutral species can be separated simultaneously in MLC[2, 3]. The amount of surfactant sorbed by the stationary phase on a C_{18} column remains constant above the CMC for SDS and CTAB containing mobile phases in pure water and 5٪ methanol [4]. Some advantages of the MLC technique compared to the conventional RP-HPLC are the low cost, non-flammability, non-toxicity and easy disposal of the mobile phase.

The general linear solvation energy relationship (LSER) equation used is[5-13].

$$\log k' = \log k_0 + m (V_x/100) + s\,\pi_2^H + a \sum \alpha_2^H +$$

$$b \sum \beta_2^H + rR_2$$

In this equation, the descriptors V_x, π_2^H, $\sum \alpha_2^H$, $\sum \beta_2^H$ and R_2 are the solute's size, dipolarity / polariz-ability , hydrogen bond (HB) donating ability, hydrogen bond accepting ability and excess molar refraction, respectively[14]. The coefficients m, s, a, b and r could be obtained through multiple linear regression analysis from experimental values of the retention factor for a group of different solutes with known descriptors by computer using the SPSS/PC program. These parameters reflect differences in the two bulk phases between which the solutes are transferring [15].

The log K_0 term is simply the intercept of the regression and is comprised of the constant contributions (c) from the solutes and the chromatographic system.

The MLC is commonly described using a three-phase model (bulk aqueous, stationary phase and micro-environment micellar) with three accompanying partition coefficients (bulk aqueous to stationary phase, bulk aqueous to micelle and stationary to micelle) [16,17].

We have studied effects of concentration of surfactants (SDS, Brij-35) and temperature with the aim of understanding the retention in these systems. Our interests specifically were in understanding the funda-mental chemical interactions responsible for retention in MLC and variations of these interactions as a function of the nature and concentration of the surfactant and the temperature. So, we used LSER, to explain retention in MLC systems using the aqueous mobile phases containing SDS and Brij-35.

EXPRIMENTAL
Reagents
Sodium dodecyl sulfate (SDS), polyoxyethylene dodecanol (Brij-35) and inorganic chemicals such as NaH2PO4, .2H2O and H3PO4 were obtained from Fluka GmbH (Buchs, Switzerland). The samples used were different compounds with descriptors and summarized in table 1.

Apparaturs
The chromatographic measurements were carried out with HPLC system equipped with a series 10 liquid chromatography pump and a model LC-95 UV/Visible spectrophotometer detector Perkin-Elmer (Norwalk, CT,USA). A Rheodyne injector Model 7125 (Cotati, CA, USA) with 10µl loop. The analytical column used was C18 (250 × 4.6mm, 10 µm) from waters (Milford, MA, USA). The UV detector was set at 254 nm to monitor the compounds.

Procedure
All mobile phases were vacuum-filtered through 0.45 µm filters (Millipore, Milford, MA, USA). Stock solution of 1 mg/ml of samples were prepared separately in methanol. A 0.5 M stock solution of SDS and 0.1M of Brij-35 were prepared and diluted with deionized doubly distilled water, organic solvent and phosphate buffer when they were needed.

RESULTS AND DISCUSSION
The influence of concentration of surfactants SDS and Brij-35, temperature and the percentage of organic modifier studied for the solutes are identified in table 1.

For a mobile phase containing 0.06 M SDS and 0.001 M Brij-35, the variation of the experimental retention factors, K´, with different organic modifiers (methanol, n-propanol, 2-propanol and butanol) showed that butanol was better than the others as shown in table 2.

The system constants and statistics derived from the solvation parameter model for 30 compounds at the appropriate concentration of surfactants (0.07 M SDS, 0.0015 M Brij-35) and different butanol percentages are summarized in table 3 and 4, respectively. The correlation coefficients obtained in this case are lower than those normally obtained for RPLC, ranging from as low as 0.930 to a quite acceptable 0.991.

Retention factor as a function of concentration of surfactants using LSER model
Plots of the system constants vs. the SDS concentration (at a constant Brij-35 concentration) shows that the m, b variations are significant as shown in Fig. 1.

The m coefficient decreases as the SDS concentration increase because of decreasing the effective cohesivity of the mobile phase. The value of b increases as the SDS concentration increases. This explains that more solutes partition out of the aqueous environment of the mobile phase into the micellar microenvironments. Therefore,

Table 1: Solute Descriptors for different compound [14].

Code	Solute	Vx	Π2	Σα	Σβ	R2
1	p-Xylene	0. 9982	0.52	0.00	0.16	0.613
2	4-Nitrophenol	0.9490	1.72	0.82	0.26	0.070
3	1-Naphthol	1.1440	1.05	0.60	0.37	1.520
4	Toluen	0. 8573	0.52	0.00	0.14	0.601
5	p-Toluic acid	1.0730	0.90	0.60	0.40	0.730
6	Benzene	0.7164	0.52	0.00	0.14	0.610
7	Naphthalene	1.0854	0.92	0.00	0.20	1.340
8	Anthracene	1.4544	1.34	0.00	0.26	2.290
9	4-Nitroaniline	0.9900	1.91	0.42	0.38	1.220
10	2-Chlorophenol	0.8980	0.88	0.32	0.31	0.853
11	Benzaldehyde	0.8730	1.00	0.00	0.39	0.820
12	2-Naphthol	1.1440	1.08	0.61	0.40	1.520
13	Bromobenzene	0.8914	0.73	0.00	0.09	0.882
14	Biphenyl	1.3242	0.99	0.00	0.22	1.360
15	2-Phenylethanol	1.0569	0.91	0.30	0.64	0.811
16	4-bromophenol	0.9500	1.17	0.67	0.20	1.080
17	Chlorobenzene	0.8388	0.65	0.00	0.07	0.718
18	Phenol	0.7751	0.89	0.60	0.30	0.805
19	m-cresol	0.9160	0.88	0.57	0.34	0.822
20	2.6-Dimethylphenol	1.0570	0.79	0.39	0.39	0.860
21	4-Chloroaniline	0.9390	1.13	0.30	0.35	1.060
22	Benzophenol	1.4810	1.50	0.00	0.50	1.447
23	m-Toluicacid	1.0730	0.90	0.59	0.38	0.730
24	o-Toluicacid	1.0730	0.90	0.60	0.34	0.730
25	3-Chlorobenzoicacid	1.0540	0.95	0.65	0.30	0.840
26	4-Chlorobenzoic acid	1.0540	0.99	0.63	0.26	0.840
27	4-Chlorophenol	0.8970	1.08	0.67	0.20	0.915
28	3-Phenylpropanoic acid	1.2480	1.20	0.60	0.58	0.730
29	Benzyl alcohol	0.9160	0.87	0.33	0.56	0.803
30	Ethylbenzene	0.9980	0.51	0.00	0.15	0.613

Table 2: System constants as a function of different organic modifiers.

Organic Modifiers	c	m	r	s	a	b	R	SE	F	n
Butanol	0.168	0.954	0.092	-0.145	-0.249	-1.406	0.947	0.08	69	30
Methanol	0.416	0.758	0.122	-0.086	-0.184	-1.243	0.930	0.104	31	30
Propanol	0.413	0.717	0.161	-0.10	-0.284	-1.284	0.936	0.111	34	30
2-Propanol	0.495	0.796	0.101	-0.101	-0.214	-1.298	0.944	0.096	39	30

R = Overall Correlation Coefficient, SE = Standard Error
F = Overall Regression F-test, n=solute number, c = system constant = log K。
Conditions: column C_{18}, 250 × 4.6 mm, dp = 10 μm; flow rate = 1.5 ml/min;
UV detector, λ= 254 nm; mobile phase = 0.06 M SDS, 0.001 M Brij-35; 5% organic modifier.

Table 3: System constants as a function of molar concentration of SDS (0.0015 M Brij-35, pH = 3.5 at 30 ℃).

SDS M	c	m	r	s	a	b	R	SE	F	n
0.03	0.248	1.104	0.115	-0.176	-0.246	-1.625	0.962	0.10	60	30
0.04	0.229	1.015	0.114	-0.146	-0.240	-1.600	0.970	0.09	76	30
0.05	0.199	0.966	0.118	-0.156	-0.237	-1.514	0.968	0.08	71	30
0.06	0.194	0.877	0.097	-0.140	-0.227	-1.415	0.974	0.07	89	30
0.07	0.159	0.845	0.100	-0.136	-0.230	-1.365	0.978	0.06	104	30

Conditions: column C_{18}, 250 × 4.6 mm,   dp = 10 μm; flow rate = 1.5 ml/min;UV detector, λ= 254 nm.

Table 4: System constants as a function of percentage of butanol for appropriate conditions
(0.07 M SDS and 0.0015 M Brij-35, pH=3.5 at 30 ℃).

%Butanol	c	m	r	s	a	b	R	SE	F	n
3	0.259	0.770	0.10	-0.112	-0.241	-1.235	0.962	0.08	60	30
5	0.156	0.842	0.10	-0.136	-0.231	-1.359	0.978	0.06	106	30
10	0.01	0.809	0.07	-0.122	-0.242	-1.289	0.983	0.05	140	30

Conditions: column C_{18}, 250 × 4.6 mm,   dp = 10 μm; flow rate = 1.5 ml/min; UV detector, λ= 254 nm.

Table 5: System constants as a function of temperature for appropriate conditions
(0.07MSDS and 0.0015 M Brij-35, 10% V/V butanol and pH=3.5).

Temperature °C	c	m	r	s	b	a	R	SE	F	n
25	0.04	0.828	0.08	-0.118	-1.362	-0.266	0.980	0.06	116	30
28	0.02	0.813	0.07	-0.119	-1.300	-0.243	0.982	0.05	130	30
30	0.01	0.809	0.07	-0.122	-1.289	-0.242	0.983	0.05	140	30
35	-0.03	0.804	0.07	-0.120	-1.230	-0.237	0.986	0.05	174	30
38	-0.004	0.796	0.07	-0.125	-1.224	-0.227	0.991	0.04	269	30

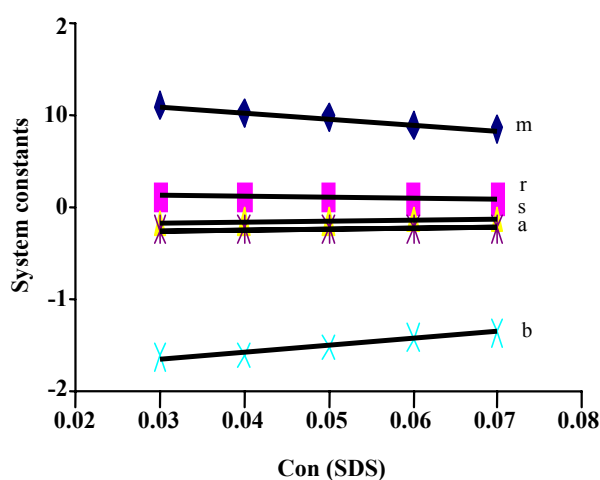*Conditions: column C_{18}, 250 × 4.6 mm,   dp = 10 μm; flow rate = 1.5 ml/min;UV detector, λ= 254 nm.*

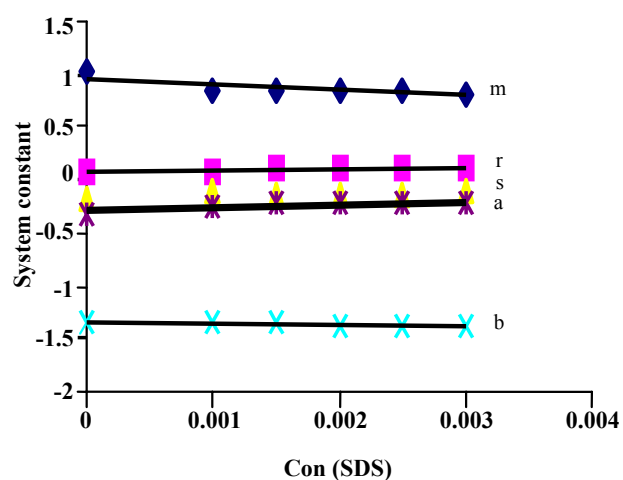**Fig.1: System constants as a function of concentration of the SDS at   0.0015M Brij-35, T = 30˚C, pH =3.5.**

Fig.2: System constants as a function of concentration of the the Brij-35 at 0/07 M SDS, T = 30˚ C, pH =3.5 .

the micellar environment shields the solutes from interactions with water.

Plots of the system constants vs. Brij-35 concentration (at a constant SDS concentration) show that the m and b values slightly decrease as the Brij-35 concentration increases (Fig. 2). Adding Brij-35 to the SDS surfactant causes an expansion of the micelle without any significant change in the surface composition of the micelle. The cohesive energy should not be significantly influenced by the entry of the nonionic surfactant into the core of the ionic micelle. So, the solute size and its basicity are the two most important solute parameters determining retention in the MLC systems.

Retention factor as a function of temperature using LSER model

Fig. 3 shows the variation of system constants with temperature (25-38˚C) at (0.07M SDS, 0.0015M Brij-35) and 10٪ butanol. Increasing the temperature has the most significant effect on m and b as seen in Fig. 3. Since the cohesion of the mobile phase reduced at higher temperatures, therefore, the formation of cavity is easier at higher temperatures as seen in table 5.

The Residual of LSER equation for the mixed micelle systems

The LSER equation was essentially developed to model the solute transfer in two - phase systems. Since, there are ion-dipole interactions between the solute and the charged head groups and their counter ions. The equation seems inadequate for a three – phase system. However, Fig. 4 shows that the systematic errors are approximately minor. Fig. 5 shows a high correlation coefficient between the predicted and the experimental capacity factors and the residual error is minor.

For the predictive ability of the model, we used the cross-validation technique. In this technique, the modeling is repeated with a randomly chosen subset of the data-rows excluded, and the resulting model is used to predict the capacity factors of the excluded data. In this study the cross-validated r^2 was calculated according to the following definition:

Cross-validated r^2 = (SD - press) / SD

The value of cross-validated r^2 determined for mixed micellar liquid chromatography was 0.973.
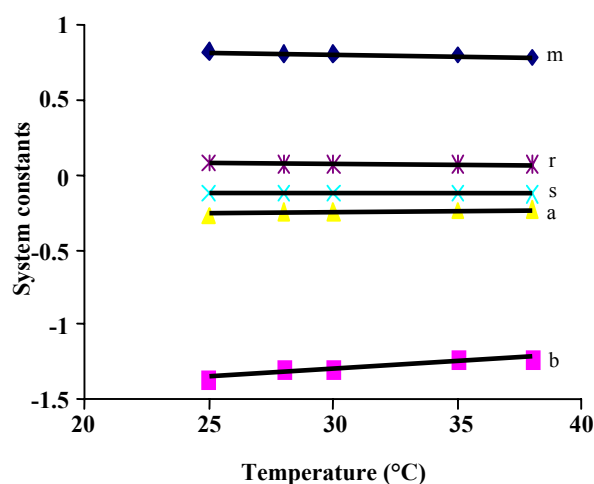

Fig.3: System constants as a function of the temperature under appropriate conditions (0.07M SDS and 0.0015M Brij-35, pH =3.5).
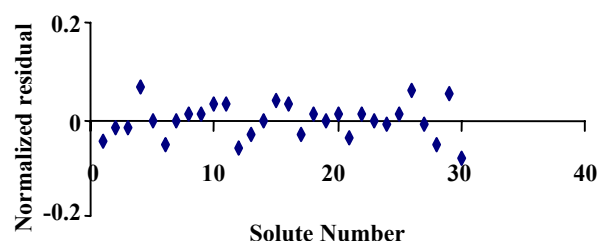

Fig.4: Normalized residuals (predicted minus experimental logK' values) of the LSER under appropriate conditions (0.07M SDS and 0.0015M Brij-35, T =38 ºC, pH=3.5).
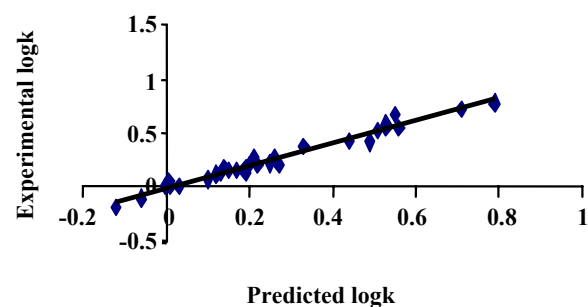

Fig.5: Predicted vs. experimental retention factors of the compounds using the solvation parameter model in mixed MLC.

CONCLUSIONS

The experimental results show that the value of m decreases as the SDS concentration increase while the value of b increases. The value of m and b slightly decrease as the Brij-35 concentration increases. Increasing the temperature has the most significant effect on m and b. Normalized residual plot show that the contribution of the systematic modeling errors are approximately minor using the LSER equation. The value of cross-validated r^2 is 0.973.

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