Journal of Chromatography A, 1217 (2010) 5137–5151

Contents lists available at ScienceDirect

Journal of Chromatography A

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

Review

A protocol for the measurement of all the parameters of the mass transfer kinetics in columns used in liquid chromatography

Fabrice Gritti[a,b], Georges Guiochon[a,b,*]

[a] Department of Chemistry, University of Tennessee, Knoxville, TN 37996-1600, USA
[b] Division of Chemical and Analytical Sciences, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6120, USA

ARTICLE INFO

Article history:
Received 30 March 2010
Received in revised form 21 May 2010
Accepted 4 June 2010
Available online 15 June 2010

Keywords:
Mass transfer
Liquid chromatography
Longitudinal diffusion
Eddy diffusion
External film mass transfer coefficient
Trans-particle mass transfer coefficient
Frictional heating
Totally porous particles
Core-shell particles

ABSTRACT

Band broadening in chromatography results from the combination of the dispersive effects that are associated with the different steps involved in the migration of compound bands along the column. These steps include longitudinal diffusion, trans-particle mass transfer, external film mass transfer, overall eddy diffusion, including trans-column, short-range inter-channel, trans-channel eddy diffusion, and the possible, additional mass transfer contributions arising from heat friction and the thermal heterogeneity of the column. We describe a series of experiments that provide the data needed to determine the coefficients of the contributions to band broadening of each one of these individual mass transfer steps. This specifically designed protocol can provide key information regarding the kinetic performance of columns used in liquid chromatography and explain why different columns behave so differently. The limitations, accuracy and precision of these methods are discussed. Further avenues of research that could improve the characterization of the mass transfer mechanisms in chromatographic columns, possibly contributing to the development of better columns, are suggested.

Contents

* Corresponding author at: Department of Chemistry, University of Tennessee, Knoxville, TN 37996-1600, USA. Tel.: +1 865 974 0733; fax: +1 865 974 2667.
E-mail address: guiochon@ion.chem.utk.edu (G. Guiochon).

0021-9673/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2010.06.016

1. Introduction

Scientists involved in chromatographic techniques, whether in its practical aspects or in fundamental studies are routinely using the van Deemter plate equations [1] for the assessment of the kinetic performance of their systems. This empirical equation formulated more than 50 years ago describes well the essence of band broadening in chromatographic columns. In all forms of chromatography (gas, liquid, and supercritical fluid chromatography, column and plate chromatography) the broadening of a compound band during its migration along a column is controlled by three main groups of contributions: (1) the longitudinal or axial diffusion (B coefficient in the van Deemter equation) accounts for the natural diffusion of sample molecules against their concentration gradient in the eluent; (2) eddy diffusion (A coefficient in the van Deemter equation) accounts for all contributions to the heterogeneity of the eluent stream in the packed bed; and (3) the overall solid–liquid mass transfer resistance (C coefficient in the van Deemter equation) accounts for the finite rates of the different steps of transfer of molecules between the bulk eluent and the stationary phase. Similar HETP equations have been proposed later, among which the empirical Knox equation is best known [2]. It differs from the van Deemter equation by the form of dependence of the eddy diffusion term on the linear velocity. These equations fits satisfactorily most of the experimental HETP data around the minimum of the curve because they contain the essence of dynamics in any chromatographic system [3]. At high eluent velocities, however, significant deviations are observed [4].

For the packed columns used in liquid chromatography, the coefficient A, B, and C of the HETP equations have hardly any physical justification, but rather hide a more subtle reality. The B term results from the sample diffusivity in the complex heterogeneous medium composed of the interstitial bulk eluent, the internal bulk eluent, and the adsorbed phase [5], with a different sample diffusivity in each of these volumes. Therefore, the B coefficient is related to an apparent, complex axial diffusion coefficient. A similar complexity applies for the eddy diffusion coefficient A. As shown by Giddings, flow velocity biases take place at different characteristic lengths inside the column and may be sorted out into trans-channel (between close particles or inside throughpores), short-range inter-channel (with a characteristic length of a few particle diameters), long-range inter-channel (with a characteristic length of ca. a hundred particle diameters) and trans-column (with a characteristic length equal to the column radius) [6]. Secondly, any molecule can be transferred from one eluent streamlet to another one by two simultaneous exchange mechanisms, diffusion and flow processes. Giddings proposed the coupling theory of eddy diffusion to account for these different contributions to eddy diffusion in packed columns [6]. The C term includes the contributions of the mass transfer resistances due to diffusion through the stationary film of eluent surrounding the particles and through the porous particles themselves. Finally, with the advent of very high pressure liquid chromatography (VHPLC), an additional HETP term caused by the generation of frictional heating inside the column should also be taken into consideration [7].

Overall, the oversimplified and superficial description of mass transfer mechanisms in LC columns that prevailed during the early developments of HPLC has now been replaced by a more sophisticated and realistic picture. The ultimate challenge in HPLC and VHPLC remains to determine experimentally and unambiguously the individual contributions of each mass transfer step taking place in chromatographic columns. Fitting to the van Deemter or Knox equation the sets of HETP and velocities data recorded cannot provide this information. Most interpretations of the mass transfer mechanisms in LC are based on arbitrary assumptions, which must be made because, otherwise, no conclusion could be reached. We recently developed and used new experimental protocols that target the most important kinetic steps in liquid chromatography, considerably limit the number of these assumptions, and are easily accessible to all practitioners.

This report reviews the standard operation procedures of these measurements, discusses their possibilities, aims, and limitations to determine the coefficients of the individual mass transfer terms in both HPLC and VHPLC. These procedures include the peak parking method (PP) [8,9], the local outlet cross-section detection method [10,11], the total pore blocking method (TPBM) [12], and surface temperature measurements [13,14]. Combined with conventional, accurate and precise measurements of HETP data, corrected for extra-column contributions to band broadening, and with models of effective axial diffusion along heterogeneous chromatographic beds [15,16], these methods have already revealed many previously unsuspected features of the dynamics of chromatography in packed columns [16–18]. These new insights are discussed and challenges to further improvement of our understanding of mass transfers in LC columns are suggested.

2. General Hetp equation

The plate height equation is generally written as

$$h = \frac{B}{\nu} + A(\nu) + C_p\nu + C_f(\nu)\nu + h_{Heat} \quad (1)$$

where B is twice the apparent longitudinal diffusion coefficient along the column, ν is the reduced interstitial linear velocity, $A(\nu)$ is the overall eddy diffusion term (including trans-channel eddy diffusion, short-range inter-channel eddy diffusion, and trans-column eddy diffusion), C_p is the trans-particle mass transfer resistance coefficient, $C_f(\nu)$ is the external film mass transfer resistance coefficient, and h_{Heat} is the additional reduced HETP term associated with the thermal heterogeneity of the column generated by frictional heating.

In a previous publication, we showed that the general plate height equation for columns packed with totally or superficially porous particles is written as follows when a parallel diffusion mechanism is assumed along the heterogeneous packed bed, in order to determine the B term [19] and to more clearly elucidate the relationships between the different components of the mass transfer resistance assumed in Eq. (1) and the relevant physico-chemical parameters characterizing the column bed and the separation involved:

$$h = \frac{2[\gamma_e + ((1-\varepsilon_e)/\varepsilon_e)(1-\rho^3)\Omega]}{\nu} \quad \text{Longitudinal molecular diffusion} \quad (2)$$

$$+ \frac{0.01\nu}{1+\omega_1\nu} \quad \text{Trans-channel eddy diffusion} \quad (3)$$

$$+ \frac{\omega_2\nu}{1+(\omega_2/2\lambda_2)\nu} \quad \text{Short-range inter-channel eddy diffusion} \quad (4)$$