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Effect of methanol concentration on the speed-resolution properties in adiabatic supercritical fluid chromatography

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ABSTRACT

The influence of the modifier concentration in supercritical mixtures of carbon dioxide and methanol on the speed-resolution properties of columns packed with 1.7 μm core–shell particles was investigated from a theoretical viewpoint. Molar fractions of methanol up to 30% were considered. The column was assumed to be operated under strict adiabatic conditions in order to maximize its efficiency. Four inlet temperatures were tested, between 297 and 337 K. Four different pressure drops along the column were considered, between 25 and 200 bar. The physico-chemical properties (density, viscosity, and heat capacity) of the mixtures of carbon dioxide and methanol were derived from the NIST REFPROP program for temperatures between 287 and 337 K and pressures between 150 and 390 bar. The axial heterogeneity of the column was taken into account by segmenting it into 500 hundreds slices in each of which all physical and chromatographic properties were assumed to be uniform. The apparent kinetic Poppe plots were built from the apparent column efficiency calculated from the sum of the increments of the retention times and time variances from the column inlet to its outlet. The numerical results showed that the axial heterogeneity of the column due to axial variations of the temperature and the equilibrium constant decreases with increasing molar fraction of methanol in the eluent when the pressure drop is increased from 25 to 200 bar. The methanol content decreases the speed-resolution of the column more particularly when the analysis is done at low pressure drops. The results demonstrate also that under adiabatic conditions, for pressure drops larger than 100 bar, an increase of methanol concentration does not cause a dramatic loss of speed-resolution. For example, at 310 K and with a pressure drop of 25 bar, the longest column is expected to deliver 17,000 plates; increasing the molar fractions of methanol from 0 to 30% decreases this efficiency by about 15% and increases the analysis time by +140%. In contrast, under the same experimental conditions except for a pressure drop of 200 bar, the maximum efficiency (130,000 plates) would remain unchanged and the analysis time increase by only 40%.

1. Introduction

Supercritical fluid chromatography (SFC) appears to be advantageous for analysts seeking to achieve faster and more efficient analyses than those provided by LC-based methods [1,2]. The main advantage of carbon dioxide/methanol supercritical mobile phase mixtures is their low viscosity (≃0.05–0.15 cP), typically one order of magnitude lower than those of conventional water-rich liquids (≃ 0.5-1.5 cP). As a result, diffusion coefficients are larger in SFC than in LC. The optimum reduced velocities of columns packed with fine particles (d_p < 5 μm) are significantly lower in SFC than in LC and it becomes possible to analyze small molecules at the large linear velocities providing optimum column efficiency. SFC could also be effective to analyze macromolecules within reasonably short times while delivering high efficiencies but provided that these macromolecules would be solubles in the mobile phase.

The thermal expansions of the mobile phases used in SFC and in LC differ significantly. The isobaric thermal expansion coefficients of supercritical fluids (≃ 10^{-3} to 10^{-2} K^{-1}) are more than an order of magnitude larger than those of liquids (≃ $10^{-4}K^{-1}$ [3]). For instance, at 312 K, the isobaric expansion coefficient of a mixture of carbon dioxide and methanol (with a 5% molar fraction of methanol) is 7.26 × 10^{-3} K^{-1} (from the NIST REFPROP program). Therefore, as pressure decreases along the column, the expansion of supercritical fluids cools them significantly [4,5] due to an absorption of heat (gain of entropy) that overcompensates for the release of heat due to frictional forces of the eluent against the packed bed. Under adiabatic conditions (no heat absorbed through the column wall), which are required to minimize the efficiency loss due to the

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formation of radial temperature gradients [6–9] (the center of the column becoming cooler than the wall region [10–12]), a temperature drop occurs along the column and the solid/supercritical fluid adsorption process can no longer be consider as isothermal along the column. Classical chromatographic theories used to predict elution times and peak widths are no longer valid in non-uniform columns. Alternative approaches were proposed in order to predict hold-up times and plate heights in axially non-uniform systems in vHPLC [13,14,6,7], in SFC [15,16], and more generally [17]. In a recent study, apparent kinetic Poppe plots were built in SFC in order to determine the stationary phase providing the best speed-resolution performance under a constant inlet pressure drop of 200 bar and under adiabatic conditions [18]. The main difficulty of that exercise was to account for the heterogeneities of the pressure, temperature, density, viscosity, specific heat capacity, thermal expansion coefficient, equilibrium constant, linear velocity, and diffusion coefficient along the column. It was shown also that the rule of additivity does not apply to the space variance in non-uniform systems because the local migration velocity of analytes depends on their abscissa along the column [2]. This rule applies only to the time variance, allowing the derivation of the apparent (average) plate height and column efficiency [18]. However, that study was limited to pure carbon dioxide, which is rarely used in practical SFC methods. An organic modifier like methanol is often added to increase sample solubility and/or modulate the apparent retention factor for achieving reasonably short analysis times.

The goal of this work is to assess from a theoretical viewpoint the influence of the concentration of organic modifier added to supercritical CO_2 on the speed-resolution performance expected from columns packed with sub-2 μm core–shell particles. The molar fraction of methanol was between 0 and 30%. The variations of the density, viscosity, and specific heat of the mobile phases for temperatures between 287 and 337 K and pressures between 150 and 390 bar were obtained from the NIST REFPROP program. These ranges include the standard temperatures and pressures used in most SFC methods. The column is assumed to be radially uniform because adiabatic conditions lead to the highest possible efficiency and to be packed with 1.7 μm core–shell particles with a core-to-particle diameter ratio $\rho = 0.71$. Extra-column effects were not included in this work since the sole effect of the mobile phase composition on the column speed-resolution performance is analyzed in this work. Four inlet temperatures between 297 and 337 K and four pressure drops between 25 and 200 bar were considered. The retention factor dependence of the compound studied, naproxen (MW = 230 g/mol), on the density and temperature was reported elsewhere [19,20]. This factor was kept constant ($\langle k \rangle$=3) for all the mobile phase compositions, inlet temperatures, and pressure drops studied. The column outlet pressure was kept constant at 150 bar. The apparent kinetic Poppe plots were built for column lengths ranging between 3 cm and 3 m. The influence of the axial heterogeneity of the column on its speed-resolution properties for increasing molar fraction of methanol are analyzed and discussed for the different temperature and pressure drop conditions studied. The advantages and inconveniences of adding methanol to supercritical CO_2 are discussed regarding its influence on the maximum column efficiency expected from the longest column (long analyses controlled by longitudinal diffusion) and on the analysis time of the shortest column (fast analyses controlled by eddy dispersion and mass transfer resistance in the stationary phase).

2. Theory

A chromatographic model designed to predict the retention times and widths of peaks eluted from non-uniform columns was used in this work. It was recently reported in [18]. To summarize, this model assumes that the column is operated under adiabatic conditions (all the physico-chemical properties inside the column are uniform in the radial direction) and that the density (ρ), viscosity (η), heat capacity (c_p), and thermal expansion coefficient (α_p) of the supercritical mobile phase, the thermodynamic equilibrium constant (K_a) of the analyte between the stationary and the mobile phases, the analyte diffusion coefficient (D_m), the intra-particle diffusion coefficient (Ω), the reduced longitudinal diffusion coefficient (B), the reduced eddy diffusion HETP (A), and the reduced solid–liquid mass transfer coefficient (C_p) vary continuously along the column. The detailed equations and calculations of these system properties between the column inlet and its outlet are in [18]. The equations used in this work to calculate the physico-chemical properties of mixtures of methanol and supercritical carbon dioxide are given in the next sections.

2.1. Assumptions

2.1.1. Properties of pure CO_2

The density (ρ in g/cm^3), the viscosity (η in Poise), and the heat capacity (c_p in dyn cm g^{-1}.K^{-1}) of pure CO_2 were provided by the NIST REFPROP software. For the assumption of an adiabatic thermal environment to be valid, we kept all experimental conditions out of the region of the phase diagram of CO_2 close to its critical point. The best relationships providing these parameters and their optimized values are given in [18]. The same mathematical functions and parameter values were used in this work when the molar fraction of methanol was set to $x = 0$.

2.1.2. Properties of mixtures of $CO_2(1-x)$ and methanol (x)

The NIST REPPPROP data obtained for methanol molar fractions of x = 5, 10, 20, and 30% were adjusted to the following empirical relationships that allow (1) a convenient decoupling of the pressure and the temperature in the calculations of these properties and (2) an excellent fitting:

$$\rho(P,T) = \rho_0(P) + \rho_1(P)(T-287) + \rho_2(P)(T-287)^2 \quad (1)$$

where $\rho_0(P)$ and $\rho_1(P)$ are two polynomials of order two and $\rho_2(P)$ is a convex downwards Langmuirian function. All these polynomials are independent of the temperature. Their expressions and their best coefficients are listed in Table 1. So,

$$\alpha_p(P,T) = \frac{1}{\rho}\frac{\partial \rho}{\partial T} = \frac{\rho_1(P) + 2\rho_2(P)(T-287)}{\rho_0(P) + \rho_1(P)(T-287) + \rho_2(P)(T-287)^2} \quad (2)$$

The viscosity data of the eluent mixtures were fitted to

$$\eta(P,T) = \eta_0(P) + \eta_1(P)(T-287) + \eta_2(P)(T-287)^2 \quad (3)$$

where $\eta_0(P)$ and $\eta_1(P)$ are two polynomials of order two and $\eta_2(P)$ is a convex downwards Langmuirian function. All these polynomials are independent of the temperature. Their expressions and their best coefficients are listed in Table 2.

Finally, the heat capacity data were fitted to

$$c_p(P,T) = c_{p,0}(P) + c_{p,1}(P)(T-287) + c_{p,2}(P)(T-287)^2 \quad (4)$$

where $c_{p,0}(P)$ and $c_{p,1}(P)$ are two polynomials of order two and $c_{p,2}(P)$ is an hyperbolic function.

Tables 1 (density data), 2 (viscosity data), and 3 (heat capacity data) are listing all the parameters obtained for these different coefficients that depend only on the pressure P.