Chemometrics and Intelligent Laboratory Systems 137 (2014) 146–154

Contents lists available at ScienceDirect

Chemometrics and Intelligent Laboratory Systems

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

Second-order calibration for simultaneous determination of pharmaceuticals in water samples by solid-phase extraction and fast high-performance liquid chromatography with diode array detector

Nadia Akvan [a], Hadi Parastar [b,*]

[a] Department of Chemistry, University of Isfahan, Isfahan 81746-73441, Iran
[b] Department of Chemistry, Sharif University of Technology, P.O. Box 11155-3516, Tehran, Iran

ARTICLE INFO

Article history:
Received 18 December 2013
Received in revised form 3 July 2014
Accepted 3 July 2014
Available online 10 July 2014

Keywords:
Parallel factor analysis
Correlation optimized warping
Chromatography
Experimental design
Pharmaceuticals
Multivariate curve resolution

ABSTRACT

A fast high-performance liquid chromatography–diode array detection (HPLC–DAD) approach combined to solid phase extraction (SPE) as a pre-concentration step is developed for simultaneous determination of five selected pharmaceuticals (carbamazepine, naproxen, diclofenac, gemfibrozil and mefenamic acid) in water samples. The effective factors on the efficiency of SPE procedure are optimized using faced-centered central composite design (FCCD). In addition, multi-response optimization by using Derringer's desirability function is used to find the optimum experimental conditions for extraction of analytes from well and river waters. Due to the complexity of water matrices and the presence of different chromatographic issues, new combination of multivariate curve resolution–correlation optimized warping to parallel factor analysis (MCR–COW–PARAFAC) and multivariate curve resolution-alternating least squares with trilinearity constraint (MCR–COW–MCR_{tril}) is proposed for simultaneous determination of five target pharmaceuticals in these samples. This strategy allowed us to overcome matrix effects and to exploit second-order advantage. Recoveries ranging from 80.12% to 102.71% and relative standard deviations below 8.0% for all pharmaceuticals proved the accuracy and precision of the proposed method. In addition, the values of relative error in calibration curves (RE, %) were below 11.24% and 12.19% for MCR–COW–PARAFAC and MCR–COW–MCR, respectively. Furthermore, the values of detection limits (LODs) and quantification limits (LOQs) were between 0.02 to 0.32 ng mL^{-1} and 0.07 to 1.07 ng mL^{-1}, respectively. In addition, analytical figures of merit using multivariate approaches were calculated for both methods. In this regard, the values of sensitivity, LOD and LOQ showed an improvement compared to univariate techniques. Inspection of the results showed that due to the efficient correction of elution time shifts using MCR–COW method and preserving trilinear data structure, both MCR–COW–PARAFAC and MCR–COW–MCR_{tril} give similar results. These results confirmed that coupling optimized SPE–HPLC–DAD method with second-order calibration algorithms can be considered as an efficient method for fast, simple and cost effective quantification of pharmaceuticals in highly contaminated samples, such as river and well waters.

1. Introduction

Determination of pharmaceutical residues in environmental matrices is a field of special interest due to the risks to human health and aquatic environment [1–3]. Pharmaceuticals are synthetic chemicals that belong to a wide group of different chemical families and may also react differently in the environment. There are very well documented evidences that some pharmaceuticals enter into the environment and they are persistent [4–6]. Pharmaceuticals can be considered as a new class of persistent pollutants which are used in a large volume every year. Pharmaceutical residues are presently found in environmental samples due to inappropriate or insufficient removal procedures in wastewater treatment plants (WWTPs) and therefore, these products were considered as remarkable sources of pollutants [5,7–9]. More than 100 different pharmaceuticals have been detected in lakes, rivers, reservoirs and streams throughout the world. Additionally, biodegradation and transformation of pharmaceuticals and their metabolites can also occur in WWTPs, which produce more toxic by-products than the parent compounds in some cases [10].

Qualitative and quantitative analysis of trace amounts of pharmaceuticals in complex environmental samples, such as waters with sufficient accuracy and precession has been a challenging task for analytical chemists because of low selectivity and sensitivity of the entire analytical procedures. Among different analytical techniques, chromatographic methods (i.e., hyphenated and/or multidimensional) have been proposed as powerful methods for determination of pharmaceuticals in water samples [10]. Gas chromatography–mass spectrometry

* Corresponding author. Tel.: +98 21 66165306; fax: +98 21 66005718.
E-mail addresses: h.parastar@sharif.edu, h.parastar@gmail.com (H. Parastar).

http://dx.doi.org/10.1016/j.chemolab.2014.07.004
0169-7439/

(GC–MS), liquid chromatography–mass spectrometry (LC–MS), high-performance liquid chromatography–diode array detector (HPLC–DAD) and comprehensive two-dimensional gas chromatography (GC × GC) are among the most frequently used chromatographic methods for determination of pharmaceuticals in environmental matrices [5,11–14].

Very often, in order to extract the analytes from complex sample matrices, an extraction step before chromatographic separation is required. Different extraction methods have been used to extract target analytes from environmental samples such as solid-phase extraction (SPE) [5,14–16], liquid-phase microextraction (LPME) [17] and solid-phase microextraction (SPME) [18]. On the other side, the optimization of extraction procedures is usually based on one-variable-at-a-time (OVAT) approach, which facilitates the interpretation of the obtained results, but interactions between variables are not taken into account [19–21]. Therefore, a false minimum or maximum may be attained, leading to the use of certain conditions in which the combination of the variables is not the one which provides the best analytical response. Experimental design methods (e.g., factorial designs and response surface methodology) have been recently applied to optimize the extraction procedures [20,21]. In this approach, the main effects of the factors, their interactions and curvatures are estimated. This is one of the greatest advantages of multivariate optimization compared to OVAT optimization. Another advantage is that the number of experiments is considerably reduced particularly in the cases with many factors [20,21].

Even under optimized conditions, these extraction processes are not usually selective; therefore, a number of interfering compounds will be extracted. In addition, in spite of the recent technological advances, current chromatographic analyses are faced with some fundamental challenges, such as baseline/background contribution, noise, elution time shifts and peak overlap that can directly affect qualitative and quantitative chromatographic results [22]. In this context, resolution, identification and quantification of target pharmaceuticals in the presence of interferences (i.e., known and/or unknown) in environmental samples are still challenging problems which are not totally solved yet with the current methods [12,23–25].

Fortunately, during the last decades, different multivariate chemometric methods (i.e., second-order calibration) have been proposed to compensate the lack of selectivity in chromatography, to overcome different fundamental chromatographic challenges during hyphenated and multidimensional chromatographic separations and to obtain pure qualitative and quantitative chromatographic information of target components in the analyzed samples [22,24,26–29]. This is achieved by mathematical resolution means based on exploiting the spectral and chromatographic features (even if they are very small) of all the components present in a particular unresolved mixture (i.e., second-order advantage) [12,26,30]. It means that despite all of these problems, faster chromatographic runs can be used which cause saving of money and time and reducing in the amount of used toxic solvents [12,25,31,32].

Parallel factor analysis (PARAFAC) [33] has a central role in multi-way chemometric methods because of the exceptional uniqueness property for resolution purposes [34–36]. This method is based on the strict fulfillment of trilinear model. Multi-run chromatographic data can be arranged in a three-way data structure where the three directions of this data array are elution times, spectroscopic channels and chromatographic runs. However, this does not imply that the trilinear model is fulfilled by these data sets. Deviation from trilinear model assumption can occur due to the changes in elution times and peak shapes between chromatographic runs (due precisely to the changes in the chromatographic conditions). Therefore, RT shifts must be corrected before PARAFAC analysis. Among different methods to correct elution time shifts, the newly developed method of multivariate curve resolution–correlation optimized warping (MCR–COW) [37] is an efficient technique for this purpose.

In our previous work, MCR–COW–PARAFAC method was developed as a new second-order calibration method for complex chromatographic data by analyzing the simulated and real HPLC–DAD data. In addition, the performance of this method was compared with other methods, such as PARAFAC, COW–PARAFAC and finally with MCR–ALS and MCR–COW–MCR. The main aim of this work was to deliver this important message to the users of PARAFAC which the use of PARAFAC for chromatographic data depends on the efficient correction of elution time shifts. Otherwise, the application of trilinear model to the chromatographic data will fail.

In the present contribution, owing to the important role of multivariate chemometric methods for studying the environmental risks of pharmaceutical residues in water matrices, combination of response surface methodology and second-order calibration is proposed to develop an optimized SPE procedure combined to a fast HPLC–DAD analysis for simultaneous determination of five target pharmaceuticals in well and river waters. In this regard, Derringer's desirability function is developed for multi-response optimization of the extraction procedure. Also, the performance of MCR–COW–PARAFAC and MCR–COW–MCR_{tril} in calibration step is compared [38]. On the other side, the estimation of analytical figures of merit for multivariate calibration models has been the object of important theoretical and experimental efforts in the past years [39]. Specifically, sensitivity, limits of detection and limits of quantitation have been calculated and employed for the comparison of the analytical performance of different methods, for the optimization of analytical methodologies, or for assessing detection capabilities. Therefore, in the present contribution multivariate analytical figures of merit are calculated according to the developed method by Olivieri and Faber [40] to evaluate the performance of the proposed strategy.

2. Theory

The MCR–COW has been recently proposed by Tistaert and Vander Heyden [37] as a novel alignment algorithm for chromatographic signals. In this method, in order to overcome the misalignment problem of COW [41] in the case of complex chromatographic signals, the complexity of the chromatographic data is reduced by proper arrangement of these data in a bilinear way and then, performing MCR bilinear decomposition to obtain pure elution and spectral profiles. The general MCR bilinear decomposition for a column-wise augmented data matrix is as follows:

$$\mathbf{X}_{aug} = \begin{bmatrix} \mathbf{X}_1 \\ \mathbf{X}_2 \\ \mathbf{X}_3 \\ . \\ . \\ . \\ \mathbf{X}_I \end{bmatrix} = \begin{bmatrix} \mathbf{C}_1 \\ \mathbf{C}_2 \\ \mathbf{C}_3 \\ . \\ . \\ . \\ \mathbf{C}_I \end{bmatrix} \mathbf{S}^T + \begin{bmatrix} \mathbf{E}_1 \\ \mathbf{E}_2 \\ \mathbf{E}_3 \\ . \\ . \\ . \\ \mathbf{E}_I \end{bmatrix} = \mathbf{C}_{aug}\mathbf{S}^T + \mathbf{E}_{aug} \quad (1)$$

where $\mathbf{X}_{aug}$ ($IJ \times K$) is the column-wise augmented data matrix, $\mathbf{C}_{aug}$ ($IJ \times N$) is the augmented matrix containing the resolved elution profiles and $\mathbf{S}^T$ ($N \times K$) is the matrix of resolved spectral profiles. In addition, $\mathbf{E}_{aug}$ ($IJ \times K$) is an augmented data matrix containing unmodeled part of data. Furthermore, I is the number of samples (e.g., concentrations), J is the number of elution time points, K is the number of wavelengths and N is the number of chemical components in the desired chromatographic region.

After MCR bilinear decomposition, the COW alignment is individually performed on the N elution profiles of I samples which minimizes the risk of aligning non-corresponding information. In other words, the $\mathbf{C}_{aug}$ ($IJ \times N$) augmented matrix is reshaped to N individual data matrices with dimensions $I \times J$. Afterwards, the folded data matrices are aligned by COW algorithm. In most of the cases, the median of the elution profiles is used as reference to avoid the effects of outliers. Using the aligned elution profiles, the N folded data matrices are unfolded to