Journal of Chromatography A 1758 (2025) 466176

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Towards biomimetic electrochromatography: Fast method for the Abraham's characterization of solute-solvent interactions in micellar and microemulsion electrokinetic systems

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ARTICLE INFO

Keywords:
Abraham solvation parameter model
Biomimetic chromatography
Chromatographic selectivity
Electrokinetic chromatography
EKC
Linear solvation energy relationships
MEEKC
MEKC

ABSTRACT

This study presents a fast method for the characterization of solute-solvent interactions in micellar and microemulsion electrokinetic chromatography based on the linear solvation energy relationships proposed by Abraham. The magnitude of the different types of interactions between solutes and chromatographic phases is determined from the differences in migration observed for pairs of solutes, and the effect of the different cohesion of the dispersed phase and the dispersive medium is determined from the injection of a mixture of homologous compounds, using in all injections nonanophenone as dispersed phase marker. For excess polarizability interactions (*e*), the compounds 8-hydroxyquinoline and 1,2-dimethoxybenzene are used. The dipolarity/polarizability coefficient (*s*) is assessed with 1,4- or 1,2-dicyanobenzene and 2-methylbenzaldehyde. To evaluate the solute hydrogen bond acceptor capacity (*a*), 3-ethoxyphenol and 2-chloroacetophenone are employed, and the hydrogen bond donor capacity (*b*) is characterized using 2,3,5,6-tetramethylpyrazine and 2,6-dimethylanisole. Finally, the cavity term (*v*) is determined using a mixture of *n*-alkyl phenone homologues in the range of acetophenone to heptanophenone, depending on the nature of the electrokinetic system. This fast approach allows for results comparable to the conventional methodology, which is based on the injection of a relatively large number of solutes and subsequent analysis using multiple linear regressions, but significantly reducing the time and resources invested in the characterization of electrokinetic chromatography systems. This novel method was assayed with micellar solutions prepared from bile salts (SC, SDC), anionic surfactants (SDS, LDS), and cationic surfactants (CTAB, TTAB), and microemulsions consisting of heptane, 1-butanol, and surfactants (SDS, SC, and TTAB) at different concentrations and pH values. Provided that electrokinetic chromatography has a high potential mimicking biological systems due to the availability of surfactants and cosurfactants of different natures and the wide operational pH range, this study aims to contribute to the development of biomimetic chromatography by proposing a screening method based on the Abraham's solvation parameter model, widely used in the characterization of biological systems.

1. Introduction

1.1. Biomimetic chromatography

The principles of liquid chromatography, which rely on the partitioning of a solute between two immiscible phases, are effectively used for physicochemical profiling and characterizing the binding properties of compounds [1–7]. Biomimetic chromatography is primarily employed in drug discovery to forecast how drug candidates will interact in biological processes, such as blood/brain distribution, plasma protein binding, tissue partitioning, skin penetration, and toxicity. This technique accelerates the drug discovery process, as chromatographic assays are easier and faster to implement and apply than biological ones. Additionally, it reduces the need for animal testing, thereby addressing ethical concerns and cutting down on costs. It is conducted in a column format, using stationary phases that contain phospholipids or proteins to mimic the biological environment, along with a buffered mobile phase that simulates physiological conditions. Biomimetic chromatography also plays a role in environmental research, applied to model aquatic toxicities and soil absorption.

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https://doi.org/10.1016/j.chroma.2025.466176
Received 27 May 2025; Received in revised form 25 June 2025; Accepted 27 June 2025
Available online 28 June 2025

Biomimetic separation techniques in the field of electrokinetic capillary chromatography have been mainly assayed with liposomes, since they are expected to better mimic biological membranes [8]. However, the required lipids are expensive, liposome preparation is complex, and these systems often encounter issues related to homogeneity and stability. The potential use of alternative electrochromatographic approaches with common non-lipidic dispersed phases (such as micellar or microemulsion-based systems) remains largely unexplored for biomimetic applications, probably due to the lack of a reliable and rapid method for the characterization of the main solute-solvent interactions affecting the chromatographic behavior.

In this work, we propose the development of biomimetic electrokinetic chromatography in capillary format, using micellar and microemulsion media as running buffers, instead of liposomes or columns with stationary phases containing lipids or proteins. Columns functionalized with proteins and lipids, unlike fused silica capillaries, must be carefully stored and used, and are much more expensive. Additionally, electrokinetic systems represent lower consumption of reagents and energy, both in the preparation of the chromatographic support and in regular operation, promoting the principles of green chemistry. Given the wide variety of surfactants that can be used to create micellar and microemulsion media, it is necessary to develop a method that allows for the simple and rapid characterization of electrokinetic chromatographic systems.

1.2. Characterization of physicochemical and biological processes: the Abraham's solvation model

In 1993 Michael H. Abraham proposed a linear relationship between the overall free energy involved in a solvation process and the sum of energies related to specific solute-solvent and solvent-solvent interactions involved [9]. The general expression for this linear solvation energy relationship (LSER) involving liquid phases and unionized solutes is:

$$\log_{10}SP = c + eE + sS + aA + bB + vV \quad (1)$$

The dependent variable in Eq. (1) is the decimal logarithm of a property related to the free energy variation of a solvation process, either physicochemical or biological. For instance, $(SP)_i$ could be the partition ratio of a solute in two immiscible solvents (such as in liquid chromatography), or some biological response as the permeation of a solute from aqueous solution through human skin or blood tissue distribution. The independent variables *E, S, A, B* and *V* are molecular descriptors of the solute, commonly in the range from 0 to 3, available from commercial [10] and open [11,12] sources. These databases provide the complete set of molecular descriptors for more than 7000 compounds and, additionally, algorithms for their estimation from molecular estructures. When the estimation of solute descriptors is required because of the lack of experimental data, an interesting option is the use of machine learning and group contribution approaches proposed by Green and collaborators, available as a web-based tool [13]. V_i is the McGowan characteristic volume [14] of the solute (in units of (mL mol^{-1})/100 to be of a similar magnitude of the other molecular descriptors [15]), which is easily calculated from the solute structure. The product terms involving the independent variables represent free energy specific contributions due to: *eE*, excess polarizability interactions of the solute *n*- and π-electrons with solvent molecules (in relation to an alkane of the same size); *sS*, dipolarity/polarizability solute-solvent interactions; *aA* and *bB*, the hydrogen bonding donation from solute to solvent (solute hydrogen bonding acidity) and from solvent to solute (solute hydrogen bonding basicity), respectively; and *vV*, the creation of a cavity in the solvent to accommodate the solute and their related dispersion interactions. In a system consisting of a solute partitioning into two condensed phases, the solvent (or system) coefficients (*e, s, a, b* and *v*) reflect the different behavior on the particular free energy contribution between the phases. For example, in the case of octanol-water partition, *v* would represent the difference between the easiness of cavity formation in the octanolic and aqueous phases and differences in general dispersion interactions. Thus, the range of solvent coefficients include negative, null and positive values. The intercept *c* in Eq. (1) accounts for system factors unaffected by solute-solvent interactions, such as the normalization or conversion of the solvation property used as dependent variable.

The Abraham's model has been widely used for the characterization of solute-solvent interactions in physicochemical and biological systems [16,17]. Among the firsts, there are a good number of liquid/liquid partitions [17–21], liquid [22–29] and electrokinetic [30–36] chromatography systems, and regarding biological processes, blood-tissue (liver, lung, kidney, heart, brain, muscle…) distributions [37–40], intestinal absorption [41], skin permeation [42,43]. Environmental processes, such as aquatic toxicities, have also been characterized through this model [36,44,45]. Thus, there are a large number of physicochemical and biological/environmental processes characterized by means of the same model, which makes it possible to compare the main solute-solvent interactions playing a fundamental role in each of them. This represents not only a valuable tool in the selection of the most promising physicochemical system for the resolution of a particular analytical challenge, or in the estimation of the expected biological behavior of a specific compound of pharmaceutical interest or the environmental impact of a molecule, but also the possibility of comparing systems within this two categories with the focus on biomimetic chromatography [46–48]. In fact, the present work aims to provide a tool for a faster characterization of chromatographic systems, fostering their study as possible physicochemical surrogate models of biological and environmental interest.

The conventional application of the model requires the measurement of the solvation property ($\log_{10}(SP)_i$ in Eq. (1)) for a relatively large set of molecules with known molecular descriptors (independent variables) and fitting the system coefficients by multilinear regression analysis. Since this method is time and reagents consuming, a fast approach based on Abraham's model was developed for the characterization of solute-solvent interactions in liquid chromatography systems, particularly reversed-phase and HILIC [49]. According to this method, a system coefficient can be measured dividing the difference in retention of two solutes with four (out of five) very similar molecular descriptors by the difference in the dissimilar descriptor:

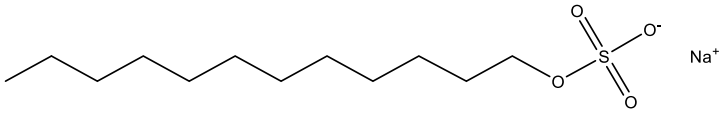
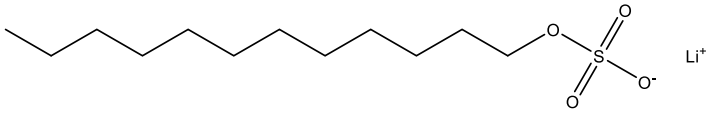
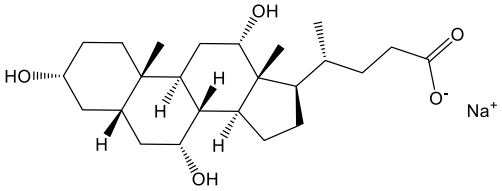
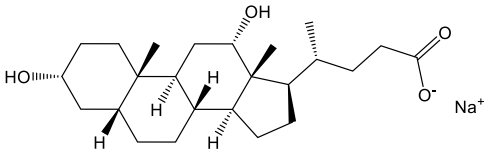
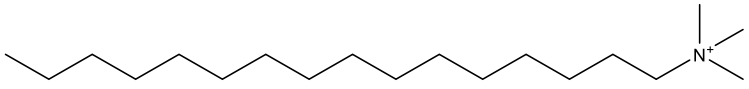
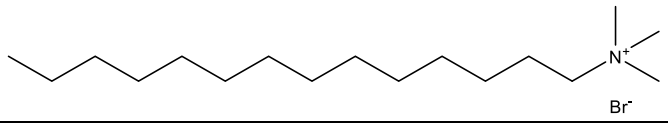
$$x = \frac{\log_{10}k_1 - \log_{10}k_2}{X_1 - X_2} \quad (2)$$

where *x* is the evaluated system coefficient (*e, s, a, b* or *v*), k_1 and k_2 are the chromatographic retention factors of the test compounds, and finally X_1 and X_2 are the respective molecular descriptors (*E, S, A, B* or *V*) responsible for the difference in retention. In liquid chromatography the retention factor is suitable solvation property, since it is related to the partition of the analyte between the mobile and stationary phases. In this study, the application of a similar approach to electrokinetic chromatography systems is evaluated.

1.3. Micelles and oil microdroplets as dispersed phase in EKC

Electrokinetic chromatography (EKC) is a capillary separation technique based on a combination of electrophoresis and interactions of the analytes with additives (e.g., surfactants, oils), which form a dispersed phase moving at a different velocity than the analytes [50]. The dispersion medium is the bulk aqueous buffer solution, and the dispersed phase commonly consists of micelles or oil microdroplets. In order to successfully separate the analytes from the dispersed phase under the action of electrophoresis, either the analytes or the micelles/micropdroplets need to be charged. Very often ionic surfactants are used in the preparation of the dispersed phase, and thus upon application of an electric field the charged micelles or microemulsion oil

Table 1
Critical micelle concentration (in pure water and 25 °C), pK_a values and structures of the surfactants used in the present study.

Surfactant	Structure	CMC (mM)	pK_a
SDS		8.2 [62] 8.1[a] [67]	< 0 [68]
LDS		9.0[a] [69]	
SC		13[b] [70]	4.98 [62]
SDC		5 [62] 10[b] [70]	5.15 [62]
CTAB		0.92 - 1.00 [62] 0.91[a] [67]	—
TTAB		3.78[a] [67]	—

Determined through [a]conductimetric and [b]surface tension measurements. [c]20 °C.

droplets migrate with an observed electrophoretic velocity, and neutral analytes with no affinity at all with the dispersed phase migrate with the electroosmotic flow velocity. These two limiting velocities set the separation window, and the closer the electrophoretic mobility of the analyte to that of the micelles or oil microdroplets, the higher its partition into the dispersed phase.

The choice of the appropriate surfactant plays a key role in the selectivity of micellar electrokinetic chromatography (MEKC) [51–53]. Common anionic surfactants consist of a long alkyl chain and a polar sulfate or sulfonate groups (e.g., sodium dodecyl sulfate –SDS, lithium dodecyl sulfate –LDS, lithium perfluorooctane sulfonate –LIPFOS) or a bile salt (sodium cholate –SC, sodium deoxycholate –SDC, sodium taurocholate –STC, sodium taurodeoxycholate –STDC). The former surfactants aggregate in a spherical micelle due to the association of their long hydrocarbon tails, remaining the hydrophilic polar head groups on the surface. The latter surfactants are usually composed of a saturated hydrophobic cyclopentanophenanthrene nucleus with alpha-oriented hydrophilic hydroxyl groups, and an aliphatic tail terminating in a hydrophilic carboxylic or sulfonate group. This planar polarity leads to complex micellar structures still under debate [54]. Cationic surfactants are commonly long-chain alkylammonium salts (e.g., hexadecyltrimethylammonium bromide (generally known as cetyltrimethylammonium bromide — CTAB), tetradecyltrimethylammonium bromide — TTAB), which are prone to be adsorbed on the negatively charged wall surface of the fused-silica capillary. Nonionic polyethyleneglycol derivatives (e.g., Brij® 35, Tween® 20, Tween® 80) and zwitterionic surfactants (e.g., CHAPS) are used, together with ionic ones, in the preparation of mixed micellar systems to obtain improved selectivities. The surfactants included in this work are presented in Table 1, together with their critical micellar concentrations (CMC) and dissociation constants. Notice that CMC is expected to decrease with the ionic strength of the medium [55], and therefore the surfactant concentration required to form micelles in a buffered solution is lower.

In microemulsion electrokinetic chromatography (MEEKC), the spheric microdroplets constituting the dispersed phase consist of an oil (e.g., octane, heptane), surfactant (e.g., SDS) and a cosurfactant (e.g., 1-butanol). Changing the nature or concentration of the surfactant, the cosurfactant or the addition of organic modifiers have a potential impact on the chromatographic selectivity [53,56].

The high tuneability of EKC (surfactant, cosurfactant, organic modifier…) and relatively low running costs makes this technique a promising candidate for biomimetic chromatography applications. However, the conventional characterization of EKC systems by multilinear regression analysis of Abraham's model is excessively time consuming for screening purposes. The present work tries to fill this gap with the proposal of a high-throughput approach for the determination of the most relevant intermolecular interactions in particular EKC systems.

1.4. EKC mass distribution ratio as a measured solvation property

The mass distribution ratio in EKC (k_{EKC}) is defined as the ratio between the chemical amounts of the analyte between the dispersed phase (n_{dp}) and aqueous buffer solution (n_{aq}), and therefore it is related to the distribution constant of the analyte (K) and the ratio of volume phases:

$$k_{EKC} = \frac{n_{dp}}{n_{aq}} = K\frac{V_{dp}}{V_{aq}} \quad (3)$$

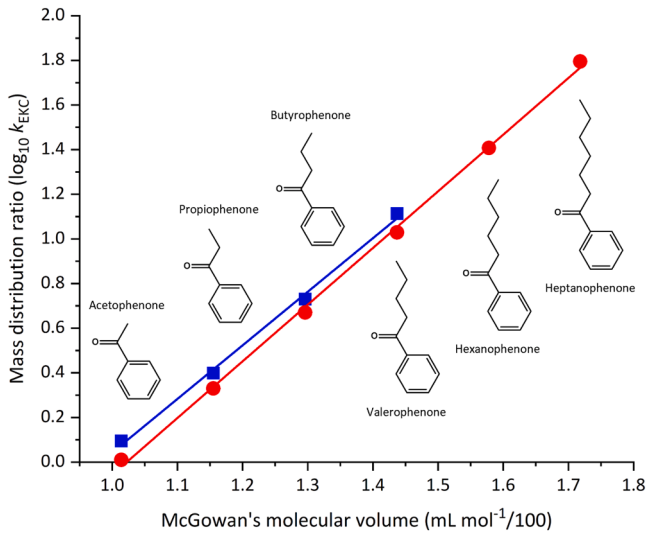


Fig. 1. Representative examples of the linear dependence of the mass distribution ratio of n-alkyl phenome homologues with the molecular volume: (■) MEKC, 1.3 % SDS, 20 mM NaH_2PO_4/Na_2HPO_4, pH 7.0; (●) MEEKC, 40 mM SDS, 8.15 % 1-butanol, 1.15 % heptane, 20 mM NaH_2PO_4/Na_2HPO_4, pH 7.0.

Table 2
Cavity coefficient values (*v*) and standard errors (in parentheses) for the studied MEKC systems reported in the literature [32] by multilinear regression analysis (Eq. (1)) of a large set of compounds (in italics) and obtained in this work by the homologous series approach (Eq. (5)).

	SDS	LDS	SC	SDC	CTAB	TTAB
Literature	*2.72 (0.06)*	*2.61 (0.06)*	*2.27 (0.10)*	*2.42 (0.13)*	*2.71 (0.05)*	*2.63 (0.05)*
Homologous	2.40 (0.10)	2.61 (0.11)	2.60 (0.12)	2.40 (0.10)	2.87 (0.13)	2.85 (0.12)

Table 3
Cavity coefficient values (*v*) and standard errors (in parentheses) for the studied MEEKC systems reported in the literature and obtained in this work by means of the homologous series approach.

	1.3 % SDS[a] [35]			1.4 % SDS[b] [31]			
	pH 7.4	pH 10.0	pH12.0	pH 7.0	pH 8.0	pH 10.0	pH 12.0
Lit.	*2.34 (0.18)*	*2.21 (0.13)*	*2.18 (0.12)*	*2.32 (0.14)*	*2.27 (0.09)*	*2.07 (0.07)*	*2.33 (0.12)*
Ho.	2.41 (0.21)	2.31 (0.05)	2.15 (0.07)	2.42 (0.06)	2.00 (0.09)	2.15 (0.07)	2.18 (0.05)
	3.3 % SDS[a] [35]			3.4 % SC[b] [31]			TTAB[c] [61]
	pH 7.4	pH 10.0	pH 12.0	pH 7.0	pH 8.0	pH 9.0	pH 10.0
Lit.	*2.46 (0.16)*	*2.15 (0.15)*	*2.18 (0.13)*	*2.17 (0.17)*	*2.20 (0.14)*	*2.29 (0.18)*	*2.35 (0.06)*
Ho.	2.01 (0.03)	2.53 (0.02)	2.09 (0.16)	1.92 (0.09)	1.84 (0.01)	1.97 (0.08)	2.15 (0.20)

[a] 25 °C, 8.15 % 1-butanol, 1.15 % heptane; [b]30 °C, 8 % 1-butanol, 1.2 % heptane; [c] 1.7 % TTAB, 8.15 % 1-butanol, 1.15 % heptane

Assuming that the volumes of secondary (V_{dp}) and aqueous (V_{aq}) phases remain constant in a particular EKC system, k_{EKC} is directly related to the distribution constant (*K*) of the analyte and thus it can be used as a measure of a solvation property (log *SP* = log k_{EKC}) in the Abraham's model. For electrically neutral analytes, which is the domain of application of the model, k_{EKC} can be directly measured from the electropherogram data using the electroosmotic hold-up time (t_{eo}) and the migration times of the analyte (t_m) and the dispersed phase (t_{dp}) [50, 53]:

$$k_{EKC} = \frac{(t_m - t_{eo})}{t_{eo}(1 - t_m/t_{dp})} \quad (4)$$

Uncharged compounds with negligible partition into the micellar or microemulsion dispersed phase, such as methanol or dimethyl sulfoxide, are commonly used as electroosmotic flow markers, whereas lipophilic uncharged solutes with a very high affinity for the micelles or oil microdroplets, such as dodecanophenone, are selected as dispersed phase markers.

2. Materials and methods

2.1. Instrumentation and equipment

All separations were performed by using a 3D Agilent 7100 (Waldron, Germany) system with UV diode array detection. Polyamide-coated capillary (Polymicrotechnologies, Phoenix, USA) with 50 μm ID, 375 μm OD, and an effective length of 50 cm was used. The cassette temperature was set to 25 or 30 °C, and an external pressure of 50 mbar was applied in all the measurements. The MEKC and MEEKC samples were injected by applying a pressure of 35 mbar for 2 s and 50 mbar for 10 s, respectively. The voltage (positive for anionic surfactants and negative for cationic ones) was set constant for a particular EKC in order to develop current intensities in the range of 30 μA. Capillary preconditioning was performed by flushing the capillary for 120 s with separation buffer and postconditioning with 1 M sodium hydroxide and water for 120 s each.

The pH was measured with a Crison GLP 22 pH meter (Barcelona, Spain) with a 5014-combination glass electrode using 3 M aqueous potassium chloride solution as salt bridge. MEKC and MEEKC solutions were sonicated at a power of 360 W in an ultrasonic bath, J.P. Selecta (Barcelona, Spain), until the solution became clear.

2.2. Chemicals and solvents

Tap water was deionized to the resistivity of 18.2 MΩ cm by a Milli-Q® plus system from Millipore (Billerica, MA, USA). All chemicals and organic solvents were of high purity grade and purchased from J.T. Baker (Phillipsburg, NJ, USA), Carlo Erba (Cornaredo, Italy) and Merck (Darmstadt, Germany).

2.3. Preparation of running buffers

The composition of the running buffers corresponds to that described in the literature, in order to compare the results of applying Abraham's fast method with the conventional approach.

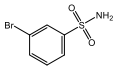
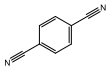
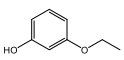
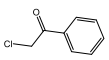
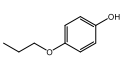
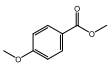
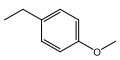
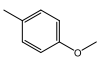
All separation solutions for MEKC system were prepared in 20 mM buffer. The following surfactants were used, all of them above their critical micelle concentrations: a) anionic surfactants: SDS (40 mM), LDS (40 mM), SC (80 mM), and SDC (40 mM); b) cationic surfactants: CTAB (20 mM) and TTAB (20 mM). SDS, SC, CTAB, and TTAB running buffers were prepared by dissolving the surfactants at room temperature in 20 mM sodium dihydrogen phosphate and then adding small amounts of a concentrated sodium hydroxide solution until pH 7.0. LDS was dissolved in 20 mM phosphoric acid and concentrated lithium hydroxide was used to adjust the pH to 7.0. The separation buffer containing SDC was prepared from sodium phosphate-sodium tetraborate (65:35) at pH 8.0. The pH values used depend on the nature of the surfactant employed and are chosen to ensure it is fully ionized under working conditions (Table 1). All the prepared solutions were filtered using syringe filter (0.45 μm) right before use.

Aqueous buffers for MEEKC were prepared according to the procedure described in the literature to reproduce the experimental

Table 4
Conditions for the selection of test compound candidates for the characterization of a particular interaction (x_i) in EKC systems.

Search within Abraham's database for pairs of solutes (1) and (2):
- fully characterized with known *E, S, A, B* and *V* molecular descriptors
- with one dissimilar molecular descriptor of interest (X_i): $\Delta X_i = \left\|X_{i,1} - X_{i,2}\right\| \geq 0.5$
- with the four remaining molecular descriptors ($X_{j\neq i}$) being similar: $dX_{i\neq j} = \sqrt{\sum_{i\neq j=1}^{4} \left(X_{j,1} - X_{j,2}\right)^2} \leq 0.05$
- unionized in a broad pH range (acid/base properties)
- with absorbance in the ultraviolet range (ease of detection)
- soluble enough in the background electrolyte and with relatively low toxicity
- commercially available and relatively unexpensive

Table 5
Abraham molecular descriptors [11] and structures of the most promising pairs of compounds for the characterization of the studied EKC systems.

	Compounds	*E*	*S*	*A*	*B*	*V*	Structures
E1	8-Hydroxyquinoline	**1.40**	1.03	0.00	0.60	1.10	
	1,2-Dimethoxybenzene	**0.83**	1.05	0.00	0.61	1.12	
E2	3-Bromobenzenesulphonamide	**1.40**	1.50	0.66	0.80	1.27	
	Monomethyl phthalate	**0.85**	1.52	0.65	0.80	1.29	
S1	1,4-Dicyanobenzene	0.87	**1.98**	0.00	0.42	1.03	
	2-Methylbenzaldehyde	0.87	**0.96**	0.00	0.40	1.01	
S2	1,2-Dicyanobenzene	0.87	**1.96**	0.00	0.41	1.03	
	2-Methylbenzaldehyde	0.87	**0.96**	0.00	0.40	1.01	
A1	3-Ethoxyphenol	0.85	1.14	**0.56**	0.48	1.12	
	2-Chloroacetophenone	0.89	1.14	**0.00**	0.47	1.14	
A2	4-Propoxyphenol	0.84	1.17	**0.57**	0.52	1.26	
	Methyl 4-methoxybenzoate	0.83	1.20	**0.00**	0.52	1.27	
B1	2,3,5,6-Tetramethylpyrazine	0.69	0.80	0.00	**0.85**	1.20	
	2,6-Dimethylanisole	0.67	0.78	0.00	**0.34**	1.20	
B2	2,3,5,6-Tetramethylpyrazine	0.69	0.80	0.00	**0.85**	1.20	
	4-Ethylanisole	0.73	0.80	0.00	**0.30**	1.20	
B3	2,3,5-Trimethylpyrazine	0.66	0.74	0.00	**0.81**	1.06	
	4-Methylanisole	0.70	0.77	0.00	**0.30**	1.06	

conditions. For 1.3 % SDS and 3.3 % SDS [35], by addition of concentrated sodium hydroxide solution to 10 mM sodium dihydrogenphosphate (pH 7.4), 20 mM boric acid (pH 10.0), 10.0 mM sodium hydrogenphosphate (pH 12.0); for 1.4 % SDS and 3.4 % SC [31], by addition of concentrated sodium hydroxide to 50 mM sodium dihydrogenphosphate (pH 7.0 or 8.0) or to 10 mM sodium hydrogenphosphate (pH 12.0), or by mixing 20 mM sodium borate and 30 mM sodium phosphate (pH 10.0). 50 mM ammonium chloride solution was used for 1.7 % TTAB and pH (10.0) was adjusted with sodium hydroxide. All separation buffers were prepared at room temperature by dissolving 1.3, 1.4 or 3.3 % w/v SDS or 1.7 % w/v TTAB or 3.4 % w/v SC in the aqueous buffer while magnetically stirring until the mixture became transparent and colorless. This was followed by the gradual addition using a burette of 1-butanol (8-8.15 % v/v) and heptane (1.15-1.2 % v/v), keeping the magnetic stirring of the turbid solution for five more minutes. The solution was then sonicated to restore its clarity. It was then allowed to sit at room temperature for a minimum of one hour and finally passed through a syringe filter (0.45 μm) just before being used as running buffer.

2.4. Sample preparation

The solutes in MEKC samples were dissolved in methanol, which also acted as electroosmotic flow marker, whereas in MEEKC the running buffer was used as sample solvent and dimethyl sulfoxide as marker. The solute concentration was in the range between 0.5 and 2.0 mg mL^{-1}.

3. Results and discussion

3.1. Selection of the dispersed phase marker and determination of v coefficient

The migration window in EKC (Eq. (4)) is defined by the behavior of two unionized UV-active compounds with opposite lipophilic behavior. The electroosmotic flow marker must be a very hydrophilic compound, which is supposed to remain exclusively in the dispersive medium, whereas the dispersed phase marker is expected to be lipophilic enough to partition exclusively into the micelles or the oil microdroplets. Typical examples of the former marker are methanol or dimethyl sulfoxide (measured log $P_{o/w}$ of -0.77 and -1.35, respectively [57]), and dodecanophenone (estimated log $P_{o/w}$ = 6.87 [57]) is commonly used for the latter purpose. However, this phenone with a 12-carbon alkyl chain, solid at room temperature, is poorly soluble in the running buffer, even in the presence of micelles or oil microdroplets. Thus, it would be interesting to evaluate the convenience of other dispersed phase markers of higher solubility, but lipophilic enough to still be excluded from the dispersive aqueous medium.

The members of a *n*-alkyl homologous series, despite their

Table 6
System coefficient values (*e, s, a* and *b*) and standard errors (in parentheses) for the studied MEKC systems reported in the literature [32] by multilinear regression analysis (Eq. (1)) of a large set of compounds (in italics) and obtained in this work by the fast approach (Eq. (2)), together with the mean absolute difference (MAD) between the results of both approaches.

	SDS	LDS	SC	SDC	CTAB	TTAB	MAD
e	*0.56*	*0.59*	*0.69*	*0.93*	*1.11*	*0.90*	—
	(0.07)	*(0.09)*	*(0.13)*	*(0.20)*	*(0.09)*	*(0.08)*	
E1	0.37	0.51	0.88	0.60	1.07	1.18	0.18
	(0.02)	(0.02)	(0.18)	(0.03)	(0.02)	(0.02)	
E2	−0.26	0.23	0.82	0.76	0.76	0.88	0.22
	(0.07)	(0.08)	(0.08)	(0.06)	(0.02)	(0.06)	
s	*−0.60*	*−0.60*	*−0.69*	*−0.87*	*−0.76*	*−0.62*	—
	(0.06)	*(0.07)*	*(0.10)*	*(0.15)*	*(0.05)*	*(0.05)*	
S1	−0.52	−0.47	−0.60	−0.52	−0.48	−0.49	0.17
	(0.01)	(0.01)	(0.01)	(0.01)	(0.16)	(0.01)	
S2	−0.45	−0.43	−0.39	−0.44	−0.26	−0.28	0.31
	(0.02)	(0.01)	(0.01)	(0.01)	(0.17)	(0.03)	
a	*−0.27*	*−0.32*	*0.12*	*0.07*	*0.82*	*0.77*	—
	(0.05)	*(0.05)*	*(0.08)*	*(0.14)*	*(0.04)*	*(0.04)*	
A1	−0.48	−0.54	−0.18	0.03	0.39	0.76	0.18
	(0.02)	(0.06)	(0.01)	(0.09)	(0.02)	(0.16)	
A2	−0.19	−0.27	−0.14	0.29	0.45	0.59	0.19
	(0.06)	(0.06)	(0.05)	(0.05)	(0.03)	(0.31)	
b	*−1.67*	*−1.57*	*−1.94*	*−1.79*	*−2.44*	*−2.41*	—
	(0.07)	*(0.07)*	*(0.11)*	*(0.15)*	*(0.05)*	*(0.06)*	
B1	−1.67	−1.36	−2.08	−1.64	−2.84	−2.50	0.17
	(0.09)	(0.01)	(0.03)	(0.02)	(0.03)	(0.05)	
B2	−1.80	−1.45	−2.02	−1.86	−3.30	−2.26	0.24
	(0.08)	(0.17)	(0.04)	(0.03)	(0.03)	(0.06)	

E1: 8-Hydroxyquinoline/1,2-Dimethoxybenzene; E2: 3-Bromobenzenesulphonamide /1-Monomethylphalate
S1: 1,4-Dicyanobenzene/2-Methylbenzaldehyde; S2: 1,2-Dicyanobenzene/2-Methylbenzaldehyde
A1: 3-Ethoxyphenol/2-Chloroacetophenone; A2: 4-Propoxyphenol/Methyl 4-methoxybenzoate
B1: 2,3,5,6-Tetramethylpyrazine/2,6-Dimethylanisole; B2: 2,3,5,6-Tetramethylpyrazine/4-Ethylanisole

differences in the number of carbon atoms (molecular volume), present very similar molecular interactions. This reasoning, in the context of the Abraham's model, implies that excess polarizability (*E*), dipolarity/polarizability (*S*), hydrogen bonding acidity (*A*) and basicity (*B*) descriptors remain nearly constant throughout the whole series of homologues. Thus, as long as the EKC system remains unchanged (same running buffer composition) and the intercept (*c*) and chromatographic coefficients (*e, s, a, b*, and *v*) are constant, the dependence of the logarithm of the mass transfer ratio ($\log_{10} k_{EKC,i}$) with the molecular volume of a homologue (V_i) can be linearized as:

$$\log_{10} k_{EKC,i} = r + v \cdot V_i \quad (5)$$

where the intercept *r* is a constant depending on the EKC system and the homologous series under study ($r = c + e \cdot E + s \cdot S + a \cdot A + b \cdot B$) and the slope *v* is the system coefficient accounting for the difference in the ease of formation of a cavity in the dispersed phase in relation to the aqueous dispersive medium.

The fitting accuracy of Eq. (5) was tested with the *n*-alkyl phenone homologous series, from the smallest and less lipophilic acetophenone (measured log $P_{o/w} = 1.58$ [57]) to the well-known dodecanophenone. In fact, in this range the homologues show similar Abraham's molecular descriptors ($E = 0.78 \pm 0.03$, $S = 0.96 \pm 0.02$, $A = 0$, $B = 0.50 \pm 0.01$) except for the molecular volume ($1.01 \leq V_i \leq 2.42$). Coelution was generally observed in the studied MEKC systems for homologues larger than valerophenone (estimated log $P_{o/w} = 3.17$ [57]), whereas for MEEKC coelution took place after heptanophenone (estimated log $P_{o/w} = 4.23$ [57]). This observation is consistent with the larger separation windows offered by MEEKC, attributed to the lower interfacial tension between oil microdroplets and the dispersive medium, allowing the solutes to penetrate more easily the surface of the droplet [58–60]. The surfactant molecules have the polar groups oriented towards the aqueous phase, with the cosurfactant molecules in between contributing to reduce electrostatic repulsion. Fig. 1 shows two representative plots of the linear dependence of $\log_{10} k_{EKC}$ with the molecular volume of the homologues for MEKC and MEEKC systems.

The smaller size of nonanophenone (9-carbon alkyl chain, est. log $P_{o/w} = 5.28$) in relation to the commonly used marker dodecanophenone (12-carbon) does not produce any difference in the migration behavior of the studied EKC systems, and both solutes partition into the dispersed phase to the same extent. However, nonanophenone shows the benefits of being more soluble in the sample and running buffers, and easier to handle because of its liquid state at room temperature. In fact, dodecanophenone precipitated inside the sample vial for some of the studied EKC systems, leading to a decrease in the marker peak in replicate analysis, whereas for nonanophenone a higher repeatability was observed along time. Therefore, nonanophenone was selected as a dispersed phase marker, instead of dodecanophenone, in the subsequent experimental work.

As shown in Tables 2 and 3, the obtained values for the cavity coefficient (*v*) are large and positive, indicating that dispersed phase, either the hydrophobic part of the surfactant molecules forming the micelles in MEKC or the oil microdroplet in MEEKC, are less cohesive than the aqueous dispersed medium. Consequently, a lower amount of energy is required to disrupt interactions (mainly of dispersive nature) within the solvent molecules in the hydrophobic phase compared to the aqueous dispersive medium, mainly governed by polarity and hydrogen bonding interactions, and thus larger solutes partition more favorably into the dispersed phase. Good agreements are found between the *v* values obtained from multilinear regression analysis in previous works and the fast approach presented in this study, either in MEKC (Table 2) or MEEKC (Table 3).

3.2. Determination of pairs of solute candidates for e, s, a, and b coefficients determination

We performed an extensive search within the Abraham's database looking for pairs of solutes with four similar molecular descriptors and one significantly dissimilar, suitable to be used in the characterization of EKC systems. The searching criteria, presented in detail in a previous work [49], is summarized in Table 4. Further refinement was carried out estimating their mass distribution ratios in EKC systems already characterized by means of the Abraham's model, in order to find solutes with significant partition in the dispersed phase and the dispersive medium, and thus preventing the solute peak from appearing at the edges of the separation window and avoiding coelution with the electroosmotic flow and micelle/microdroplet markers. Solutes with negative values of log k_{EKC} are prone to coelute with the electroosmotic marker, and compounds with relatively large ones, with nonanophenone. All pairs of compounds assayed in this work are described in the supplementary material (Table SP1), and the compounds that have provided results most similar to those in the literature are highlighted in Table 5. Notice that some of the test compounds selected as final candidates for the fast characterization of column liquid chromatography systems, such as pentacene and dibenz [*a,c*]anthracene for dipolarity/polarizability interactions or dibenzofuran for polarizability contributions from *n*- and π-electrons, are not suitable in EKC systems due to their low solubility in the running buffers (and insufficient UV detection) or because of the coelution with the dispersed phase marker.

Table 6 allows the comparison of system coefficients obtained for the studied MEKC systems using the proposed fast method and by applying Abraham's model through the injection of a large number of solutes followed by multiple linear regression analysis (Eq. 1). In the extensive characterization work conducted in 2002 with the collaboration of Prof. Abraham [32], chemometric methods were used to ensure the representativeness of the 71 selected solutes for characterization, which were

Table 7
System coefficient values (*e, s, a* and *b*) and standard errors (in parentheses) for the studied MEEKC systems reported in the literature (in italics) and obtained in this work, together with the mean absolute difference (MAD) between the results of both approaches.

	1.3 % SDS [35]			1.4 % SDS [31]				3.3 % SDS [35]			3.4 % SC [31]			TTAB [61]	MAD
	pH 7.4	pH 10.0	pH 12.0	pH 7.0	pH 8.0	pH 10.0	pH 12.0	pH 7.4	pH 10.0	pH 12.0	pH 7.0	pH 8.0	pH 9.0	pH 10.0	
e	*0.38*	*0.36*	*0.43*	*0.50*	*0.28*	*0.35*	*0.35*	*0.09*	*0.25*	*0.40*	*0.40*	*0.33*	*0.26*	*0.47 (0.08)*	—
	(0.11)	*(0.10)*	*(0.08)*	*(0.11)*	*(0.05)*	*(0.04)*	*(0.08)*	*(0.17)*	*(0.21)*	*(0.08)*	*(0.11)*	*(0.07)*	*(0.09)*		
E1	0.60	0.62	0.49	0.34	0.23	0.09	0.67	0.01	0.13	0.05	0.25	0.27	0.44	0.89	0.19
	(0.05)	(0.06)	(0.20)	(0.04)	(0.09)	(0.16)	(0.04)	(0.07)	(0.12)	(0.02)	(0.02)	(0.02)	(0.12)	(0.01)	
E2	0.51	0.20	0.44	0.15	0.12	0.23	0.02	0.11	0.02	0.01	−0.19	0.02	0.31	0.90	0.23
	(0.04)	(0.04)	(0.02)	(0.03)	(0.07)	(0.10)	(0.03)	(0.01)	(0.08)	(0.07)	(0.09)	(0.04)	(0.03)	(0.01)	
s	*−0.70*	*−0.47*	*−0.67*	*−0.89*	*−0.41*	*−0.44*	*−0.62*	*−0.61*	*−0.52*	*−0.66*	*−0.71*	*−0.41*	*−0.40*	*−0.69 (0.06)*	—
	(0.11)	*(0.10)*	*(0.09)*	*(0.20)*	*(0.06)*	*(0.05)*	*(0.09)*	*(0.10)*	*(0.11)*	*(0.09)*	*(0.19)*	*(0.09)*	*(0.15)*		
S2	−1.24	−0.59	−0.58	−0.56	−0.39	−0.60	−0.57	−0.55	−0.61	−0.58	−0.40	−0.49	−0.31	−0.45	0.16
	(0.01)	(0.01)	(0.04)	(0.01)	(0.19)	(0.09)	(0.06)	(0.01)	(0.01)	(0.01)	(0.15)	(0.01)	(0.02)	(0.01)	
S1	−1.33	−0.66	−0.65	−0.94	−1.30	−0.70	−0.66	−0.65	−0.74	−0.66	−0.54	−0.67	−0.57	−0.69	0.21
	(0.01)	(0.01)	(0.05)	(0.01)	(0.07)	(0.09)	(0.06)	(0.04)	(0.07)	(0.01)	(0.06)	(0.01)	(0.12)	(0.01)	
a	*−0.22*	*−0.10*	*0.07*	*−0.18*	*−0.26*	*−0.26*	*−0.22*	*−0.04*	*−0.09*	*0.02*	*−0.03*	*0.05*	*0.07*	*0.19 (0.04)*	—
	(0.22)	*(0.16)*	*(0.14)*	*(0.11)*	*(0.08)*	*(0.09)*	*(0.15)*	*(0.11)*	*(0.19)*	*(0.14)*	*(0.14)*	*(0.11)*	*(0.14)*		
A1	−0.27	−0.29	0.17	−0.17	−0.37	−0.08	−0.01	−0.73	−0.48	−0.03	−0.25	−0.18	−0.03	0.44	0.20
	(0.03)	(0.01)	(0.13)	(0.06)	(0.03)	(0.15)	(0.02)	(0.02)	(0.02)	(0.08)	(0.02)	(0.02)	(0.06)	(0.01)	
A2	−0.08	−0.08	0.06	−0.08	−0.57	−0.68	−0.02	−1.16	−0.03	−0.02	−0.30	0.33	0.16	0.58	0.25
	(0.06)	(0.08)	(0.02)	(0.08)	(0.05)	(0.16)	(0.08)	(0.01)	(0.16)	(0.04)	(0.04)	(0.05)	(0.02)	(0.13)	
b	*−1.90*	*−2.14*	*−1.83*	*−1.72*	*−2.06*	*−2.15*	*−2.02*	*−1.90*	*−1.88*	*−1.83*	*−1.66*	*−2.06*	*−2.15*	*−2.07 (0.07)*	—
	(0.18)	*(0.13)*	*(0.10)*	*(0.14)*	*(0.11)*	*(0.15)*	*(0.11)*	*(0.14)*	*(0.15)*	*(0.10)*	*(0.18)*	*(0.11)*	*(0.15)*		
B1	−2.26	−2.38	−1.94	−1.45	−2.33	−2.63	−2.43	−2.20	−1.97	−1.86	−1.77	−1.91	−2.14	−2.56	0.24
	(0.03)	(0.02)	(0.03)	(0.21)	(0.18)	(0.47)	(0.01)	(0.02)	(0.07)	(0.05)	(0.15)	(0.04)	(0.02)	(0.01)	
B3	−2.16	−2.20	−2.34	−1.48	−1.70	−1.71	−2.14	−2.12	−2.21	−2.30	−2.05	−1.99	−1.94	−2.46	0.29
	(0.01)	(0.01)	(0.02)	(0.01)	(0.01)	(0.01)	(0.24)	(0.01)	(0.08)	(0.01)	(0.06)	(0.01)	(0.06)	(0.15)	

E1: 8-Hydroxyquinoline/1,2-Dimethoxybenzene; E2: 3-Bromobenzenesulphonamide /1-Monomethylphalate
S1: 1,4-Dicyanobenzene/2-Methylbenzaldehyde; S2: 1,2-Dicyanobenzene/2-Methylbenzaldehyde
A1: 3-Ethoxyphenol/2-Chloroacetophenone; A2: 4-Propoxyphenol/Methyl 4-methoxybenzoate
B1: 2,3,5,6-Tetramethylpyrazine/2,6-Dimethylanisole; B3: Trimethylpyrazine/4-Methylanisole

structurally different and covered the largest possible chemical space. The chosen micellar marker was dodecanophenone and all measurements were performed in triplicate, implying the need of more than two hundred injections for the characterization of a single chromatographic system. In contrast, the fast approach requires only a single injection of solute pairs to obtain the *e, s, a*, and *b* coefficients, and a single injection of a series of homologs for *v*; even in triplicate, the approach requires only a total of fifteen injections. Using the values from the article as a reference, Table 6 presents the two pairs of solutes that show the greatest similarity for each coefficient along the various surfactants included in the study, calculated as the mean absolute difference. The selected pairs of candidates for *e, s, a* and *b* coefficients are, respectively, 8-hydroxyquinoline / 1,2-dimethoxybenzene (E1), 1,4-dicyanobenzene / 2-methylbenzaldehyde (S1), 3-ethoxyphenol / 2-chloroacetophenone (A1), and 2,3,5,6-tetramethylpyrazine / 2,6-dimethylanisole (B1). Although the different nature of the surfactant, all micelles present a higher capacity of interaction with the solutes in relation to aqueous buffer through loose electrons ($e > 0$), and a lower ability to donate hydrogen bonding ($b < 0$) and stablish polarity/polarizability interactions ($s < 0$). However, significant differences can be observed in the hydrogen bond acceptance capacity of the micelle of cationic surfactants, which is greater than that of the dispersive medium (CTAB, TTAB: $a > 0$), while the opposite phenomenon is observed for anionic surfactants (SDS, LDS: $a < 0$). For a more detailed analysis of the physicochemical implications of the signs and magnitudes of the chromatographic coefficients, readers are referred to the original article [32]

The results obtained for the different microemulsion systems are summarized in Table 7. Similarly to MEKC systems, the characterization presented in the literature was carried out considering an extensive number of solutes (85 for 1.3 % and 3.3 % SDS (38 neutral, 36 acidic, and 11 basic) [35], 57 for 1.4 % SDS and 3.4 % SC [31], and 61 for TTAB [61]), and thus the rapid method we propose represents a significant saving of time, laboratory resources, reagents, and solvents. The three pairs we proposed for the characterization of *e, a* and *b* in MEKC are also the most suitable for MEEKC. In the case of dipolar interactions, the pair recommended for MEKC ranked second, behind the first choice 1, 2-dicyanobenzene / 2-methylbenzaldehyde (S2). In microemulsions, the trends and differences previously discussed for micellar systems formed from different surfactants are observed, but they are more attenuated, likely due to the presence of oil (heptane) and the cosurfactant (1-butanol) in the dispersed phase.

Some of the molecules presented in Table 5 show acid/base properties. The hydroxyquinoline has a basic pyridine nitrogen and acidic phenol groups, with pK_a values of 4.91 and 9.81, respectively [62]. Therefore, ionization of the phenolate group is expected to be significant in water at pH 10 and above. Similar pK_a values are expected for 3-ethoxyphenol and 4-propoxyphenol (9.6±0.1 and 10.3±0.2, respectively [63]), and even for the acidic hydrogen of the 3-bromobenzenesulfonamide (9.8±0.6 [63]). Before experimentally testing these compounds, we thought that the ionization of the molecules would represent a difficulty in the application of the fast characterization approach, since the molecular of ionized compounds are different from those of the uncharged ones. For instance, a reduction in the hydrogen bond acidity, but an increase in basicity and polarity, would be expected upon deprotonation of the phenol group. This effect would even be more pronounced for the carboxylic group of the monomethyl phthalate, with a pK_a of 3.3±0.1 [63], which is expected to be fully ionized yet in moderately acidic running buffers. The first consequence would be the migration of the ionized analytes inside the capillary upon the influence of the electric field, as an additional mechanism to the partition with the charged dispersive phase. Secondly, the differences in the migration behavior of a pair of test compounds could not be uniquely attributed to a dissimilar molecular descriptor and the application of Eq. (2) would be inaccurate. Despite these issues, the correspondence of the system coefficients obtained with these presumably ionized compounds with the reference ones obtained from literature is better than that achieved with

fully unionized solutes. The reasons behind these observations are not yet clear and deserve further investigation. In the 1930s Hartley observed the effect of positive and negative micelles on the color of acidimetric indicators [64], reviewed in [65], and proposed the existence of a pH gradient between the interface of an ionic micelle and the bulk solution [66]. Thus, the interactions of the solutes with the charged dispersive phase (or its interface) might indeed change the acid/base behavior of the compounds. However, it cannot be ruled out that the effect of the migration of the charged might be less significant than the partition into the dispersive phase, or the differences between molecular descriptors of the same kind for the two solutes remain similar despite the ionization. The basic nitrogen atoms of both pyrazines, with pK_a values below 3.2 [63], are expected to be fully deprotonated and therefore neutral at the working pH values of the studied EKC systems.

4. Conclusions

In this study, we propose a method based on Abraham's solvation parameter model that allows the characterization of micellar electrokinetic chromatography and microemulsion systems with only five injections, using nonanophenone as a marker for the dispersed phase. For the determination of the cavity term (*v*), mixtures containing different homologues of *n*-alkyl phenones are used, and for the rest of the model coefficients, the following pairs of compounds are injected: 8-hydroxyquinoline and 1,2-dimethoxybenzene for the characterization of dispersion interactions due to the solute's π- and *n*-electrons (*e*); 1,4- or 1,2-dicyanobenzene and 2-methylbenzaldehyde for dipolarity/polarizability type forces (*s*); 3-ethoxyphenol and 2-chloroacetophenone to characterize the hydrogen bond acceptor capacity of the dispersed phase relative to the dispersive medium (*a*), and 2,3,5,6-tetramethylpyrazine and 2,6-dimethylanisole for the donor capacity (*b*). The method has been tested with micellar systems containing bile salts (80 mM SC and 40 mM SDC), anionic (40 mM SDS and 40 mM LSD) and cationic surfactants (20 mM CTAB and 20 mM TTAB), and microemulsions consisting of heptane, 1-butanol and SDS at different concentrations (1.3 –3.3 %) and pH values (7 — 12), or 3.4 % SC and pH 7 —9 or 1.7 % TTAB and pH 10. This fast approach constitutes a more efficient alternative to conventional characterization of EKC systems by means of multilinear regression analysis of a relatively large set of test compounds, aligned with the Green Chemistry principles of waste prevention and energy efficiency. It is expected that the implementation of the proposed methodology will allow an increase in the pace of characterization of EKC systems, thus raising the possibilities of developing chromatographic configurations suitable for biomimetic applications in pharmaceutical and environmental sciences.

CRediT authorship contribution statement

Rabia Idrees: Writing – original draft, Visualization, Investigation, Formal analysis. **Xavier Subirats:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Susana Amézqueta:** Writing – review & editing, Supervision. **Martí Rosés:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This publication is part of grant PID2023-150245NB-I00 funded by MICIU/AEI/10.13039/501100011033 and by "ERDF A way of making Europe". Research recognition by the Catalan Government (2021 SGR 00248) is acknowledged, too.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2025.466176.

Data availability

Data will be made available on request.

References

[1] C. Giaginis, A. Tsantili-Kakoulidou, Quantitative structure–Retention relationships as useful tool to characterize chromatographic systems and their potential to simulate biological processes, Chromatographia 76 (2013) 211–226, https://doi.org/10.1007/s10337-012-2374-6.
[2] K. Valkó, Physicochemical and Biomimetic Properties in Drug Discovery, Wiley, Hoboken, NJ, USA, 2014.
[3] F. Tsopelas, T. Vallianatou, A. Tsantili-Kakoulidou, Advances in immobilized artificial membrane (IAM) chromatography for novel drug discovery, Expert Opin. Drug. Discov. 11 (2016) 473–488, https://doi.org/10.1517/17460441.2016.1160886.
[4] S. Bunally, R.J. Young, The role and impact of high throughput biomimetic measurements in drug discovery, Admet. Dmpk. 6 (2018) 74–84, https://doi.org/10.5599/admet.530.
[5] K.L. Valkó, Application of HPLC measurements for the determination of physicochemical and biomimetic properties to model in vivo drug distribution in support of early drug discovery, in: 2020: pp. 667-758. https://doi.org/10.1016/B978-0-444-64070-3.00013-8.
[6] K.L. Valko, Biomimetic chromatography—A novel application of the chromatographic principles, Analyt. Sci. Adv. 3 (2022) 146–153, https://doi.org/10.1002/ansa.202200004.
[7] E. Grządka, I. Malinowska, Selected chromatographic methods for determining the biological activity of substances, Appl. Sci. 14 (2024) 4265, https://doi.org/10.3390/app14104265.
[8] F. Tsopelas, C. Stergiopoulos, P. Danias, A. Tsantili-Kakoulidou, Biomimetic separations in chemistry and life sciences, Microchim. Acta 192 (2025) 133, https://doi.org/10.1007/s00604-025-06980-x.
[9] M.H. Abraham, Scales of solute hydrogen-bonding: their construction and application to physicochemical and biochemical processes, Chem. Soc. Rev. 22 (1993) 73, https://doi.org/10.1039/cs9932200073.
[10] ACD/Labs. Advanced Chemistry Development, Inc. Toronto, ON, Canada. Software V11.02.
[11] N. Ulrich, S. Endo, T.N. Brown, N. Watanabe, G. Bronner, M.H. Abraham, K.-U. Goss, UFZ-LSER database v 3.2 [Internet], (2017). http://www.ufz.de/lserd.
[12] C.F. Poole, The complete 2025 Wayne State University compound descriptor database for use with the solvation parameter model, J. Chromatogr. A 1752 (2025) 465958, https://doi.org/10.1016/j.chroma.2025.465958.
[13] Y. Chung, F.H. Vermeire, H. Wu, P.J. Walker, M.H. Abraham, W.H. Green, Group contribution and machine learning approaches to predict Abraham Solute parameters, solvation free energy, and Solvation enthalpy, J. Chem. Inf. Model. 62 (2022) 433–446, https://doi.org/10.1021/acs.jcim.1c01103.
[14] J.C. McGowan, Estimates of the properties of liquids, J. Chem. Technol. Biotechnol. 28 (1978) 599–607, https://doi.org/10.1002/jctb.5700280902.
[15] M.H. Abraham, J.C. McGowan, The use of characteristic volumes to measure cavity terms in reversed phase liquid chromatography, Chromatographia 23 (1987) 243–246, https://doi.org/10.1007/BF02311772.
[16] W.E. Acree Jr., L.M. Grubbs, M.H. Abraham, Prediction of Toxicity, Sensory Responses and Biological Responses with the Abraham Model, in: Toxicity and Drug Testing, InTech, 2012, https://doi.org/10.5772/29972.
[17] W.E. Acree Jr., L.M. Grubbs, M.H. Abraham, Prediction of partition coefficients and permeability of drug molecules in biological systems with Abraham Model solute descriptors derived from measured solubilities and water-to-organic solvent partition coefficients. Toxicity and Drug Testing, InTech, 2012, https://doi.org/10.5772/19082.
[18] M.H. Abraham, H.S. Chadha, F. Martins, R.C. Mitchell, M.W. Bradbury, J. A. Gratton, Hydrogen bonding part 46: a review of the correlation and prediction of transport properties by an lfer method: physicochemical properties, brain penetration and skin permeability, Pestic. Sci. 55 (1999) 78–88, https://doi.org/10.1002/(SICI)1096-9063(199901)55:1<78::AID-PS853>3.0.CO;2-7.
[19] W.E. Acree, M.H. Abraham, Solubility of crystalline nonelectrolyte solutes in organic solvents: mathematical correlation of benzil solubilities with the Abraham General Solvation Model, J. Solution Chem. 31 (2002) 293–303, https://doi.org/10.1023/A:1015853220711.
[20] J.-C. Bradley, M.H. Abraham, W.E. Acree, A.S. Lang, Predicting Abraham model solvent coefficients, Chem. Cent. J. 9 (2015) 12, https://doi.org/10.1186/s13065-015-0085-4.
[21] J. Li, Application of Abraham's solvation parameter model to extractables and leachables studies in pharmaceutical and medical device industries: A tutorial, J. Chromatography Open 6 (2024) 100158, https://doi.org/10.1016/j.jcoa.2024.100158.

[22] M.H. Abraham, M. Rosés, Hydrogen bonding. 38. Effect of solute structure and mobile phase composition on reversed-phase high-performance liquid chromatographic capacity factors, J. Phys. Org. Chem. 7 (1994) 672–684, https://doi.org/10.1002/poc.610071205.

[23] M.H. Abraham, M. Rosés, C.F. Poole, S.K. Poole, Hydrogen bonding. 42. Characterization of reversed-phase high-performance liquid chromatographic C18 stationary phases, J. Phys. Org. Chem. 10 (1997) 358–368, https://doi.org/10.1002/(SICI)1099-1395(199705)10:5<358::AID-POC907>3.0.CO;2-N.

[24] L.C. Tan, P.W. Carr, Study of retention in reversed-phase liquid chromatography using linear solvation energy relationships, J. Chromatogr. A 799 (1998) 1–19, https://doi.org/10.1016/S0021-9673(97)01054-6.

[25] M. Vitha, P.W. Carr, The chemical interpretation and practice of linear solvation energy relationships in chromatography, J. Chromatogr. A 1126 (2006) 143–194, https://doi.org/10.1016/j.chroma.2006.06.074.

[26] C.F. Poole, N. Lenca, Applications of the solvation parameter model in reversed-phase liquid chromatography, J. Chromatogr. A 1486 (2017) 2–19, https://doi.org/10.1016/j.chroma.2016.05.099.

[27] H. Riering, N. Bilmann, Characterisation of RP Sorbents by Linear Solvation Energy Relationships (LSER), Labmate, 2019, pp. 8–12. https://www.labmate-online.com/article/chromatography/1/macherey-nagel-gmbh/characterisation-of-rp-sorbents-by-linear-solvation-energy-relationships-lser/2583 (accessed November 27, 2024).

[28] C.F. Poole, Solvation parameter model: tutorial on its application to separation systems for neutral compounds, J. Chromatogr. A 1645 (2021) 462108, https://doi.org/10.1016/j.chroma.2021.462108.

[29] X. Subirats, L. Casanovas, L. Redón, M. Rosés, Effect of the solvent on the chromatographic selectivity in reversed-phase and HILIC, Adv. Sample Preparat. 6 (2023), https://doi.org/10.1016/j.sampre.2023.100063.

[30] S.K. Poole, C.F. Poole, Characterization of surfactant selectivity in micellar electrokinetic chromatography, Analyst 122 (1997) 267–274, https://doi.org/10.1039/a605799c.

[31] S.K. Poole, D. Durham, C. Kibbey, Rapid method for estimating the octanol–water partition coefficient (log Pow) by microemulsion electrokinetic chromatography, J. Chromatogr. B Biomed. Sci. Appl. 745 (2000) 117–126, https://doi.org/10.1016/S0378-4347(00)00072-4.

[32] E. Fuguet, C. Ràfols, E. Bosch, M.H. Abraham, M. Rosés, Solute–solvent interactions in micellar electrokinetic chromatography III. Characterization of the selectivity of micellar electrokinetic chromatography systems, J. Chromatogr. A 942 (2002) 237–248, https://doi.org/10.1016/S0021-9673(01)01383-8.

[33] E. Fuguet, C. Ràfols, E. Bosch, M.H. Abraham, M. Rosés, Selectivity of single, mixed, and modified pseudostationary phases in electrokinetic chromatography, Electrophoresis 27 (2006) 1900–1914, https://doi.org/10.1002/elps.200500464.

[34] S.K. Poole, C.F. Poole, Quantitative structure–retention (property) relationships in micellar electrokinetic chromatography, J. Chromatogr. A 1182 (2008) 1–24, https://doi.org/10.1016/j.chroma.2007.12.080.

[35] X. Subirats, H.-P. Yuan, V. Chaves, N. Marzal, M. Rosés, Microemulsion electrokinetic chromatography as a suitable tool for lipophilicity determination of acidic, neutral, and basic compounds, Electrophoresis 37 (2016) 2010–2016, https://doi.org/10.1002/ELPS.201600080.

[36] A. Fernández-Pumarega, S. Amézqueta, S. Farré, L. Muñoz-Pascual, M.H. Abraham, E. Fuguet, M. Rosés, Modeling aquatic toxicity through chromatographic systems, Anal. Chem. 89 (2017) 7996–8003, https://doi.org/10.1021/acs.analchem.7b01301.

[37] M.H. Abraham, The factors that influence permeation across the blood–brain barrier, Eur. J. Med. Chem. 39 (2004) 235–240, https://doi.org/10.1016/j.ejmech.2003.12.004.

[38] M.H. Abraham, A. Ibrahim, W.E. Acree, Air to muscle and blood/plasma to muscle distribution of volatile organic compounds and drugs: linear free energy analyses, Chem. Res. Toxicol. 19 (2006) 801–808, https://doi.org/10.1021/tx050337k.

[39] X. Subirats, L. Muñoz-Pascual, M.H. Abraham, M. Rosés, Revisiting blood-brain barrier: A chromatographic approach, J. Pharm. Biomed. Anal. 145 (2017) 98–109, https://doi.org/10.1016/j.jpba.2017.06.027.

[40] X. Liu, W.E. Acree, M.H. Abraham, Descriptors for some compounds with pharmacological activity; calculation of properties, Int. J. Pharm. 617 (2022) 121597, https://doi.org/10.1016/j.ijpharm.2022.121597.

[41] M.H. Abraham, Human intestinal absorption—Neutral molecules and ionic species, J. Pharm. Sci. 103 (2014) 1956–1966, https://doi.org/10.1002/jps.24024.

[42] M.H. Abraham, F. Martins, Human skin permeation and partition: general linear free-energy relationship analyses, J. Pharm. Sci. 93 (2004) 1508–1523, https://doi.org/10.1002/jps.20070.

[43] K. Zhang, M.H. Abraham, X. Liu, An equation for the prediction of human skin permeability of neutral molecules, ions and ionic species, Int. J. Pharm. 521 (2017) 259–266, https://doi.org/10.1016/j.ijpharm.2017.02.059.

[44] K.R. Hoover, W.E. Acree, M.H. Abraham, Chemical toxicity correlations for several fish species based on the Abraham solvation parameter model, Chem. Res. Toxicol. 18 (2005) 1497–1505, https://doi.org/10.1021/tx050164z.

[45] K.R. Bowen, K.B. Flanagan, W.E. Acree, M.H. Abraham, C. Rafols, Correlation of the toxicity of organic compounds to tadpoles using the Abraham model, Sci. Total Environ. 371 (2006) 99–109, https://doi.org/10.1016/j.scitotenv.2006.08.030.

[46] C.F. Poole, S.N. Atapattu, Recent advances for estimating environmental properties for small molecules from chromatographic measurements and the solvation parameter model, J. Chromatogr. A 1687 (2023) 463682, https://doi.org/10.1016/j.chroma.2022.463682.

[47] C.F. Poole, S.N. Atapattu, Predicting biophysical properties of small molecules from chromatographic measurements and the solvation parameter model, J. Chromatogr. A 1738 (2024) 465461, https://doi.org/10.1016/j.chroma.2024.465461.

[48] E. Fuguet, M. Rosés, Tutorial on modelling chromatographic surrogation of biological processes, J. Chromatogr. Open 6 (2024), https://doi.org/10.1016/j.jcoa.2024.100189.

[49] L. Redón, M. Safar Beiranvand, X. Subirats, M. Rosés, Characterization of solute-solvent interactions in liquid chromatography systems: A fast method based on Abraham's linear solvation energy relationships, Anal. Chim. Acta (2023) 1277, https://doi.org/10.1016/j.aca.2023.341672.

[50] M.-L. Riekkola, J.Å. Jönsson, R.M. Smith, Terminology for analytical capillary electromigration techniques (IUPAC Recommendations 2003), Pure Appl. Chem. 76 (2004) 443–451, https://doi.org/10.1351/pac200476020443.

[51] M.-L. Riekkola, Electrophoresis | micellar electrokinetic chromatography. Encyclopedia of Separation Science, Elsevier, 2000, pp. 1280–1286, https://doi.org/10.1016/B0-12-226770-2/04401-X.

[52] S. Terabe, Capillary separation: micellar electrokinetic chromatography, Annu. Rev. Anal. Chem. 2 (2009) 99–120, https://doi.org/10.1146/annurev.anchem.1.031207.113005.

[53] U. Pyell, Micellar and microemulsion electrokinetic chromatography, in: capillary electromigration separation methods, Elsevier (2018) 113–142, https://doi.org/10.1016/B978-0-12-809375-7.00005-8.

[54] O. Pabois, R.M. Ziolek, C.D. Lorenz, S. Prévost, N. Mahmoudi, M.W.A. Skoda, R.J. L. Welbourn, M. Valero, R.D. Harvey, M.M.-L. Grundy, P.J. Wilde, I. Grillo, Y. Gerelli, C.A. Dreiss, Morphology of bile salts micelles and mixed micelles with lipolysis products, from scattering techniques and atomistic simulations, J. Colloid Interface Sci. 587 (2021) 522–537, https://doi.org/10.1016/j.jcis.2020.10.101.

[55] P. Palladino, R. Ragone, Ionic strength effects on the critical micellar concentration of ionic and nonionic surfactants: the binding model, Langmuir 27 (2011) 14065–14070, https://doi.org/10.1021/la202897q.

[56] W. Buchberger, Microemulsion Electrokinetic Chromatography, in: P. Schmitt-Kopplin (Ed.), Springer New York, New York, NY, 2016: pp. 91-109. https://doi.org/10.1007/978-1-4939-6403-1_6.

[57] Bio-Loom, (n.d.). http://www.biobyte.com/(accessed December 5, 2024).

[58] T. Wen, X. Zhao, G. Luo, J. Wang, Y. Wang, B. Yao, J. Zhao, J. Zhu, Z. Yu, Comparison of microemulsion electrokinetic chromatography and solvent modified micellar electrokinetic chromatography on rapid separation of heroin, amphetamine and their basic impurities, Talanta 71 (2007) 854–860, https://doi.org/10.1016/j.talanta.2006.05.051.

[59] R. Ryan, S. Donegan, J. Power, K. Altria, Advances in the theory and application of MEEKC, Electrophoresis 31 (2010) 755–767, https://doi.org/10.1002/elps.200900568.

[60] R. Ryan, K. Altria, E. McEvoy, S. Donegan, J. Power, A review of developments in the methodology and application of microemulsion electrokinetic chromatography, Electrophoresis 34 (2013) 159–177, https://doi.org/10.1002/elps.201200375.

[61] B.Martín Sanz, Characterization of tetradecyltrimethylammonium bromide (TTAB) microemulsion by microemulsion electrokinetic chromatography. Bachelor's Thesis in Chemistry, University of Barcelona, 2018.

[62] (Editor-in-Chief)J.R. Rumble (Ed.), CRC Handbook of Chemistry and Physics, 105th ed., CRC Press, 2023.

[63] Calculated using Advanced Chemistry Development (ACD/Labs) Software, CAS SciFinder, American Chemical Society (ACS), 2024 (n.d.).

[64] G.S. Hartley, The effect of long-chain salts on indicators: the valence-type of indicators and the protein error, Trans. Faraday Soc. 30 (1934) 444, https://doi.org/10.1039/tf9343000444.

[65] G.S. Hartley, State of solution of colloidal electrolytes, Q. Rev. Chem. Soc. 2 (1948) 152, https://doi.org/10.1039/qr9480200152.

[66] G.S. Hartley, J.W. Roe, Ionic concentrations at interfaces, Trans. Faraday Soc. 35 (1940) 101, https://doi.org/10.1039/tf9403500101.

[67] E. Fuguet, C. Ràfols, M. Rosés, E. Bosch, Critical micelle concentration of surfactants in aqueous buffered and unbuffered systems, Anal. Chim. Acta 548 (2005) 95–100, https://doi.org/10.1016/j.aca.2005.05.069.

[68] S. Das, M. Bonn, E.H.G. Backus, The surface affinity of cations depends on both the cations and the nature of the surface, J. Chem. Phys. 150 (2019), https://doi.org/10.1063/1.5065075.

[69] C. Das, B. Das, Effect of tetraalkylammonium salts on the micellar behavior of lithium dodecyl sulfate: A conductometric and tensiometric study, J. Mol. Liq. 137 (2008) 152–158, https://doi.org/10.1016/j.molliq.2007.06.005.

[70] A. Roda, A.F. Hofmann, K.J. Myselsn, The Influence of Bile Salt Structure on Self-association in Aqueous Solutions (1983).