Journal of Chromatography A, 1218 (2011) 6135–6143

Contents lists available at ScienceDirect

Journal of Chromatography A

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

Controlled-cycle pulsed liquid–liquid chromatography. A modified version of Craig's counter-current distribution

Artak E. Kostanyan*, Andrei A. Voshkin, Nikolai V. Kodin

Kurnakov Institute of General & Inorganic Chemistry, Russian Academy of Sciences, Leninsky Prospekt 31, Moscow 119991, Russia

ARTICLE INFO

Article history:
Available online 4 January 2011

Keywords:
Counter-current chromatography
Craig distribution
Liquid chromatography
Pulsed extraction columns
Controlled-cycle operation
Modelling

ABSTRACT

A new liquid–liquid chromatography technique developed from a combination of controlled-cycle operation and a pulsed-mixing technique is suggested and validated. The controlled-cycle pulsed liquid–liquid chromatography (CPLC) system operates without involving a centrifuge and consists, of a series of multistage units, and a method for imparting pulsation motion to the liquids inside the units (the pulsation cycle). This chromatography technique can be considered as an improved continuous form of Craig's counter-current distribution method, or, alternatively, as a form of droplet chromatography with the cycling mode of operation. The theoretical model has been designed to account for the effects of the basic parameters influencing the CPLC operation. The theoretical model's suitability was proved by direct comparison between the experimental and model responses. The CPLC devices containing 1, 2, 4 and 5 multistage columns (each column was divided into 26 stages) have been designed, fabricated and tested; experiments were conducted to test the chromatographic behavior of organic (monocarboxylic) and mineral acids. The mass transfer rate in the stages depends on the nature of both—phase and sample systems: the highest values were achieved in experiments with acetic acid by using the octane/water biphasic system, where an equilibrium concentration distribution between stationary and mobile phases in the stages was attained. The results obtained demonstrated the potential of the new technique for preparative and industrial scale separations.

1. Introduction

The development of support-free liquid–liquid chromatography methods called counter-current chromatography (CCC), having started many decades ago [1–5], has led to a number of new chromatography techniques for the separation and purification of natural products and synthetic substances on analytical, preparative and pilot scales [6–18]. Originating from Craig's counter-current distribution method [19], most of these techniques use a centrifugal force field to retain the stationary liquid phase inside the column. Several CCC methods were developed, that did not use any centrifuge: droplet CCC, rotation locular CCC and gyration locular CCC [3,4].

The CCC columns can be considered as extraction columns with an extremely high length to the diameter ratio, operating under non-steady state conditions [20]. The fundamental principle of separation is the same in both the chromatographic and the extraction columns. It is based on differential partitioning of individual components between two immiscible solvent phases. The distribution of components between the phases and along the extraction and chromatographic columns is governed by two phenomena: interphase mass transfer and longitudinal dispersion of components caused by axial mixing in the phases.

In the development of highly efficient techniques for preparative and industrial separations it is vital to combine both the high separation efficiency and the low fabrication cost of the apparatus. To meet these requirements of industrial practice in the field of CCC techniques we have suggested and evaluated two approaches: the application of the technique of controlled-cycle operation to counter-current chromatography [21–24] and the application of a periodic pulsation to supply the additional energy necessary to intensify the interphase mass-transfer [25–27]. Both approaches have long been known and used to increase the separation efficiency of distillation and extraction columns [28–38].

In previous work [27], a support-free liquid chromatography technique based on the application of a periodic pulsation to force the mobile phase through the stationary phase in a coiled column was described. Since the peak resolution was poor, a system of pulsed mixing and controlled cycle is proposed to improve the separation efficiency. In this paper, we present such a controlled-cycle pulsed liquid chromatography system. For a better evaluation and

* Corresponding author. Fax: +7 495 9554834.
E-mail address: kost@igic.ras.ru (A.E. Kostanyan).

0021-9673/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2010.12.103

understanding of the basics of the new method a brief review of the theory follows.

1.1. Theory of support-free liquid–liquid chromatography

One of the specific features of support-free liquid chromatography is that the mathematical description of the separation process is less complex compared to the other forms of chromatography due to the lack of geometrical complexities of the packing materials. The complications of flow, diffusion, and mass transfer processes in the packing caused by adsorptive and capillary forces are not present in support-free liquid chromatography. The migration rates and the spreading of individual chromatographic peaks depend only on the partition coefficient, the rate of interphase mass transfer and the degree of axial mixing in the two liquid phases. The combined effect of the longitudinal mixing in the phases and the mass transfer between them on the partitioning behavior of a solute can be described on the basis of continuous (diffusion) or discrete (cell) models [20,39–43]. For low degrees of axial mixing (which is the case in chromatography) the calculations by both—continuous and cell models, lead to identical results.

1.2. Consider two operation modes

1.2.1. Continuous mode of operation

The cell model for continuous operation of a chromatographic column represents a chain of perfectly mixed, equally-sized cells. The thorough analysis of the model equations for linear chromatography was carried out in [41]: the model equations were solved in the Laplace domain and peaks were calculated by numerical inversion of the transfer function. The analytical solution of the model equations, obtained in [43], may be presented in the following dimensionless form:

$$X = \left[\lambda\frac{(\gamma - r_1)}{(r_2 - r_1)}\right]^n \exp(-nr_1 t)\sum_{j=0}^{n-1}\frac{t^j}{j!}n^{j+2}B_j \tag{1}$$

with

$$\lambda = \frac{1}{1-S_f};\quad \nu = \frac{T_c}{1-S_f};\quad \gamma = \frac{T_c}{K_D S_f};\quad r_1 = 0.5(\omega - \sqrt{\omega^2 - 4\lambda\gamma});$$

$$r_2 = 0.5(\omega + \sqrt{\omega^2 - 4\lambda\gamma});\quad \omega = \lambda + \nu + \gamma;$$

$$B_j = \sum_{k=0}^{n-1-j}\frac{(-1)^{n-1-j-k}(2n-2-j-k)!}{k!(n-k)!(n-1-j-k)!(\gamma - r_1)^k(r_2 - r_1)^{n-1-j-k}}$$

where $k' = K_D S_f/(1-S_f)$ is the retention factor (the ratio of amounts of solute in the stationary and mobile phases under equilibrium conditions), K_D is the partition coefficient, S_f is the fractional volume of the stationary phase; n is the number of perfectly mixed cells (a measure of the degree of the axial mixing in the column); $T_c = a_c k_x V_c/(Fn)$ is the number of mass transfer units in a cell (a measure of the interphase mass transfer rate), a_c is the interphase contact area per unit volume of the contacting liquids, F is the volumetric flow rate of the mobile phase, k_x is the overall mass transfer coefficient, V_c is the column volume; $t = \tau F/V_c$ and $X = x/\bar{x}$ are the dimensionless time and concentration, respectively, τ is time, $\bar{x} = Q/V_c$ is the mean concentration in the column, Q is the amount of the compound in the sample.

If the partition equilibrium in each cell is reached, the model reduces to the equilibrium cell model, which is usually considered as the model of theoretical plates:

$$X = \frac{n^n}{(n-1)!}\left(\frac{\tau}{\bar{\tau}}\right)^n\frac{V_c}{\tau F}\exp(-n\tau/\bar{\tau}) \tag{2}$$

where $\bar{\tau} = (1 - S_f + S_f K_D)V_c/F$ is the mean residence (retention) time of a solute in the column.

The following relationship between the non-equilibrium and equilibrium models can be established:

$$n_e = \frac{nT_c(1+k')^2}{T_c(1+k')^2 + 2k'^2} \tag{3}$$

where n_e is the effective number of theoretical plates (a measure of column efficiency in terms of the equilibrium model).

Replacing n in Eq. (2) with n_e provides:

$$X = \frac{n_e^{n_e}}{(n_e-1)!}\left(\frac{\tau}{\bar{\tau}}\right)^{n_e}\frac{V_c}{\tau F}\exp(-n_e\tau/\bar{\tau}) \tag{4}$$

For $n_e \geq 30$ chromatographic peaks calculated using Eqs. (1) and (4) become identical.

1.2.2. Cycling mode of operation

The concept of cycling mode we have first used [44,45] in the comparative analysis of CCC and Craig's counter-current distribution (CCD) processes. Sutherland and Folter have proposed the application of CCD as eluting counter-current distribution model for mathematical description of CCC [46–48]. While this approach from our point of view is not the best way to describe the CCC processes, it should be noted that the idea of the controlled-cycle chromatography emerged through the analysis of the works of the afore-mentioned authors. Actually, the eluting CCD model describes the cycling mode of operation of a cascade of equilibrium stages, which is the way the Craig's apparatus would operate, if the CCD process could be extended beyond the number of transfers equal to the chain of CCD stages. In these circumstances, the concentrations in the portions of the mobile phase leaving the Craig's apparatus would be [44]:

$$X = \frac{n_{es}}{(1-S_f)}\frac{(n_{es}+i-1)!\lambda^{n_{es}}\gamma^i}{(n_{es}-1)!i!}\quad i = 0,\ 1,\ 2,\ 3,\quad \ldots$$

with

$$\lambda = \frac{1}{(1+k')},\quad \gamma = \frac{k'}{(1+k')} \tag{5}$$

where n_{es} is the number of equilibrium stages in the Craig's apparatus; i is the number of the portions of the mobile phase leaving the apparatus (the number of transfers): $i = 0$ corresponds to the solvent front elution.

The application of the controlled-cycle method to the processes of column chromatography in general [22], and to the centrifugal partition chromatography [21], in particular, was recently suggested and discussed. Considering a cascade of equilibrium stages, it was shown that the controlled-cycle technique can provide greater efficiencies (measured with the number of theoretical plates) than conventional operation of a chromatographic column. The following relationship between the efficiencies of continuous and controlled-cycle chromatography processes can be established:

$$n_{cyc} = n\frac{1+k'}{k'} \tag{6}$$

where n and n_{cyc} are the numbers of theoretical plates reached in the continuous and cycling modes of a chromatographic column operation, respectively.

2. Description of the general principle and operation of the controlled-cycle pulsed liquid–liquid chromatography (CPLC)

The fundamental principle of the CPLC is the combination of two techniques: