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Suitable interface for coupling liquid chromatography to inductively coupled plasma-mass spectrometry for the analysis of organic matrices. 1 Theoretical and experimental considerations on solute dispersion

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ABSTRACT

Liquid chromatography (LC) hyphenated to a specific detection such as inductively coupled plasma-mass spectrometry (ICP-MS) is a technique of choice for elemental speciation analysis. However, various instrumental limitations may considerably reduce the expected sensitivity of the technique. Among those, we were interested by the solute dispersion into the interface located between LC and ICP-MS. The interface consists of a Sample Introduction System (SIS) and a possible flow-splitter prior to SIS. Flow splitting can be required in case of organic matrices to reduce the organic solvent amount entering plasma which may lead to plasma instabilities.

Although extra-column dispersion is usually well taken into account with conventional UV detection it has been little studied in the context of LC-ICP-MS and moreover never quantified. Our objective is to assess the loss in column plates and hence in both separation quality and sensitivity which may be generated by the coupling of LC and ICP-MS in the specific case of organic matrices. In this first study, this is done (1) from a theoretical approach; (2) from 55 experimental studies reported in LC-ICP-MS and (3) from our experimental results highlighting the critical impact of the flow splitter on extra-column dispersion depending on both flow-rate and split ratio. It turns out by evaluating the 55 reported studies by means of theoretical calculations, that the loss in plates due to extra-column dispersion was most of the time beyond 50% and even often beyond 90%. Moreover, from our experiments, it has been shown that a very low split ratio (1:50) could generate an additional variance around 200 μL^2 which induces a loss in theoretical plate of 90% for ultra-high performance LC (UHPLC) column (5 cm × 2.1 mm, 1.7 μm).

1. Introduction

The need for determining elemental species concentrations rather than total element concentrations has grown within the past decades. According to Templeton et al. [1,2] speciation analysis consists in identifying and quantifying different chemical species of a particular element in a given sample. It has become an important field of research over the past few years in several areas including biochemistry, environmental chemistry, ecotoxicology, pharmaceuticals, petrochemicals, and nutrition science [3].

Nowadays hyphenated techniques such as Liquid Chromatography (LC) hyphenated with Inductively Coupled Plasma Mass Spectrometry (LC-ICP-MS) are widely used both to obtain elemental information and to discriminate species in a given matrix. LC techniques, including ion exchange chromatography (IEC) [4], reversed-phase liquid chromatography (RPLC) [5], ion-pairing chromatography (IPC) [6], size exclusion chromatography (SEC) [7,8] and hydrophilic interaction liquid chromatography (HILIC) [9,10], have been used for speciation analysis [11]. Different hyphenated techniques can be combined together to achieve more exhaustive characterization of complex matrices. For example, LC-ESI-MS can be associated to LC-ICP-MS to obtain both structural information and elemental information [5,12–14].

Most speciation analyses are performed in aqueous matrices by using ion-exchange chromatography and deal with environmental

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samples [15]. In this specific case, the mobile phase is not critical for the coupling of both techniques since the amount of organic solvent in the mobile phase is limited (small percentage of organic modifier sometimes added, usually without disturbing plasma stability). However, when using RPLC [16–28] or HILIC [9,10,29–34], a large amount of organic solvent is introduced into the plasma. The problems involved by this introduction was thoroughly discussed by Leclercq et al. [35,36] in a recent review.

Some key issues have to be considered for coupling LC to ICP-MS in case of organic matrices [3]: (i) metal contamination from the chromatographic system and/or the stationary phase and/or the mobile phase [3], (ii) plasma instabilities due to the solvent load, especially in case of organic mobile phases [3], (iii) signal fluctuations in gradient elution depending on plasma parameters [37] and (iv) solute dispersion into the interface located between LC and ICP-MS. The interface is made of a sample introduction system (SIS) and a possible flow splitter prior to SIS which may be required, in case of organic matrices, to reduce the amount of solvent entering plasma and hence to decrease plasma instabilities [3]. The solute dispersion in the interface unit is a critical issue because that can result in additional solute band broadening and hence in significant loss in both sensitivity and separation quality. Although extra-column dispersion is usually well taken into account with conventional UV detection, it has been little studied in the context of LC-ICP-MS. In the present study, we made therefore an attempt to assess the extent to which the interface contributes to solute band broadening. This was done by (i) estimating from published studies the likely loss in plates due to solute dispersion in the interface and (ii) showing the critical impact of the flow splitter on extra-column dispersion depending on both flow-rate and split ratio. To support the first approach, a synoptic table has been built (Table 2) which summarizes 55 studies carried out on organic matrices in LC-ICP-MS and gives, for each study, an estimation of the interface contribution to solute band broadening. A further second part of our study will be dedicated to the comparison of a large number of commercially available SIS regarding the extra-column dispersion.

2. Theoretical considerations

Solute dispersion can be assessed by the peak variance. The total solute dispersion (total variance, σ^2_{total}) comes from both dispersion inside the column (column variance, σ^2_{col}) and extra-column dispersion (extra-column variance, σ^2_{ext}).

Extra-column dispersion results from the injection process ($\sigma^2_{injection}$), the different tubing (σ^2_{tubing}) and the detection ($\sigma^2_{detector}$) [38].

Because variances can be added if the corresponding dispersion process are independent of each other, the total peak variance can be written as

$$\sigma^2_{total} = \sigma^2_{col} + \sigma^2_{ext} \quad (1)$$

Similarly, the extra-column variance is the sum of individual contributions according to

$$\sigma^2_{ext} = \sigma^2_{injection} + \sigma^2_{tubing} + \sigma^2_{detector} \quad (2)$$

For Gaussian peaks, the total peak variance in volume units can be given by the measured peak width at half peak height ($w_{0.5}$) according to

$$\sigma^2_{total,v} = \frac{F^2 w^2_{0.5}}{5.54} \quad (3)$$

Where F is the mobile phase flow-rate.

For asymetrical peaks, the second order central moment has to be used to provide a reliable variance value. These latter, in volume units, is given by

$$\sigma^2_{total,v} = F^2 \frac{\int_0^\infty (t - t_R)^2 I(t)\,dt}{\int_0^\infty I(t)\,dt} \quad (4)$$

Where t_R is the mean residence time and $I(t)$ the intensity as a function of time.

Extra-column variance can be approximated by removing the column and replacing it by a zero dead volume union connector. In this case, extra-column variance is calculated from Eq. (3).

The column variance, expressed in length units ($\sigma^2_{col,x}$) is related to both the column length and the column plate height, H_{col}, by

$$\sigma^2_{col,x} = L H_{col} \quad (5)$$

H_{col} varies with the mobile phase linear velocity, u, and its variation may be fitted by the van Deemter equation [39] or by the Knox equation [40] using reduced parameters h_{col} (H_{col}/d_p) and ν ($u.d_p/D_m$, d_p being the average particle diameter and D_m the molecular diffusion coefficient of the solute in the mobile phase). At the minimum of the curve, typical values for h_{col} and ν are 3 and 5 respectively.

Considering the solute linear velocity at the time the solute is eluted from the column ($u/(1+ k_e)$, k_e being the retention factor at elution), the column variance can be expressed in volume units according to

$$\sigma^2_{col,v} = \frac{V_0^2 (1 + k_e)^2 H_{col}}{L} \quad (6)$$

V_0 is the column dead volume, related to the column length, the internal diameter, d_i and the column porosity, ε_t by

$$V_0 = \pi L \varepsilon_t (d_i^2/4) \quad (7)$$

Under isocratic conditions, k_e depends on the retention volume and is given by

$$k_e = \frac{V_R}{V_0} - 1 \quad (8)$$

Under gradient conditions, k_e depends on both the gradient conditions and the solute properties. However a rough estimation of k_e can be made when the linear solvent strength theory (LSST) can be applied and the solvent strength parameter, S is known [41,42], using the following relation

$$k_e = \frac{1}{2.3\, S\, t_0 \frac{\Delta C}{t_G}} \quad (9)$$

With t_0 the column dead time, ΔC the gradient composition range, and t_G the gradient time. Typical values of S (S being the absolute value of the slope of the linear relationship between the logarithm of the retention factor and the stronger solvent volume fraction) are 4 for small molecules, 20 for peptides and much higher for larger molecules [42].

Thus, From Eqs. (6) and (7), the column variance for a given peak in a given chromatogram can be estimated provided that the column geometry is known, and the retention factor can be determined.

Similarly to Eq. (6), the total variance in volume units can be written

$$\sigma^2_{total,v} = \frac{V_0^2 (1 + k_e)^2 H_{total}}{L} \quad (10)$$

Where H_{total} is the total plate height resulting from the two dispersion processes.

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