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UROP Final Paper
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Effect of the Cooling Coefficient on Efficiency Loss in SFC

Abstract

Supercritical fluid chromatography (SFC) is becoming a rapid alternative to high performance liquid chromatography (HPLC) because the lower viscosity and higher diffusivity of the mobile phase due to critical conditions enables faster separations and the ability to use smaller stationary phase particle sizes. However, radial temperature gradients that form from expansion of the mobile phase across the column reduce its efficiency. The net cooling coefficient of the mobile phase at the column outlet is a major factor controlling that temperature drop. The experimental correlation between the net cooling coefficient and efficiency loss was examined by performing two series of experiments: one where the oven temperature was held constant at 50.0 °C and the column outlet pressure was varied to yield nominal net cooling coefficients ranging from 0.10 to 0.25 K/bar and another where the column outlet pressure was held constant at 148 bar and the oven temperature was varied to yield the same range of nominal net cooling coefficients. Plate height curves of both sets of experiments were produced to examine column efficiency. It was found that the elution profiles that shared the same net cooling coefficient but had different experimental conditions had nearly identical column efficiencies, indicating that the net cooling coefficient strongly predicts column efficiency.

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1. Introduction

Chromatography is one of the most widely used separation techniques. Supercritical fluid chromatography (SFC) employs the use of mobile phase CO_2 at or near critical temperatures and pressures and is used as an alternative to high performance liquid chromatography (HPLC). The lower viscosity and higher diffusivity of the mobile phase compared to that of HPLC due to critical conditions enables faster separations and the ability to use smaller stationary phase particle sizes. It is most often used to separate low to moderate molecular weight compounds that are thermally labile, and its ability to separate chiral compounds leads to the practical use in pharmaceutics to purify drugs.

Radial and axial temperature gradients that form within the column during separations are responsible for efficiency loss in both HPLC and SFC. However, while the temperature gradients in HPLC form mainly from viscous heating of the mobile phase, enthalpic expansion and consequential cooling of the mobile phase due to the pressure drop from column inlet to outlet is the main factor in SFC. Indeed, the pressure drop is generally less than what is seen in HPLC, but the efficiency loss that results is substantial under some conditions.[1-2]

Operating under temperatures and pressures close to the critical point of the mobile phase where its compressibility is the highest leads to the most significant losses in column efficiency. Recently, Zauner et al. have shown that the efficiency here can be improved by optimizing the thermal conditions to minimize radial temperature gradients. Specifically, wrapping the column in foam insulation greatly improved efficiency, and there was no measureable loss in efficiency when the column was operated in still air by using a commercially available column heater.[3] In contrast, convective air conditions caused significant efficiency loss.

The net cooling coefficient of the mobile phase provides a physical basis for its temperature drop observed experimentally.[4] It quantifies the temperature drop of the mobile phase from column inlet to outlet due to its expansion, and to a lesser extent, viscous heating. The following experiment will attempt to establish an experimental correlation between the net cooling coefficient at the column outlet under convective air conditions and efficiency loss.

2. Experimental Work

2.1. Apparatus and chemicals

The experimental apparatus and conditions were the same as reported in reference [3], and are repeated in this section for completeness.

All chromatograms were obtained using a Hewlett-Packard SFC Model G1205A equipped with a Rheodyne 5092 injector with a 5-mL injection loop and a series 1050 HP diode array detector (DAD). The DAD wavelength was set at 208 nm with a bandwidth of 4 nm, and the reference wavelength was set at 450 nm with the same bandwidth. A Phenomenex 5-micron Luna-C18(2), 250 mm x 4.6 mm i.d. column was use for all separations. The exact particle size provided by the manufacturer was 4.82 microns. The operating system was HP-SFC Chemstation Revision A.02.02 running under Microsoft Windows 3.1.

The pressure and temperature at various points in the system were monitored to the nearest 0.1 bar and 0.1 K, respectively. The pressure transducers, Sensotec Model TJE or Model Super TJE, had an absolute pressure range up to 600 bar. The TJE units were calibrated against the Super TJE to the nearest 0.1 bar over the pressure region of interest. The inlet pressure was monitored at a tee placed upstream from the injector, and the outlet pressure was monitored at a tee downstream from the column outlet. Three Fisher Digital Thermometers with a small bead-type probe were used to monitor the oven temperature, the inlet temperature, and the column wall temperature at a position approximately 200 mm from the column inlet. The digital thermometers were calibrated to the nearest 0.1 K against an NIST-traceable digital thermometer (Fisher Scientific) accurate to ± 0.05 K.

All connections from the injector to the column outlet tee were made using 0.18-mm I.D. x 1/16” o.d. stainless steel tubing, and Valco zero-dead-volume fittings were used to make all connections in the flow stream between the injector and the outlet pressure tee. Connection from the outlet pressure tee to the UV detector was made using 0.18-mm i.d. x 1/32” o.d. EFI-Ni tubing from Valco Instruments, Inc. The length of tubing from the column outlet to the detector was approximately 90 cm.

A capillary heater (AgileSleeve model PTC050, from Analytical Sales and Products, Inc.) was used to preheat the mobile phase to the desired inlet temperature. A 200-mm length of 0.18-mm i.d. x 1/16” o.d. stainless steel tubing was inserted into the capillary preheater. The column inlet temperature was monitored using a temperature probe placed on the capillary supply tubing approximately 60 mm upstream from the column inlet, and covered with a short strip of insulating foam. The setting for the preheater was adjusted at each flow rate to yield the desired inlet temperature. After a period of equilibration of up to 15 minutes, temperatures measured at this point were constant to within ± 0.1 K.

The total length of the tubing from the injector to the column inlet was 76 cm, and from the column outlet to the outlet pressure tee it was 5 cm. The extra-column contributions to pressure drop at different flow rates and temperatures were determined by injecting the sample mixture with the column replaced by a zero-dead-volume union.

Alkylbenzenes (98.0% minimum purity) were purchased from Tokyo Chemical Industry Co. Methanol, acetonitrile, and methylene chloride were HPLC grade. Medical grade CO_2

(Praxair) was purified by slow room temperature distillation through a 1/8" stainless steel transfer tube into a second tank with a dip tube prior to its use as mobile phase. HPLC methanol (Fisher) was used as modifier.

For all separations an alkylbenzene test mixture consisting of 0.50 mg/mL each of n-decylbenzene, n-dodecylbenzene, n-tetradecylbenzene, n-hexadecylbenzene and n-octadecylbenzene in a ternary injection solvent was used. The ternary injection solvent was a mixture of acetonitrile, methylene chloride and methanol, equal parts by volume. The column was operated under the convective air thermal mode. In other words, the column was suspended in the oven in the usual fashion with the fan running and no special modifications. All chromatograms were obtained at flow rates from 1 to 5 mL/min in 0.5 mL/min interval increments. The temperature of the mobile phase was adjusted to match the oven temperature using the preheater. At each flow rate three separate injections were made using a 5-mL injection loop with full-loop loading.[3]

2.2. Experiments conducted for this study

Two series of experiments were conducted to examine the trend between the cooling coefficient of the mobile phase at the column outlet and efficiency loss. For the first series the oven temperature was held constant at 50 °C, and the outlet pressure was varied to yield nominal cooling coefficients at the column outlet ranging from 0.10 K/bar to 0.25 K/bar. For the second series the column outlet pressure was held constant at 148 bar, and the oven temperature was varied to yield the same range of nominal cooling coefficients. These two series of experiments shared the same experimental condition of 50 °C and 148 bar, where the cooling coefficient is equal to 0.150 K/bar.

3. Results and Discussion

3.1. Enthalpic expansion and heating coefficients

The following discussion on heating coefficients is largely taken from reference [3].

While viscous heating of the mobile phase influences its temperature change to a lesser extent, both this and its enthalpic expansion need to be considered to quantify the temperature change from column inlet to outlet. The rate of heat generation h_g of the mobile phase in watts for an infinitesimal volume element ∂V is given by: (1)

$$hg = -u_z(\partial P/\partial z)$$

The rate of heat consumption h_c due to expansion of the mobile phase is:

$$h_c = u_z\alpha T(\partial P/\partial z) \tag{2}$$

where u_z is the superficial velocity, $\alpha = -(1/\rho)(\partial\rho/\partial T)$ is the thermal expansion coefficient, T is temperature, and $\partial P/\partial z$ is the local pressure gradient. Assuming the column is adiabatic and operated under steady-state conditions, all of this heat goes towards changing the temperature of the mobile phase. The rate of heat generation or consumption in watts per unit volume and in terms of the heat capacity and temperature change is then:

$$h = mC_p(\partial T/\partial V) \tag{3}$$

where m is the mass flow rate and C_p is the heat capacity of the mobile phase. Using the relation $m/A = u_z\rho$, where A is the cross sectional area of the column, and combining Eqs. (1)-(3) gives the net incremental temperature change of the mobile phase in a column operated under adiabatic conditions:

$$\partial T = -(1/(\rho C_p) - (\alpha T)/(\rho C_p))\partial P \tag{4}$$

The net cooling coefficient of neat CO_2 mobile phase is then $(1 - \alpha T)/\rho C_p$ and is in units of K/bar.[4] While operating under convective air conditions is not adiabatic and the mobile phase used consisted of 5% methanol modifier, this relationship demonstrates how the net cooling coefficient is related to the temperature drop. The net cooling coefficients were evaluated for the conditions here and the contours plotted on a pressure-temperature plane

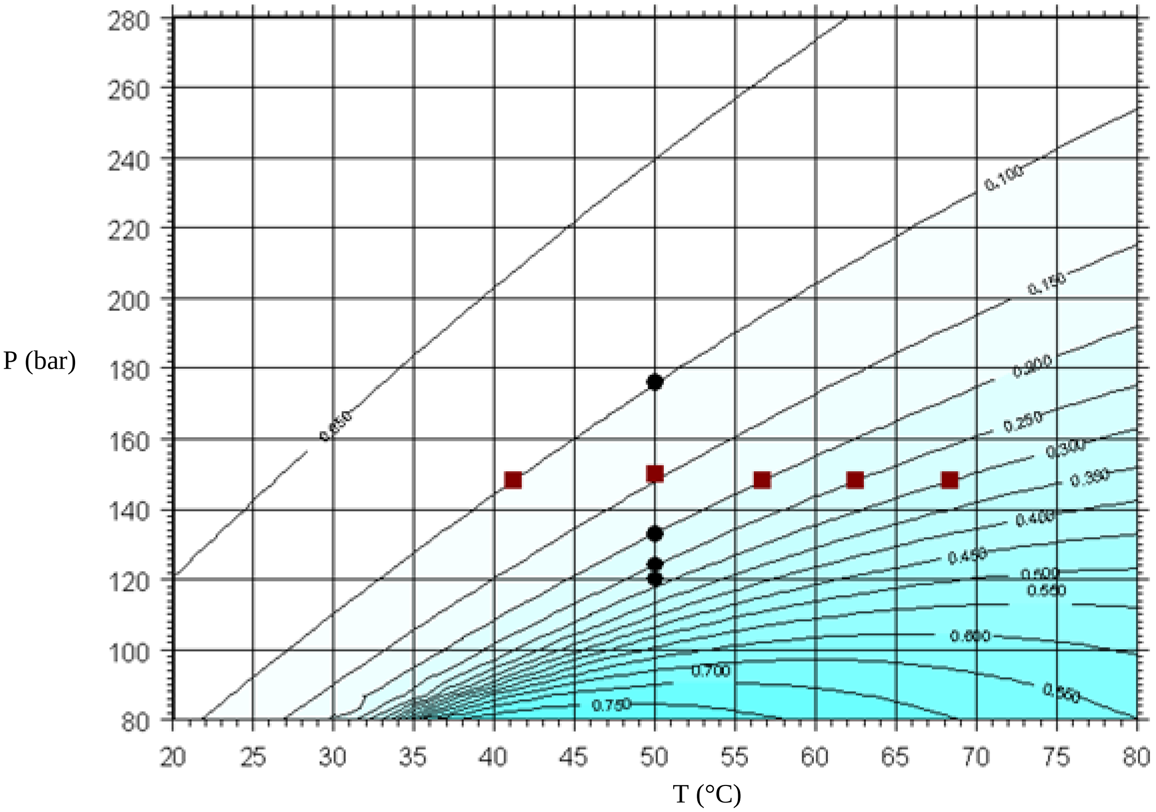

Figure 1 Diagram of the cooling coefficient contours plotted on the P-T plane for the 5% methanol/95% carbon dioxide mobile phase. The marks on the diagram represent the experimental conditions where data were collected. The red marks represent the experimental series where pressure was held constant, and the black marks represent the experimental series where temperature was held constant.

A positive net cooling coefficient across the entire range of temperatures and pressures corresponds to an endothermic process and indicates that the cooling effect from expansion dominates the viscous heating.

Plate height curves for the net cooling coefficients examined in the two series of experiments were determined and used to evaluate column efficiency. The peak profile observed at the column outlet provides a measure of the apparent plate height $\hat{H}$, and the apparent reduced plate height $\hat{h}$ is defined as $\hat{h} = \hat{H}/d_p$ where d_p is the mean particle size (4.82 microns). The apparent reduced plate heights were estimated from the width of the peak at half height w_h using the following equation:

$$\hat{h} = (L/d_p) \times (w_h^2/5.54t_r^2) \tag{5}$$

where L is the length of the column and t_r is the retention time. This relationship assumes a Gaussian band profile, which is not always the case. For such peaks Eq. (5) probably underestimates the apparent plate height, but for the purposes here of examining the trend between the cooling coefficient and efficiency loss, this relationship suffices.[3]

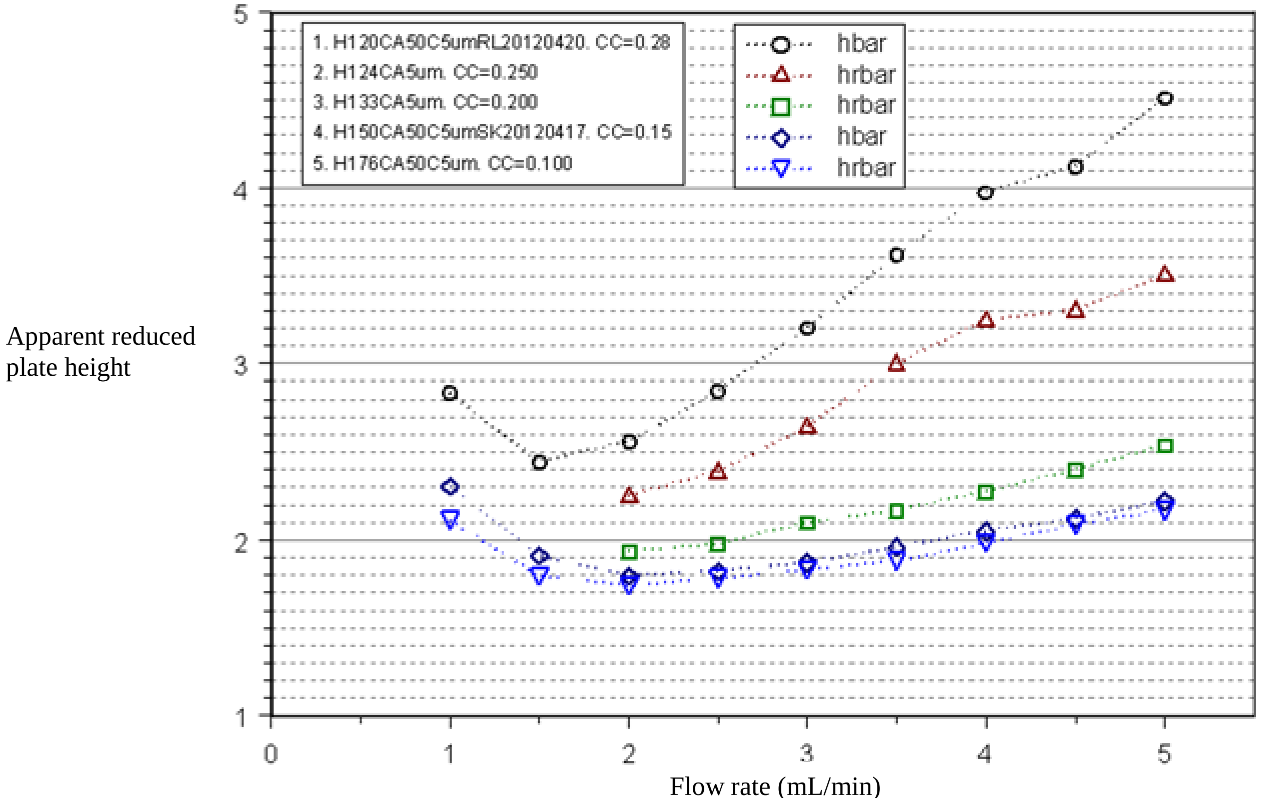

Figure 2 Plate height curve of the series represented by black circles in Fig. 1. The oven temperature was held constant at 50.0 °C while the outlet pressure was varied to yield net cooling coefficients of 0.10, 0.15, 0.20 0.25, and 0.28 K/bar.

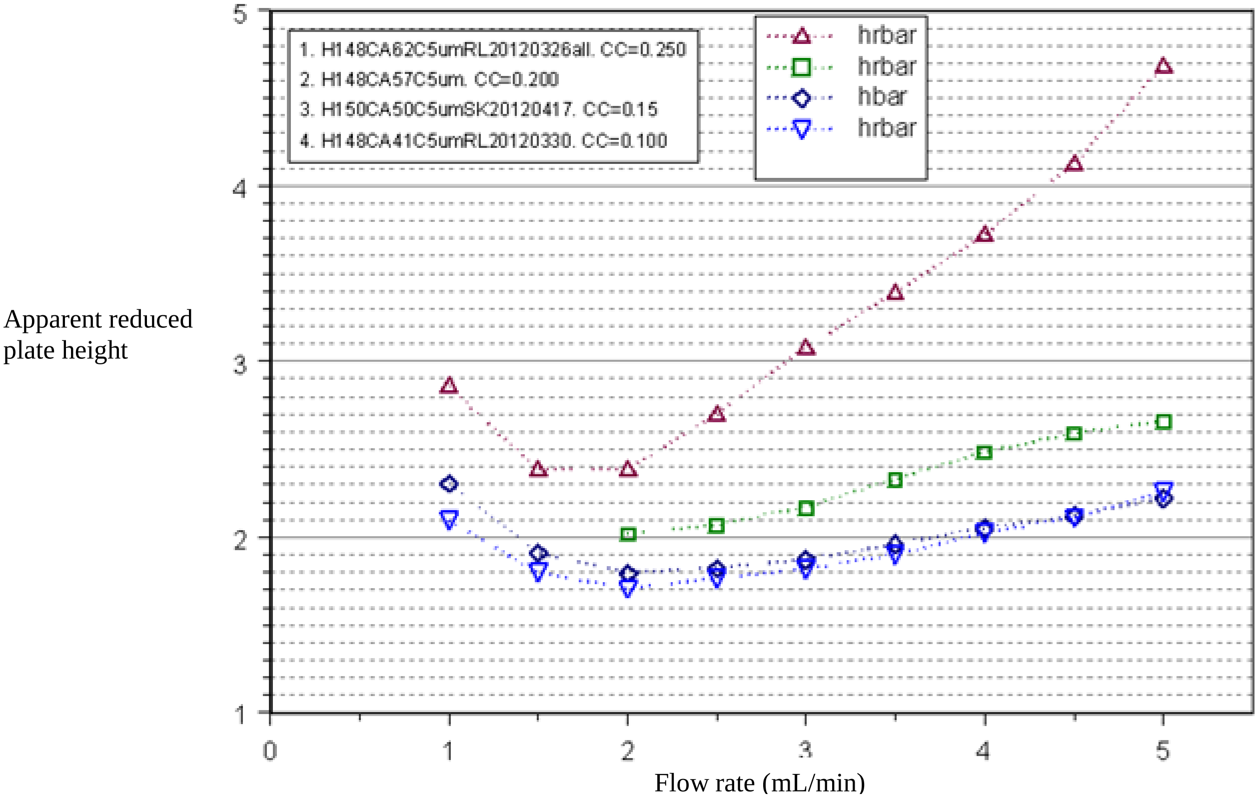

Figure 3 Plate height curve of the series represented by red squares in Fig. 1. The outlet pressure was held constant at 148 bar while the oven temperature was varied to yield net cooling coefficients of 0.10, 0.15, 0.20, and 0.25 K/bar.

The apparent reduced plate height is directly proportional to the net cooling coefficient, which means that column efficiency is indirectly proportional to the net cooling coefficient. Furthermore, elution profiles sharing the same net cooling coefficients but different experimental conditions had similar column efficiencies. For example, setting the outlet pressure to 176 bar when the oven temperature was held constant at 50.0 °C gave a net cooling coefficient of 0.10 K/bar. This net cooling coefficient was also achieved when the outlet pressure was 148 bar and the oven temperature was set to 41 °C. Fig. 2 and Fig. 3 show that these elution profiles had an almost identical apparent reduced plate height of approximately 2.7 at their optimum flow rate of 2.0 mL/min. The two sets of experimental conditions that produced net cooling coefficients of

0.15 and 0.25 K/bar also had nearly identical column efficiencies at the optimum flow rate. The experimental conditions that yielded the net cooling coefficient of 0.20 K/bar were the same in the two series of experiments, so the agreement in column efficiency seen here was expected.

4. Conclusion

Efficiency loss associated with pressure drop in SFC is mainly due to enthalpic expansion and consequential cooling of the mobile phase as the pressure drops across the column, which creates radial temperature gradients within the column. The net cooling coefficient of the mobile phase at the column outlet is a major factor affecting that temperature drop. There appears to be an experimental correlation between the net cooling coefficient of the mobile phase at the column outlet and efficiency loss in SFC. Under pressure and temperature conditions that differed but yielded the same net cooling coefficient, the apparent reduced plate heights were nearly identical. The strong correlation between the net cooling coefficient and efficiency loss supports the idea that radial temperature gradients that form from the mobile phase cooling are largely responsible for the loss in efficiency in SFC. Furthermore, the net cooling coefficient was directly related to efficiency loss. Wrapping the column in foam insulation or operating under still air conditions to reduce the formation of radial temperature gradients would improve the efficiency, and Zauner et. al have recently shown this.[3]

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