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Solute–solvent interactions in micellar liquid chromatography Characterization of hybrid micellar systems of sodium dodecyl sulfate–pentanol

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Abstract

The solvation parameter model has been applied to the characterization of hybrid micellar chromatographic systems with mixtures of sodium dodecyl sulfate (SDS) and pentanol as mobile phases. Retention factors for 22 compounds in two groups, phenethylamines and antihistamines, were used for the characterization of the systems after the calculation of their Abraham descriptors. Three equations were developed as multiple linear regressions using Abraham descriptors and properties, such as $\log P_{oct}$ and polar surface area to correlate the retention factors. A group of 30 data points was used as an independent test set to assess the predictive capability of the equations. Micellar chromatographic systems were compared against other separation systems using principal components analysis. Conventional RPLC chromatography using mobile phases with high amounts of organic solvents are close to the micellar mobile phases that only use small amounts of alcohol.

Keywords: Solvation parameter model; Micellar liquid chromatography; Sodium dodecyl sulfate; Pentanol

1. Introduction

Micellar liquid chromatography (MLC) is a chromatographic technique that uses surfactants as part of the mobile phase composition, at a concentration higher than the critical micellar concentration (cmc) [1]. Anionic sodium dodecyl sulfate (SDS) is the most widely used surfactant in MLC, but neutral Brij-35 or cationic CTAB, are also used. Pure micellar solutions are often not very useful as mobile phases, and it is usual to add a small amount of an organic modifier to the micellar solution to improve the chromatographic efficiencies and decrease the analysis time [2].

In MLC a wide range of solute with different polarities can be separated in the same run without the requirement of gradient elution. This is achieved due to the differential association of the solutes between the micelles in the mobile phase and to the stationary phase which is modified by the adsorption of monomers of surfactant. Non-polar solutes are only affected by hydrophobic interactions, but charged solutes experience also electrostatic attraction or repulsion [3].

An advantage of using hybrid micellar mobile phases against the organic solvents used in conventional RPLC is the low amount of organic modifiers used and hence the lower toxicity. Propanol, butanol and pentanol are less toxic than those conventionally used in RPLC, methanol and acetonitrile, and are highly retained in the micellar solution, which reduces the risk of evaporation. Several studies have been performed using MLC on different groups of compounds such as phenethylamines [4], antihistamines [5], barbiturates [6], benzodiazepines [7], and stimulants [8].

The solvation parameter model is based on a linear free energy relationship (LFER), and can be written as:

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

where SP is the dependent solute property (e.g. $\log P$, $\log k$, where k is the HPLC retention factor) and E, S, A, B and V are the Abraham solute descriptors. E is an excess molar refraction, S the solute dipolarity/polarizability, A and B are parameters charac-

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terizing the effective hydrogen-bond acidity and hydrogen-bond basicity, respectively, and V is McGowan's characteristic volume.

The values of the coefficients of the correlation (e, s, a, b and v) are related to the chemical nature of the chromatographic system, mobile and stationary phase. These coefficients reflect differences in the two phases between which the compound is transferred, that is the chromatographic stationary phase and the mobile phase that consists of the miceller surfactant and the aqueous buffer. Thus, e depends on the difference in capability of the mobile and stationary phase to interact with solute n- or π-electrons; s is a measure of the difference in dipolarity/polarizability between the two phases, a and b are measures of the difference in hydrogen-bond acidity and basicity, respectively, between the two bulk phases, and v is a measure of the relative ease of forming a cavity for the solute in the phases [9].

Several papers have been published on the use of the solvation parameter model in MLC. Retention data in various micellar systems have been studied in this way [10–12] and Mutelet et al. [13] have used retention data to determine Abraham descriptors for polyaromatic hydrocarbons.

The purpose of the present work is to calculate Abraham descriptors for a number of solutes [9,14], and to apply Eq. (1) to retention data in MLC in order to characterize the micellar system.

2. Experimental

2.1. Reagents and materials

Studied drugs were phenethylamines and antihistamines. The following compounds were kindly donated by the pharmaceutical laboratories indicated: amphetamine (Miquel, Barcelona, Spain), ephedrine, phenylephrine (Fardi, Barcelona), phenylpropanolamine (Boehringer Mannheim, Terrassa, Barcelona), and pseudoephedrine (Lasa, Sant Feliu de Llobregat, Barcelona), carbinoxamine, dexbrompheniramine, pheniramine, phenyltoloxamine, pyrilamine (Pfizer, Madrid, Spain), azatadine, chlorpheniramine (Schering-Plough, Madrid), cyclizine (Gayoso-Wellcome, Madrid), cyproheptadine (Reig Jofré, Barcelona), diphenhydramine (Aldo Unión, Barcelona), doxylamine (ICN Biochemicals, Barcelona), tripelennamine (Wassermann, Barcelona), and triprolidine (ICN Biochemicals, Aurora, OH, USA). Other phenethylamines, arterenol, mephentermine, methoxyphenamine and tyramine, were from Sigma (St. Louis, MO, USA).

Stock solutions containing 200 μg/ml of the drugs were prepared in distilled-deionized (Barnstead, Sybron, Boston, MA, USA) water, and conveniently diluted to 20 μg/ml for chromatographic analysis.

The micellar mobile phases consisted of the surfactant sodium dodecyl sulphate (99% purity, Merck, Darmstadt, Germany), and the modifier 1-pentanol (Scharlau, Barcelona), which were buffered with 0.01 M disodium hydrogenphosphate (Panreac, Barcelona) and 0.1 M HCl (Probus, Badalona, Spain) used to adjust the pH to 7. Mobile phases and drugs solutions were filtered through 0.45 μm nylon membranes (Micron Separations, Westboro, MA, USA).

Experimental MLC data used in this work have been determined previously for phenethylamines [4] and antihistamines [5], thus some additional information of experimental procedure can be found in the references cited below. Table 1 gives the retention factors, as $\log k$, for the 22 compounds studied in the various given mobile phases.

2.2. Apparatus and conditions

The chromatographic system was an Agilent Technologies Series 1100 (Palo Alto, CA, USA) equipped with a quaternary pump, an autosampler (20 μl injection volume), and UV–vis detector (190–700 nm range). An ODS-2 column of 5 μm particle size, 120 mm × 4.6 mm I.D. was used (Scharlau, Barcelona). Injection of the solutions into the chromatograph was made through a Rheodyne valve (Cotati, CA, USA). The flow-rate was 1.0 ml/min.

The dead time was determined as the mean value of the first significant deviation of the base-line in the chromatograms of the analytes. Chromatographic signals were acquired and processed with an Agilent ChemStation (Rev. A.10.01).

2.3. Calculation and procedure

Solver was used in the determination of Abraham descriptors for the studied compounds. It is a tool in Microsoft Excel which can be used to determine the maximum or minimum value of one cell by changing other cells. It is based on the generalised reduced gradient (GRG2) nonlinear optimisation code developed by Leon Lasdon, University of Texas at Austin, and Allan Waren, Cleveland State University. The statistical software used in the data treatment, including principal component analysis, was Minitab Version 14 [15].

3. Results and discussion

3.1. Calculation of Abraham descriptors for the studied drugs

Phenethylamines, such as amphetamine, ephedrine, phenylpropanolamine and pseudoephedrine, are characterized by a phenyl ring having an alkylamine chain [16]. On the other hand, antihistamines have a different basic structure. Most of them are substituted ethylamines consisting of three portions, a nucleus, an ethylamine group, and a linkage such as oxygen (the ethanolamine derivatives diphenhydramine, doxylamine, carbinoxamine and phenyltoloxamine), nitrogen (the ethylenediamine derivatives tripelennamine and pyrilamine, and the piperazine cyclizine), or carbon (the propylamine derivatives pheniramine, dexbrompheniramine, chlorpheniramine and dexchlorpheniramine) [17].

The determination of descriptors is based on Eq. (1). A property of a given compound such as the partition coefficient, P, is correlated by Eq. (1), where SP is now $\log P$. If we have values of $\log P$ for several water–solvent systems, we can set up