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Matrix solid-phase dispersion followed by liquid chromatography tandem mass spectrometry for the determination of selective ciclooxygenase-2 inhibitors in sewage sludge samples

Sara Triñanes, Mª Carmen Casais*, Mª Carmen Mejuto, Rafael Cela

Dpto. Química Analítica, Nutrición y Bromatología. Instituto de Investigación y Análisis Alimentario, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain

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ABSTRACT

A straightforward single-step extraction method based on matrix solid-phase dispersion (MSPD), followed by high-performance liquid chromatography with hybrid quadrupole time of flight mass spectrometry (LC–QTOF-MS), was developed and optimized to determine five non-steroidal anti-inflammatory drugs (Valdecoxib, Etoricoxib, Parecoxib, Celecoxib and 2,5-Dimethylcelecoxib) in sewage sludge samples. The influence of different operational parameters on the extraction efficiency a well as in the matrix effects of the produced extracts was evaluated in detail. Under final working conditions, freeze dried samples (0.2 g) were first soaked with 100 μL of aqueous potassium hydroxide solution (60%, w/v), mixed with 1 g of anhydrous sodium sulfate and dispersed with 1 g of Florisil. This blend was transferred to the top of a polypropylene column cartridge containing 3 g of silica. Analytes were recovered using 15 mL of hexane/acetone (1:2, v/v) mixture. The extracts were concentrated by evaporation and reconstituted with 1 mL of methanol/water (1:1, v/v), filtered and injected in the LC system. Quantification limits from 0.005 and 0.05 ng g^{-1} and absolute recoveries between 86 and 105% were achieved. Results indicated the presence of two of the targeted COXIBs in real samples of sewage sludge, the highest average concentration (22 ng g^{-1}) corresponding to celecoxib. Moreover, the screening capabilities of the LC–QTOF-MS system demonstrated that the developed MSPD extraction procedure might be useful for the selective extraction of some other pharmaceuticals (e.g. amiodarone and their metabolite *N*-desethylamiodarone, miconazole, clotrimazole and ketoprofen) from sludge samples.

1. Introduction

Active pharmaceutical ingredients (APIs) are a very large and diverse group of compounds used in considerable quantities through the world designed to prevent, cure and treat diseases and improve health. Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most consumed groups [1,2]. As with many other API residues and metabolites, one of the most important routes into the environment is sewage treatment plants (STPs) and some studies have reported the occurrence of NSAIDs in treated wastewater effluents, indicating that some of these compounds are not efficiently removed in STPs [3–5]. On the other hand, when STPs appear efficient in removing pharmaceutical residues as judged by the absence in treated aqueous effluents, these residues frequently may remain intact accumulated in sludge. In contrast to the many studies of pharmaceutical residues in the aquatic environment, the occurrence and fate of pharmaceuticals in solid matrices, such as sludge, soil and sediments have been rarely studied [6], possibly because the matrix complexity, especially in the case of sludge. This means that several NSAIDs drugs (including the selective ciclooxygenase-2 (COX-2) inhibitors (COXIBs)), especially the more hydrophobic, low biodegradable compounds are likely re-entering into the environment through the sludge [6,7].

The amount of sewage sludge produced per year in the UE is estimated over 10 million tones [8,9]. In particular, Spain produces around 1.13 million tons per year and, 81% are employed in agriculture, 7% are eliminated in landfill, another 7% is incinerated and 5% of tons go to other uses [10]. Consequently, it is a real technological challenge the elimination of these compounds as well as the analytical control of its levels in these complex matrices.

Pharmaceutical residues in soils, sediments and sludge have been extracted by ultrasonic solvent extraction (USE) [4],

* Corresponding author.
E-mail address: carmela.casais@usc.es (M.C. Casais).

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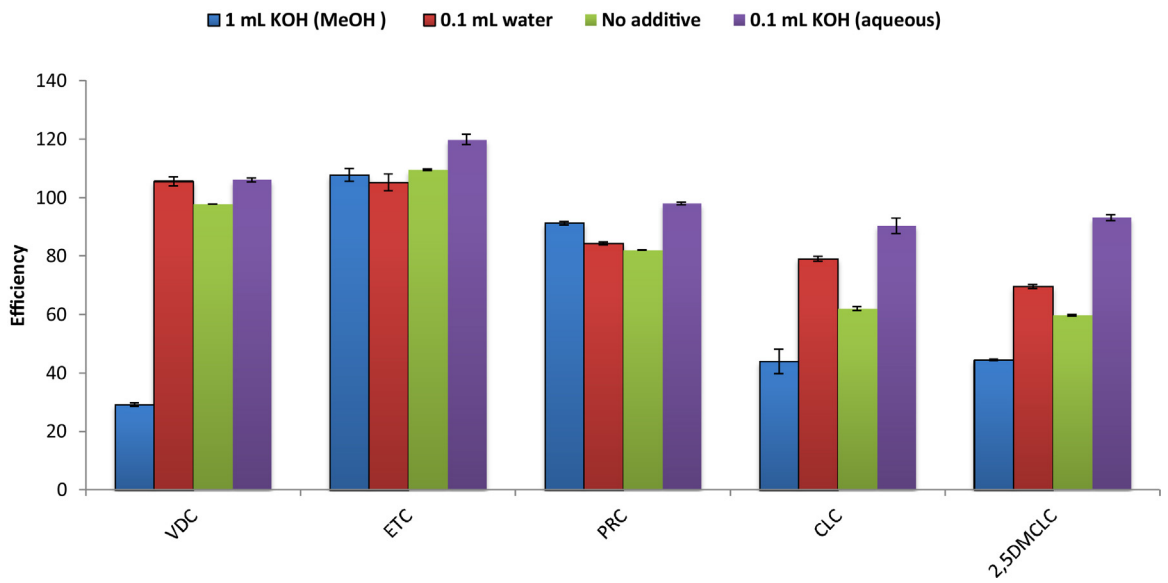

Fig. 1. Efficiency of MSPD extraction as a function of the additive. (Sample: 0.2 g; Elution solvent: 30 mL hexane/acetone (1:1, v/v)), n = 3.

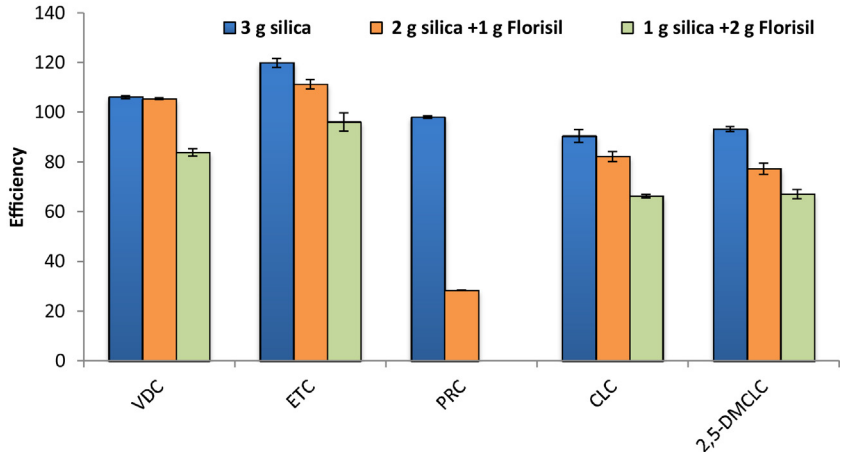

Fig. 2. Efficiency of MSPD extraction as a function of the co-column. (Sample: 0.2 g; Elution solvent: 30 mL hexane/acetone (1:1, v/v)), n = 3.

microwave assisted extraction (MAE) [11] and pressurized liquid extraction (PLE, ASE) [4,12–14]. In most cases, the extracts need further clean-up using solid phase extraction (SPE) and concentration to provide analytical extracts allowing the reliable quantification of analytes. An alternative strategy for the extraction of organic environmental pollutants is matrix solid-phase extraction (MSPD), developed by Baker et al. [15], that has been applied for the extraction of a large variety of analytes from solid, semi-solid, viscous and biological matrices [16]. This technique involves a process allowing simultaneous extraction and clean-up of analytes from solid or semi-solid samples with significant reduction in solvent consumption not requiring particularly expensive instrumentation [6].

In this study, five COXIBs were selected on the basis of their recent use as a convenient alternative to the traditional non-steroidal anti-inflammatory drugs (t-NSAIDs) [17]. The aim was to assess the suitability of the matrix solid-phase dispersion technique (MSPD) for the one-step extraction of COXIBs from sludge samples. While the necessary selectivity in the determination is provided by LC-ESI-Q/TOF, the objective was to develop a simple process allowing the quantitative extraction of the analytes while providing clean extracts with a minimum of sample preparation operations. As far as we know this is the first time MSPD has been applied to process sludge samples for the analysis of COXIBs. Different important parameters, such as solid sorbent types, eluting solvents or the amount of additives were studied and optimized. The complete procedure was evaluated for linearity, sensitivity, matrix effects, repeatability and reproducibility demonstrating satisfactory performance. Additionally, using the information gathered by the LC–QTOF-MS instrument, other non-target pharmaceutical residues were screened in the LC–MS chromatograms of samples which extends the practical applicability of the developed sample preparation procedure.

2. Experimental

2.1. Reagents, standards and materials

Acetonitrile (ACN), methanol (MeOH) (gradient-grade, Lichrosolv), *n*-hexane, acetone, ethyl acetate (EtOAc) and dichloromethane (DCM) (Suprasolv) were purchase from Merck (Darmstadt, Germany). Ultrapure water was produced by means of a Milli-Q gradient A-10 system (Millipore, Billerica, MA, USA). The commercial selective COXIBs standards (*Valdecoxib (VDC)* (4-(5-methyl-3-phenyl-4-isoxazolyl) benzenesulfonamide), *Parecoxib (PRC)* (*N*-{[4-(5-Methyl-3-phenyl-1,2-oxazol-4-yl)phenyl]sulfonyl}propanamide),