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Electromembrane extraction (EME) and HPLC determination of non-steroidal anti-inflammatory drugs (NSAIDs) in wastewater samples

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ABSTRACT

In this paper, an electromembrane extraction (EME) combined with a HPLC procedure using diode array (DAD) and fluorescence detection (FLD) has been developed for the determination of six widely used non-steroidal anti-inflammatory drugs (NSAIDs): salicylic acid (SAC), ketorolac (KTR), ketoprofen (KTP), naproxen (NAX), diclofenac (DIC) and ibuprofen (IBU). The drugs were extracted from basic aqueous sample solutions, through a supported liquid membrane (SLM) consisting of 1-octanol impregnated in the walls of a S6/2 Accurel® polypropylene hollow fiber, and into a basic aqueous acceptor solution resent inside the lumen of the hollow fiber with a potential difference of 10 V applied over the SLM. Extractions that were carried out in 10 min using a potential of 10 V from pH 12 NaOH aqueous solutions shown concentration enrichments factors of 28–49 in a pH 12 NaOH aqueous acceptor solution. The proposed method was successfully applied to urban wastewaters. Excellent selectivity was demonstrated as no interfering peaks were detected. The procedure allows very low detection and quantitation limits of 0.0009–9.0 and 0.003–11.1 $\mu g\,L^{-1}$, respectively.

1. Introduction

The analysis of complex samples and the analytes detection or quantitation at very low levels are nowadays two of the main analytical problems. The analytical complexity increases in those cases where both problems are present. The use of clean-up procedures is an old analytical tool that in the last years has undergone very important developments. Traditionally, liquid–liquid extraction (LLE) has been an important sample-preparation technique prior to chemical analysis. Recently, solid phase extraction (SPE), using several sorbent types, has been the preferred sample-preparation technique to extract pharmaceuticals from several environmental and biological matrices [1–3], but in the last years, there has been a high interest in developing new extraction and clean-up procedures.

Liquid phase microextraction (LPME), also known as supported liquid membranes (SLM) extraction, is an attractive alternative to the widely used solid phase extraction (SPE). Audunsson [4] introduced an alternative concept for LPME that was developed by Thordarson et al. [5], and Pedersen-Bjergaard and Rasmussen [6], based on the use of single, low-cost, disposable, porous, hollow fibers made of polypropylene (HF-LPME) that allows in most cases, not only a efficient clean-up procedure, but it can also produce high degree of pre-concentration. Additionally, the low organic solvent consumption makes HF-LPME an interesting and environmental friendly analytical procedure. Some reviews on hollow fiber-based LPME have been reported [7–10].

The ionic nature of several of the interesting analytes in liquid extraction procedures led to some authors to propose the use of electrical fields to enhance and to manipulate LLE. Early attempts of analytical LLE driven by an external electrical field (from 1 to 15 kV dc) were reported by van der Vlis et al. between 1994 and 1996 [11–13]. After this period, no other papers emerged on the electro extraction concept. In 2005, Arrigan and co-workers proposed another approach to LLE driven by electrical potential with the development of "electrochemically modulated LLE of ions" [14–16]; where the analytes were extracted from a flowing aqueous phase of a flow-injection system with a stationary organo-gel phase (pseudo-liquid) using electrical potentials in the −1 to +1 V range.

In 2006, Pedersen-Bjergaard and Rasmussen demonstrated, for the first time, that an electrical potential produces analytical extraction through a supported liquid membrane (SLM) [17,18]. This system was termed electromembrane extraction (EME) and the analytes were extracted from an aqueous sample through an organic solvent (2-nitrophenyl octylether, NPOE) immobilized as SLM in the wall of a polypropylene porous hollow fiber to an aqueous acceptor solution placed inside the lumen of the hollow

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fiber. Essentially, it is similar to a HF-LPME where the migration through the SLM is forced by the electrical field generated from two electrodes placed outside the fiber and inside the lumen (electromigration, EMI). In order to ensure efficient electrokinetic mobility in the EME system, pH must be adjusted to provide total ionization of the analytes in the two aqueous solutions. In these first works, basic analytes were analyzed using acid pHs and electrical potential of 300 V.

In 2007, the same authors publish an article [19] where EME was discussed in more detail from a theorical point of view. It was demonstrated that the flux of analytes across the membrane can be described using a mathematical model based on the Nernst–Planck equation. The model demonstrated that the magnitude of the electrical potential difference, the ion balance of the system, and the absolute temperature influenced the flux of analyte through the SLM. These conclusions were verified by experimental data with five basic drugs and NPOE as SLM. Other articles related to the extraction of basic drugs using EME have also been published by these authors [20–25] using lower voltages than those used in the first published papers.

The electromembrane extraction procedure using hollow fibers as support for the SLM has been also applied to the separation of peptides [26,27]. Other EME configuration, called by the authors drop-to-drop [28], shown poor recoveries and repeatability.

There is only a single previous article about the electrokinetic migration of acidic drugs through SLM in a hollow fiber configuration [29] where the influence of some parameters (pH of donor and acceptor solutions, voltage, extraction time and agitation) on the electromigration process was studied. Some of the drugs analyzed in the present work were studied with recoveries between 25% and 82% and enrichment factors of 2.5–8.2. Repeatability and linearity was briefly tested for some of the acidic drugs analyzed with not very good results; authors attribute this fact to the experiments were performed with home-built equipment.

In this work, a HPLC/DAD-FLD method combined with prior EME was developed for the determination of six widely used non-steroidal anti-inflammatory drugs (NSAIDs): salicylic acid (SAC), ketorolac (KTR), ketoprofen (KTP), naproxen (NAX), diclofenac (DIC) and ibuprofen (IBU). The method was applied to their determination in urban wastewaters. The EME provides very clean extracts that can be directly injected into the chromatographic system allowing excellent baselines. The proposed EME is an easy and rapid sample pretreatment procedure that additionally, provides high sample preconcentration which enhances the applicability of the proposed method. EME reduces the organic solvents consumption to several microlitres in contrast to other clean-up/preconcentration alternatives which is according to the current trends to a “Green Chemistry”.

2. Experimental

2.1. Chemicals and reagents

All chemicals were of analytical-reagent grade or better. All solutions and dilutions were prepared with ultrapure water form a Milli-Q Plus water purification system (Millipore, Billerica, MA, USA). SAC, KTR, KTP, NAX, DIC and IBU, dihexyl ether, 2-nitrophenyl octyl ether (NPOE), 1-heptanol, benzyl alcohol, cyclohexanol, and 1-octanol were purchased from Fluka–Sigma–Aldrich (Madrid, Spain) and the rest of products were obtained from Merck (Darmstadt, Germany).

Aqueous working solutions of NSAIDs were daily prepared by adequate dilutions from methanolic (KTP, NAX) and aqueous (SAC, KTR, DIC, IBU) 100 mg L^{-1} stock solutions.

2.2. Chromatographic conditions

The chromatographic separation was performed at 10 °C using a LaChrom® VWR-Hitachi (Barcelona, Spain) liquid chromatograph with a quaternary L-2130 pump. The injector was a autosampler L-2200. Separations were carried out at 10 °C (VWR Refrigerated Circ Model 1160S, West Chester, Pennsylvania, USA) using a LiChroCART® 75-4 Purosphere® STAR RP-18e 3 μm (75 mm × 4.0 mm i.d.) (VWR, Darmstadt, Germany) preceded by a guard column Kromasil® 100 Å, C18, 5 μm (15 mm × 4.6 mm i.d.) (Scharlab S.L., Barcelona, Spain).

The mobile phase consisted of 0.1% formic acid (pH 2.6) (component A) and acetonitrile (component B) at a flow rate of 0.8 mL min^{-1}. An initial 60% component A was used in isocratic mode for 5 min and then a linear elution gradient was programmed from 60% to 0% A for other 5 min, finally an isocratic mode for 2 min was programmed. Five minutes were waited between injections which allowed re-equilibration of the column to the initial conditions. Table 1 shows the monitoring wavelengths for DAD and fluorescence detection (FLD) detections and the retention times for the analyzed compounds.

2.3. Supported liquid membrane preparation and extraction procedure

The electrical equipment consisted in a dc power supply model Power Source 300 V (VWR International, West Chester, Pennsylvania, USA) with programmable voltage in the range 2–300 V, providing currents in the range 4–500 mA. Simple platinum wires with a diameter of 0.25 mm were used as electrodes in the sample and acceptor solutions with an average inter-electrode distance of 2 mm which resulted in an electrical field of 50 V cm^{-1} (for a typical 10 V dc). As sample compartment, 10 mL glass vials were used with a height of 48 mm and with an internal diameter of 20 mm (VWR International, West Chester, Pennsylvania, USA). Hollow fiber used for immobilization of the supported liquid membrane and for housing the acceptor solution was a S6/2 Accurel® polypropylene hollow fiber (1800 μm i.d., 450 μm wall thickness and 0.2 μm pore size) that was purchased from Membrana (Wuppertal, Germany). The sample solution was stirred with a FB15107 Magnetic Stirrer (Fisher Scientific, Pittsburgh, PA, USA).

Hollow fibers were cut into 24 mm pieces, washed with acetone in an ultrasonic bath and dried; the fiber was closed in the lower end by thermal and mechanical pressure, whereas the upper end was connected to a piece of 8 mm length from a pipette tip of polypropylene (Rodelab, Seville, Spain) as a guiding tube. The fiber was soaked with 1-octanol during 5 s to impregnate the pores, and the excess of organic solvent was removed with a medical wipe. The lumen of the prepared fiber piece was filled with 50 μL of acceptor phase (pH 12 aqueous solution) using a HPLC syringe and the positive electrode was placed in the acceptor solution. Hollow fiber with acceptor solution was placed into the 10 mL sample solution (pH 12) and voltage (10 V) was applied for 10 min during the sample stirring at 600 rpm.

After electromigration, the fiber was taken out and the acceptor phase was extracted using a HPLC syringe and placed into a HPLC microvial to be injected (20 μL) into the HPLC system through the autosampler unit.

2.4. Preparation of environmental water samples

Wastewater samples were obtained from E.D.A.R. Punta Umbría-AQUALIA Wastewater Treatment Plant which is located in Punta Umbría, Huelva, Spain. The WWTP essentially receives urban wastewaters. The capacity of this WWTP is 140,000 inhabitants and

Table 1
Monitoring wavelengths and retention times.

	DAD			FLD			
	λ_{max} (nm)	t_R (min)	SD (min)	λ_{exc} (nm)	λ_{em} (nm)	t_R (min)	SD (min)
SAC	235	2.72	0.021	230	445	3.00	0.024
KTL	315	3.73	0.009	–	–	–	0.011
KTP	255	6.45	0.014	–	–	–	0.013
NPX	230	7.01	0.008	239	251	7.24	0.015
DIC	280	10.27	0.018	–	–	–	0.017
IBU	224	10.41	0.017	224	290	10.65	0.022

the discharged flow is 21,250 m^3/day. Samples from the influent (raw water, WWR), after the primary sedimentation tank (WW1) and the effluent (treated water after anaerobic digestion, WWT) were analyzed.

All samples were filtered through a GDU1 glass fibre filter bed (10–1 μm) (Whatman, Mainstone, UK) and through Pall Nylaflo™ nylon membrane filter 0.45 μm (Pall Corporation, Ann Arbor, Michigan, USA) and adjusted to pH 4 with HCl. Filtered samples were stored in the dark at 4 °C prior to electromigration procedure. Water samples, were directly analyzed after NaOH addition just to obtain pH 12 prior to be submitted to the electromigration procedure.

3. Results and discussion

3.1. Chromatographic conditions

Looking for a fast and high resolution separation a LiChroCART® 75-4 Purosphere® STAR RP-18e 3 μm was selected as working column. This column is a small size particle HPLC column that allows high resolution separations and lower retention times than other 5 μm ones. The selected column also provides good resolution and good peak symmetry.

Table 2
Four-level factorial design (X_1: donor pH, X_2: voltage, X_3: extraction time and X_4: stirring speed).

X_1	X_2	X_3	X_4
+1	+1	+1	+1
+1	+1	+1	−1
+1	+1	−1	+1
+1	+1	−1	−1
+1	−1	+1	+1
+1	−1	+1	−1
+1	−1	−1	+1
+1	−1	−1	−1
−1	+1	+1	+1
−1	+1	+1	−1
−1	+1	−1	+1
−1	+1	−1	−1
−1	−1	+1	+1
−1	−1	+1	−1
−1	−1	−1	+1
−1	−1	−1	−1
α	0	0	0
$-\alpha$	0	0	0
0	α	0	0
0	$-\alpha$	0	0
0	0	α	0
0	0	$-\alpha$	0
0	0	0	α
0	0	0	$-\alpha$
0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0
0	0	0	0

The mobile phase consisted of 0.1% formic acid and acetonitrile. Different gradient elution conditions were tested searching for the shortest time of analysis without sacrificing peak shape. The gradient elution program described in the previous section was the best option in terms of time of analysis, shape of the peaks and reproducibility. The peak resolution for the analyzed substances oscillates between 1.60 and 12.33 (all above the critical value, 1.5). Additionally, asymmetry factors, retention factors, and selectivity factors for the obtained peak are according to their critical values.

3.2. Optimization and evaluation of experimental conditions for electromigration

First, some preliminary tests were carried out in order to check the electromembrane extraction behaviour according to the organic solvent used as supported liquid membrane; the solvents checked were dihexyl ether, 2-nitrophenyl octyl ether (NPOE), 1-heptanol, benzyl alcohol, cyclohexanol, 1-octanol and 1:1, 1:2, 1:3 and 1:5 dihexyl ether: 1-octanol mixtures. Dihexyl ether can not be used as supported liquid membrane due to produces an interruption in the electrical conduction. Much better results were obtained when 1-octanol was used as SLM; the rest of solvents and mixtures only lead to recoveries of 2–20% respect to the 1-octanol one. Additionally, an impregnation time of 5 s was established as optimum.

The inter-electrode distance was also checked between 1 and 5 mm and an optimum distance of 2 mm was obtained. Lower a higher inter-electrode distances lead to a general decrease in the analytes extraction.

Some tests concerning to the effect of the ionic strength of the donor phase in the electromigration process were realized. Sodium sulfate concentrations between 0.1 and 1.5 M were checked without relevant results. It is remarkable that sodium sulfate concentrations over 1 M produce the burning of the fiber.

Some preliminary tests related to the pH effect on the electromigration efficiency were carried out showing that electromigration increases for all the analytes with the increase of the pH of acceptor phase. However, pH values higher than 12 produce analytes degradation, so pH 12 was fixed in the acceptor phase for the later optimization of the rest of experimental variables that, as it is described below, was realized using an experimental design.

On the other hand, we have checked that, in the experimental conditions, if no electrical power is applied the extraction of the analytes is null, which shows that there is not liquid phase

Table 3
Coded factors used for the experimental design.

Levels					
Factors	−2	−1	0	1	2
X_1 (pH)	9	9.75	10.5	11.25	12
X_2 (V)	2	6	10	14	18
X_3 (time) min	5	7.5	10	12.5	15
X_4 (speed) rpm	150	300	450	600	750

Table 4
Detection limits, linear ranges, % linearity and enrichment factors for the HPLC method (DAD and FLD detection) combined with prior EME.

	DAD			FLD			Enrichment
	LOD[a]	Linear range [a]	% Linearity	LOD[a]	Linear range[a]	% Linearity	
SAC	0.16	0.55–100	99.45	0.12	0.41–100	99.87	40
KTR	0.18	0.61–100	99.75	–	–	99.71	35
KTP	0.12	0.40–100	99.67	–	–	99.63	43
NAX	0.08	0.29–100	99.89	0.0009	0.003–30	99.79	32
DIC	0.23	0.77–100	99.91	–	–	99.84	49
IBU	3.36	11.1–100	99.73	0.94	3.1–50	99.65	28

[a] $\mu g\,L^{-1}$.

microextraction (LPME) contribution to the proposed electromembrane extraction procedure.

In order to optimize the experimental extraction parameters an experimental design was applied. The fundamental objectives of the experimental planning are to identify controllable factors that significantly influence the outcome of the experiment, minimizing the effects of uncontrollable factors and optimizing the objective function to get the best response. It is interesting to obtain as much information as possible with the least number of experiences.The influence of the experimental variables to find the best conditions to quantify the six NSADs studied (donor phase pH (X_1), voltage (X_2), electromigration time (X_3) and stirring speed (X_4)) has been considered.

As it has been previously described that the pH of the acceptor phase is a critical parameter during the extraction so it was not considered a variable to optimize in the experimental design and it was fixed at pH 12.The optimization has been carried out using a central composite design (CCD) for four factors at two levels. These designs account for the main factors and binary interactions that influence the signal, with a low number of assays. The design matrix corresponds to four factors and thirty experiments, as illustrated in Table 2. The thirty runs are split into three groups: sixteen runs on the basis of levels +1 or −1, eight runs on the basis of levels $+\alpha$ or $-\alpha$ and six runs at the center of design. Table 3 shows the coded levels of selected factors ($-\alpha$, −1, 0, 1, α) where $\alpha = 2$.The computer program used on the experimental design was ECHIP ver. 6.4.1 (Velocity Pointe, Wilmington, DE, USA). After a scrutiny of the optimal conditions, it was considered a slight modification of some of them in order to favor the extraction for those compounds with higher detection limits (analytical optimal conditions). So, the optimal conditions used were those described in Section 2.3, pH 12 for the donor and acceptor, a voltage of 10 V, an electromigration time of 10 min and a stirring speed of 600 rpm. Respecting to the optimum time and voltage, it has been observed that the optimum value voltage is 10 whatever the value taken by any other of the variables. On the other hand, most of the compounds get better enrichment factor 10 min after extraction. After 10 min extraction, the enrichments are constant or lower for some of the compounds.

3.3. Linearity, sensitivity, precision and robustness for the electromigration

Linearity of the response function was studied from external calibration. A 10-point (in triplicate) calibration curve, was constructed using a least-square linear regression analysis of standards mixtures of the analytes at different concentrations. Using the selected electromigration conditions, aqueous pH 12 solutions with different analytes concentrations were submitted to the electromigration procedure and analyzed according to the described HPLC procedure. Peak areas are proportional to concentrations in the

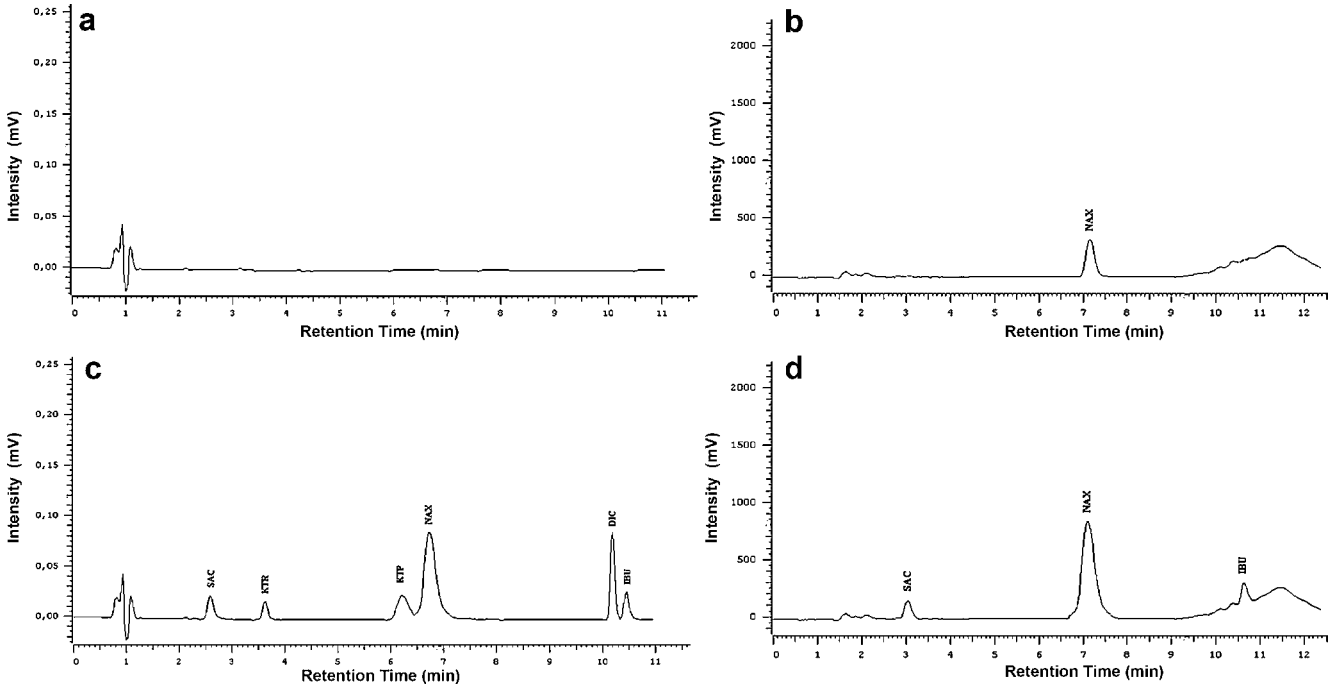

Fig. 1. DAD (a) and FLD (b) chromatograms from blank and spiked (DAD: all 5 ng mL^{-1} except IBU 20 ng mL^{-1} and FLD: SAC 2 ng mL^{-1}, NPX 0.05 ng mL^{-1}, IBU 5 ng mL^{-1}) wastewater (WWR) sample.

donor phase. A linear relationship was obtained with correlation coefficients $r \geq 0.999$ and the calibration curves obtained showed no changes over the course of 1 month. Detection and quantitation limits were calculated as the minimum concentration of an analyte giving peaks whose signal-to-noise ratio is 3 and 10, respectively. Enrichment factor was calculated as the increase in the concentration between the aqueous external donor phase and the internal (acceptor) phase. Table 4 shows the corresponding data and, as can be seen, the high enrichment values obtained for all the analytes allow their determination at low concentration levels.

To evaluate the repeatability and the intermediate precision, aqueous samples at three concentrations levels 0.8 (0.1 for IBU), 5 and 20 $\mu g\,L^{-1}$ (in triplicate) were subjected to the entire analytical procedure and measured in one single day and 1 day per week during 2 months, respectively. Intermediate precision was performed using the prediction of actual concentrations from the validation standards selected for the analytical assay in the *mxpxn* design (m = analytical levels, p = days and n = replications). From the corresponding ANOVA, the intermediate precision was computed [30]. The repeatability, expressed as relative standard deviation, was in the range 2.4–5.2%. Intermediate precision also expressed as relative standard deviation, was in the range 2.7–5.3%.

The robustness study is based on the procedure suggested by Youden [31]. A design matrix with two factors in eight experiments was used where the +1 and −1 levels correspond to slight modifications in the more critical variables: pH values of donor and acceptor phases and stirring time.

The effect of a given factor, say x_i can be estimated as the difference of result averages at levels +1 and −1:

$$D(x_i) = \frac{1}{4}\left[\sum R_{(x_i=+1)} - \sum R_{(x_i=-1)}\right]$$

where R is the corresponding experimental result obtained.

A significance t-test [32] was used to determine whether variations have a significant effect on the result,

$$t(x_i) = \frac{\sqrt{2}|D(x_i)|}{S_{IP}}$$

where S_{IP} is the standard deviation of the intermediate precision, evaluated in the precision study. The $t(x_i)$ values were compared with the corresponding critical t values ($n = 4$) at 5% significance level and three degrees of freedom. The results obtained indicated that the procedure can be considered robust against the considered factors for all the analyzed compounds.

3.4. Wastewater samples analysis

Wastewater samples described in Section 2.4 were submitted to the EME proposed procedure and analyzed. Some of the NSAIDs were detected in the samples analyzed (SAC in WWR and WWT, NAX in WWT, DIC in WWR and WW1, and IBU in WWR) and only contents of NAX could be measured in the samples WWR (0.043 $\mu g\,L^{-1}$) and WW1 (0.023 $\mu g\,L^{-1}$).

In order to check the suitability of the proposed procedure, spiked samples at some concentration levels: 0.8, 2, 5 and 20 $\mu g\,L^{-1}$ (plus 0.1 $\mu g\,L^{-1}$ for NAX and 50 $\mu g\,L^{-1}$ for IBU) were analyzed. Results obtained are shown in Table 5. Wastewater samples are, in general, complex samples from the analytical point of view, that frequently require complex clean-up processes. The direct application of the proposed HF-LPME procedure to the different kind of wastewater samples analyzed show, in general, good results in terms of recovery, approximately of 60% and high for SAC, KTR, KTP and NAX in all samples; 70% and high for IBU and nearly 100% for DIC. No significant differences have been observed in relation to the depuration process suffered by wastewaters. Urban wastewaters have extremely high surfactants concentrations that could modify the supported liquid membrane behaviour [33] which could lead to recovery decreases. Despite this fact, the good preconcentration and clean-up obtained implies a great advantage over other sample treatment procedures which could justify the use of the proposed EME procedure.

Table 5
Recoveries (%) using EME/HPLC from wastewater spiked samples. (Average of three determinations ± standard deviation).

	Spiked level[a]	Wastewater sample ([b])		
		WWR	WW1	WWT
SAC	0.8	66 ± 5.3	67 ± 6.4	69 ± 6.2
	2	67 ± 7.1	66 ± 6.8	69 ± 6.3
	5	65 ± 6.1	65 ± 7.6	66 ± 6.0
	20	68 ± 4.6	69 ± 5.9	70 ± 4.8
KTR	0.8	55 ± 6.8	56 ± 7.2	57 ± 5.3
	2	55 ± 3.1	56 ± 4.5	57 ± 4.4
	5	55 ± 3.6	57 ± 3.9	56 ± 3.6
	20	57 ± 2.6	57 ± 3.1	59 ± 2.5
KTP	0.8	62 ± 4.8	63 ± 5.2	65 ± 3.7
	2	62 ± 4.0	62 ± 4.3	63 ± 3.5
	5	63 ± 4.3	61 ± 4.4	64 ± 4.1
	20	62 ± 4.4	64 ± 4.7	62 ± 5.0
NAX	0.1	58 ± 4.2	58 ± 4.3	60 ± 4.1
	0.8	59 ± 4.3	60 ± 4.4	60 ± 4.5
	2	59 ± 4.1	61 ± 4.1	61 ± 3.6
	5	59 ± 3.7	58 ± 3.3	60 ± 2.8
	20	61 ± 3.5	60 ± 3.1	62 ± 3.3
DIC	0.8	100 ± 2.4	99 ± 2.5	100 ± 2.5
	2	99 ± 2.6	99 ± 2.6	99 ± 2.8
	5	100 ± 2.7	99 ± 2.7	100 ± 2.7
	20	100 ± 2.7	100 ± 2.5	100 ± 2.6
IBU	5	74 ± 3.4	73 ± 3.6	74 ± 3.9
	20	74 ± 4.5	75 ± 4.0	73 ± 4.1
	50	75 ± 3.8	75 ± 3.5	76 ± 3.8

[a] ($\mu g\,L^{-1}$).
[b] Average recovery (%) ± standard deviation ($n = 3$).

Fig. 1 shows representative DAD and FLD chromatograms obtained from blank and spiked wastewater (WWR) sample. This samples has been selected as the more complex wastewater. As it can be seen, both FLD chromatograms show excellent baselines, showing the blank FLD chromatogram the NAX peak above mentioned. Spiked chromatograms show well defined peaks corresponding only to the added substances.

4. Conclusions

This study presents a hollow fiber-based electromembrane microextraction method combined with an HPLC (DAD-FLD) determination using a small size particle chromatographic column that allows a rapid, simple, low-cost, accurate, high sensitive and selective methodology for the determination of six widely used non-steroidal anti-inflammatory drugs. The proposed extraction procedure has a very low (few μL) organic solvent consumption. The excellent clean-up obtained implies a great advantage over other sample treatment procedures.

The proposed procedure has been demonstrated adequate for the determination of the analytes in urban wastewater samples that usually require tedious clean-up and preconcentration steps.

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