Journal of Chromatography A, 1218 (2011) 2276–2283

Contents lists available at ScienceDirect

Journal of Chromatography A

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

Preconcentration of emerging contaminants in environmental water samples by using silica supported Fe_3O_4 magnetic nanoparticles for improving mass detection in capillary liquid chromatography

Yolanda Moliner-Martínez [a], Antonio Ribera [b,c], Eugenio Coronado [b], P. Campíns-Falcó [a,*]

[a] Departamento de Química Analítica, Facultad de Química, Universidad de Valencia, Dr. Moliner 50, E46100 Burjassot, Valencia, Spain
[b] Instituto de Ciencia Molecular (ICMol), Universidad de Valencia, Catedrático José Beltrán 2, E46980 Paterna, Valencia, Spain
[c] Fundación General de la Universidad de Valencia (FGUV), Amadeu de Savoia n° 4, 46010 Valencia, Spain

ARTICLE INFO

Article history:
Received 12 November 2010
Received in revised form 26 January 2011
Accepted 14 February 2011
Available online 19 February 2011

Keywords:
Magnetic nanoparticles
Emerging contaminants
Capillary LC–MS
Environmental water

ABSTRACT

A magnetic material based on Fe_3O_4 magnetic nanoparticles incorporated in a silica matrix by using a sol–gel procedure has been used to extract and preconcentrate emerging contaminants such as acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen from environmental water samples prior to the analysis with Capillary LC–MS. The use of the proposed silica supported Fe_3O_4 magnetic nanoparticles enables surfactant free extracts for the analysis with MS detection without interferences in the ionisation step. Under the optimum conditions, we demonstrated the reusability of the magnetic sorbent material during 20 uses without loss in the extraction efficiency. In addition, no cleanup was necessary. The preconcentration factor was 100 and the detection limits were between 50 and 150 ng/L. The proposed procedure has been applied to the analysis of water samples obtaining recoveries between 80 and 110% and RSD values lower than 12%. Concentrations of the target analytes over the range 1.7 and 0.1 μg/L have been found in different water samples.

1. Introduction

Development of analytical methodologies for the determination of emerging contaminants in environmental samples has suffered a dramatic progress in recent years. These methodologies are focussed on the evaluation of the occurrence of pharmaceuticals [1,2], personal care products [3,4], hormones [5,6] and other organic compounds [7,8] in environmental water samples. In this sense, special attention has been paid on the determination of pharmaceuticals in waters as they are biological active substances and so they could acted as endocrine disrupters [9–11].

Several analytical methods have been reported in the recent years for pharmaceutical determination in environmental water samples. Generally, these determinations involve a preconcentration step followed by the separation with chromatographic technique [12–18]. Recently, many research studies have been focussed on the development of nanosized adsorbent materials for preconcentration of organic pollutants. Magnetic nanoparticles have become increasingly popular for the development of magnetic sorbents. These sorbents combine the high surface area of nanomateriales with the magnetic properties, so they can be isolated from the solutions simply by applying a magnetic field, this property is especially attractive as high sample volume can be processed [19–21]. Recently, a review dealing with the analytical applications of magnetic nanoparticles has been published [22].

Coating of magnetic NPs with silica is a commonly used procedure to obtain magnetic sorbents owing to its stability and versatility of surface modification [23–27]. In these works the addition of surfactants to assist the extraction of organic compounds is generally necessary. The main drawback of these procedures is the presence of high surfactant concentrations in the extracts, thus the use of MS detection could be limited as surfactant suppressed ionisation of compounds [20]. Therefore, the analysis of environmental organic pollutants is also limited due to the low concentration of these compounds in such matrices. Efforts in order to overcome these problems have been made. For example, hemimicelles of alkylcarboxilate magnetic materials have been successfully used for the determination of PAHs in environmental samples. But, to our knowledge, silica supported magnetic materials to obtain surfactant free extracts have not been developed [20].

Thus, the aim of this paper was (i) the synthesis of a controlled polarity magnetic material based on the use of magnetite nanoparticles (Fe_3O_4-NPs) and cetyltrimethylammonium bromide (CTAB) supported on a silica matrix that allows the surfactant free extracts and (ii) the application of this material for the preconcentration of pharmaceuticals in environmental water samples for

* Corresponding author. Tel.: +34 96 3543002; fax: +34 96 3544436.
E-mail address: pilar.campins@uv.es (P. Campíns-Falcó).

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doi:10.1016/j.chroma.2011.02.036

the subsequent analysis with capillary LC–MS detection. In this work, pharmaceuticals such as acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen have been selected as target analytes in order to evaluate the properties of the synthesised materials.

2. Experimental

2.1. Chemicals

Iron(III)acetylacetanoate ($Fe(acac)_3$), 1,2-hexadecandiol, oleyamine, oleic acid, acetylsalicylic acid, acetaminophen, diclofenac, ibuprofen, tetraethylorthosilicate (TEOS), CTAB, sodium dodecylsulphate (SDS) and phenyl ether were purchased from Sigma–Aldrich (Steinheim, Germany). Methanol and acetonitrile were purchased from Panreac (Barcelona, Spain). Stock standard solutions (100 mg/L) of acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen were prepared in water. Working standard solutions were made by appropriate dilution of the stock standard solutions in water.

2.2. Characterisation measurements

HRTEM images were obtained with a Philips Tecnai F20 equipment operating at 200 kV. The samples were prepared by deposition of a drop of the synthesised material suspension onto a lacey carbon/formvar-coated copper grid. The digital analysis of the HRTEM micrographs was done using Digital Micrograph TM 1.80.70 for GMS1.8.0 Gatan. Atom composition of the material was determined by electron probe microanalysis (EPMA) performed on a Philips SEM XL30 equipped with an EDAX microprobe. IR spectra were recorded with a FT-IR Nicolet 5700 spectrophotometer using powdered samples in KBr pellets. X-ray powder profiles were collected at 293 K with a Siemens D-500 X-ray powder diffractometer equipped with 2.2 kW sealed Cu-K_α radiation source (λ_α = 1.54184 Å), diffracted beam monochromator, rotator sampler and a rotating anode D-max Rigaku at 80 mA and 45 kV. Samples were grounded and mounted on a flat sample plate. Typically, profiles were collected as step scans in the $1^\circ < 2\Theta < 70^\circ$ range with a 0.05° step and 6 s/step.

2.3. Chromatographic analysis.

The capillary chromatographic system used consisted of a LC capillary pump (Agilent 1100 series, Waldbronn, Germany). Chromatographic separation of the analytes was done with a Zorbax SB C18 capillary column 150 mm × 0.5 mm i.d., 5 μm (Agilent). An injection valve with an internal loop of 2 μL was used for direct injection of the analytes into the chromatographic column. Detection was carried out with a UV–Vis diode array detector (Agilent, 1200 series) equipped with a 80 nL flow cell coupled in series with a MS detector (Agilent, 6140 series) equipped with a atmospheric pressure ionisation source electrospray (API-ES). The wavelength was set at 230 nm. The optimal operating parameters for the MS detector in negative ion mode were: drying glass flow 4 ml/min, nebulizer pressure 12 p.s.i. and capillary voltage 3000 V. Single ion monitoring (SIM) was used to quantify the target analytes using external calibration. Previously, full scan mode (SCAN) was used to identify the analytes by matching the retention time and mass spectra with standards. The main mass spectra ions were 137, 150, 205 and 294 for acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen, respectively.

The mobile phase was a mixture of water (solvent A) and acetonitrile (solvent B) in gradient elution mode at a flow rate of 10 μL/min. The gradient program was 30% B during the first 4 min. The acetonitrile content was increased to 50% at 5 min and was constant over the next 10 min. Re-equilibration of the column was done in 2 min after each run. All solvents were filtered through a 0.45 μm nylon membranes (Teknokroma) before use.

2.4. Synthesis of silica supported magnetite nanoparticles

2.4.1. Synthesis of Fe_3O_4 nanoparticles

Organic-phase synthesis of Fe_3O_4 nanoparticles was based on Sun and Zeng procedure [27]. 0.706 g of $Fe(acac)_3$ were mixed with 2.013 g of 1,2-hexadecanodiol, 1.695 g of oleic acid, 1.605 g of oleyamine and 20 mL of phenyl ether under Ar stream (20 min). The mixture was refluxed at 263 °C during 30 min. After cooled to room temperature, 80 mL of ethanol was added to the reaction mixture and centrifugation (10,000 rpm, 10 min) was used to separate the dark-brown material. This material was redissolved in hexane (20 mL) to give 5 nm nanoparticles.

2.4.2. CTAB transfer to obtain water soluble nanoparticles

Water soluble Fe_3O_4 nanoparticles (Fe_3O_4–CTAB) were obtained under different CTAB concentrations, 0.03, 0.06 and 0.1 M. Fe_3O_4 nanoparticles hexane extracts (20 mL) were mixed with 20 mL of 0.03, 0.06 and 0.1 M CTAB solutions, respectively. Water Fe_3O_4–CTAB colloidal solutions with different CTAB content (0.03–0.1 M) were then rotaevaporated until complete elimination of hexane.

2.4.3. Silica supported Fe_3O_4 nanoparticles (Fe_3O_4–SiO_2)

Different magnetic materials were synthesised as function of the Fe_3O_4–CTAB content (10–100% Fe_3O_4–CTAB content, taken into account that the total volume of the solution was kept constant, so the CTAB solution was used to dilute the nanoparticles suspension). 10 mL of Fe_3O_4–CTAB water dispersion was adjusted to pH 11 with NaOH 1 M. Then, 2.10 mL of TEOS was added and stirred overnight. After, the resulted gel was heated at 50 °C during 30 min. The magnetic material was isolated by centrifugation (10,000 rpm, 10 min) and vacuum dried during 24 h to obtain the magnetic sorbent material.

2.5. Extraction and preconcentration procedure

A typical magnetic solid phase extraction was carried out by addition of 30 mg of magnetic sorbent material to 20 mL of standards or water samples. After stirring during 10 min, the magnetic sorbent was isolated from the solution with a Nd disk magnet. The sorbent was air dry to eliminate the excess of water (30 s). The extraction of target analytes was carried out by the addition of 200 μL of methanol to the isolated magnetic sorbent. The extract was isolated from the sorbent with the Nd disk magnet and directly injected into the capillary LC system. Nevertheless, the parameters here indicated were ranged in order to optimise the extraction and preconcentration procedure.

2.6. Analysis of water samples

Six water samples from different water treatment plants effluents along river Jucar (water samples 1, 3 and 6) and Turía (water samples 2, 4 and 5) (Region of Valencia) were analysed. Samples were collected in dark glass containers and stored at 4 °C until analysis.

3. Results and discussion

3.1. Silica supported Fe_3O_4 nanoparticles

The preparation of small Fe_3O_4 nanoparticles with a narrow particle size distribution depends on the reaction media in which

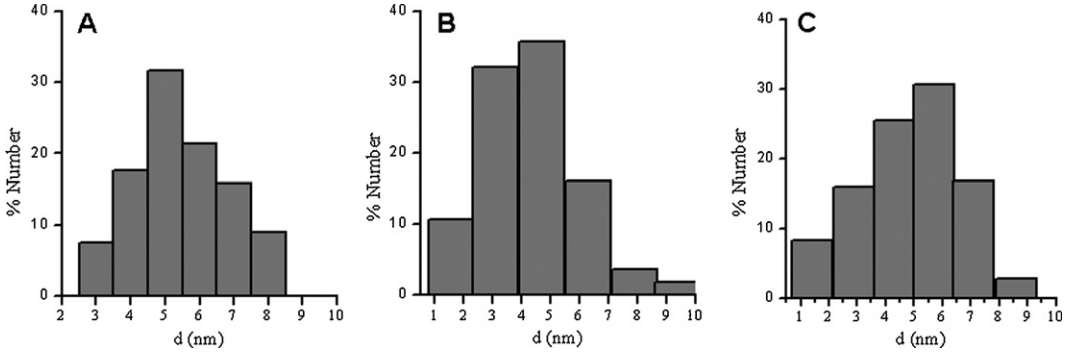

Fig. 1. Size distribution of Fe_3O_4 NPs: (A) in hexane, (B) after CTAB transfer and (C) in the SiO_2 matrix.

the nanoparticles are synthesised. Although aqueous solution syntheses are commonly used with this aim [24–26], the preparation of small monodisperse nanoparticles (<20 nm) has limited success. Recent advances have demonstrated that the preparation of small Fe_3O_4 nanoparticles with a narrow particle size distribution can be reach with organic-phase synthesis [28,29]. In fact is very important to obtain Fe_3O_4 NPs with uniform physical and chemical properties. In particular, this process is based on the reaction of $Fe(acac)_3$ in phenyl ether in presence of hexadecanodiol, oleic acid and oleyamine [27]. These NPs were finally solubilised in hexane. HRTEM has been used to obtain the NPs size and size distribution. Fig. 1A shows size distribution of the synthesised Fe_3O_4–oleate NPs obtained from the HRTEM measurements.

In the second step, Fe_3O_4–oleate NPs were incorporated in surfactant micelles by evaporating the organic solvent (hexane) and following a previously proposed procedure [30,31] used to transfer Fe_3O_4–oleate NPs to aqueous solution. CTAB was selected as surfactant to transfer Fe_3O_4–oleate NPs to aqueous media. CTAB concentrations between 0.1 and 0.03 M were tested. At these CTAB concentrations we did not observe differences in the resulting dispersions. Nevertheless, we expected the presence of two kinds of micelles: CTAB capped Fe_3O_4–oleate NPs micelles (hereafter called magnetic micelles, Fe_3O_4–CTAB and CTAB micelles resulting from the excess of CTAB. Probably, the hydrophobicity of the proposed material will depend on these CTAB micelles, considering that these micelles were not eliminated before the use of the material as sorbent, thus the higher CTAB concentration the higher hydrophobicity of the material. Later, we will discuss the dependence of the CTAB concentration with the sorbent capacity of the magnetic material. Fig. 1B shows the size distribution of the Fe_3O_4 NPs when they are as Fe_3O_4–CTAB. As can be seen the distribution was around 5 nm. In addition, the size distribution did not depend on the CTAB concentration. In summary, the Fe_3O_4–oleate NPs were transferred to water phase by using CTAB. The nonpolar chain of CTAB strongly interacts with the oleate and the hydrophilic parts stabilized the NPs in water [30,31]. In addition, CTAB micelles could be also found in the reaction media.

The last step was the preparation of silica supported Fe_3O_4 nanoparticles (Fe_3O_4–SiO_2) as magnetic sorbent for extraction of emerging contaminants in water samples. The preparation was carried out following a simple sol gel procedure (see Section 2). As previously reported by Fan et al. [31], Fe_3O_4–CTAB and surfactant micelles interact with the oligosilic species formed by TEOS under basic conditions to form a silica matrix containing Fe_3O_4–CTAB and surfactant micelles. The strategy relied on the interaction between both the Fe_3O_4–CTAB with the silanol groups of the silica to form a magnetic silica matrix and the CTAB micelles with the silanol groups providing a hydrophobic material to use it as sorbent for organic compounds in water samples. Fig. 2A shows a simplified illustration of a part of the silica matrix. The mechanisms by the way these NPs are incorporated to the final material would be presumably the same presented by Fan et al. [31]. HRTEM image of the magnetic material is showed in Fig. 2B. This figure shows the silica matrix in which the Fe_3O_4–CTAB NPs are incorporated.

X-ray measurements revealed the amorphous structure of the material. The presence of CTAB was confirmed by FT-IR using the strong band of N–H around 1085 cm^{-1}. Elemental analysis of CHN also confirmed the presence of C and N in the structure of the magnetic material. Notice that CTAB is a structural unit. As suggested by Fan et al. [31], ammonium groups of CTAB are involved in the interaction with silica units, so, the main interaction mechanism between the target analytes and the magnetic sorbent could be attributed to hydrophobic interactions between the alkyl chains of CTAB micelles and so the responsible of the extraction of these organic compounds from water samples.

We also studied the influence of the Fe_3O_4–CTAB content in the material. Percentages of 10, 50 and 100% (percentages referred to the 10 mL of Fe_3O_4–CTAB dispersion used to form the gel) were tested using 0.1 M CTAB. Table 1 shows the elemental analysis for each material. As was expected, the Fe/Si relation increased when the % of NPs increases while the Si/Br relation remains constant. The study of the Fe_3O_4–CTAB content was done as follows: 30 mg of each final material (Fe_3O_4–SiO_2) was added to 20 mL of ultrapure water. After, we tried to completely separate the magnetic material with the Nd disk magnet placed at the bottom of the vial. Only the use of the magnetic material with a Fe_3O_4–CTAB content of 100% allowed the quantitative separation of the sorbent material from the solution. In fact, a content of 10% of Fe_3O_4–CTAB did not show any magnetism.

Finally, we evaluated the influence of the sol–gel procedure on the Fe_3O_4 NPs size by estimating the distribution size of the NPs when using 0.1 M CTAB and 100% of Fe_3O_4–CTAB. Fig. 1C represent the size distribution of Fe_3O_4 NPs inside of the silica matrix. As can be seen, no changes in this parameter were observed.

3.2. Optimisation of the extraction and preconcentration of target analytes

Acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen were selected as target analytes as they are some of the pharmaceuticals of major consumption in Spain. Fig. 3 shows

Table 1
Composition of the magnetic material as function of the Fe_3O_4 content (%).

Fe_3O_4 content (%)	Composition		
	Fe/Si	Fe/Br	Si/Br
10	0.0091	0.2	21
50	0.034	0.8	23
100	0.091	2.1	22

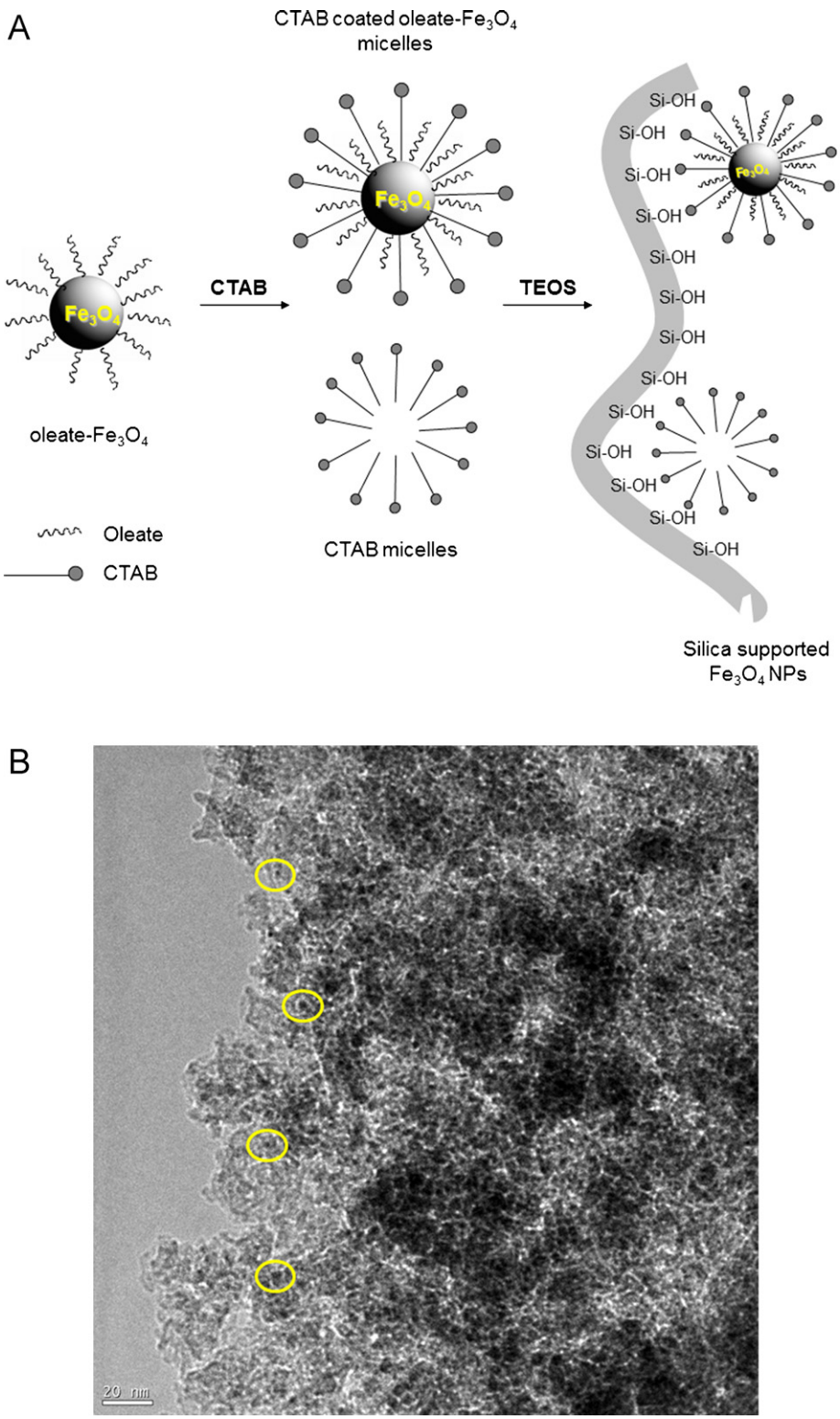

Fig. 2. (A) Schematic illustration of the proposed magnetic sorbent. (B) HRTEM of the magnetic material showing some of the Fe_3O_4 NPs (marked in yellow) supported inside the magnetic material. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

the chemical structures of the target analytes. Being these compounds the most abundant (low μg/L) as revealed several studies [2,31–33]. The extraction efficiency of the magnetic sorbent material was carried out by studying several experimental variables such as type of sorbent, amount of sorbent, extraction time, volume of sample processed, reusability, volume of elution solvent and type of eluent were studied. The extraction efficiency was studied as function of recovery values and with UV detection at 230 nm.

3.2.1. *Type of magnetic sorbent*

We used as sorbent material that with 100% of Fe_3O_4–CTAB obtained from a 0.1 M water solution of CTAB, as this is the only one that can be completely separated from the solution.

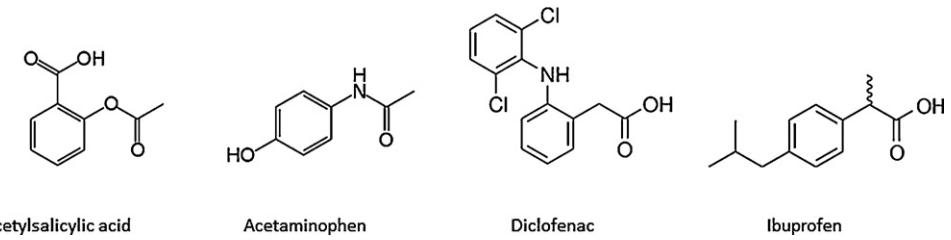

Fig. 3. Chemical structures of the target analytes.

Table 2
Composition of the magnetic sorbents synthesised as function of the CTAB concentration and recoveries obtained after the use of each magnetic material as magnetic sorbent (for more details see the text).

	Microanalysis results			Recoveries (%)			
	Si/Fe	Fe/Br	Si/Br	Acetylsalicilic acid	Acetaminophen	Diclofenac	Ibuprofen
Fe_3O_4 (CTAB, 0.1 M)	12	1.90	24	87 ± 5	89 ± 6	93 ± 4	90 ± 4
Fe_3O_4 (CTAB, 0.06 M)	11	3.80	42	15 ± 2	33 ± 3	31 ± 3	47 ± 2
Fe_3O_4 (CTAB, 0.03 M)	13	4.80	58	–	–	–	29 ± 5

Additionally, we studied the sorbent capacity of the magnetic materials as function of the CTAB concentration. Firstly, we studied the sorption capacity of the magnetic material when 30 mg of the sorbent material were added to a solution containing a mixture of the target analytes (0.5 mg/L). We observed that the analytes were quantitatively adsorbed on the magnetic sorbent material, as the percentages of the analytes in the solution were lower than 4%. In an attempt to elucidate the retention mechanism and to confirm the proposed structure in Fig. 2, we studied the concentration of CTAB (0.1, 0.06 and 0.03 M) in the synthesis of the magnetic material. Table 2 shows the elemental composition of the magnetic materials synthesised as function of the CTAB concentration and the recoveries obtained after the elution of the analytes with 200 μL. Microanalysis confirmed the reduction of CTAB in the material while iron content remains constant. The recoveries obtained showed that a decrease in the CTAB concentration resulted in the lost of the extraction efficiency of the material as this feature has a more pronounced influence with the polarity of the analytes. As has been commented in Section 3.1, the interaction mechanism should be based on hydrophobic interactions between the analytes and aliphatic chains of CTAB micelles while the magnetic micelles are the responsible of the magnetism of the sorbent material. Thus, we synthesised a reversed phase magnetic material that could be used as extracting phase for organic compounds from environmental waters that additionally, provided surfactant-free extracts.

3.2.2. Type and volume of eluent

We also studied the nature of the eluent and the volume. As it was expected, the addition of water to the eluent (methanol) resulted in worse extraction recoveries (from 60 to 70% for all the analytes), even at percentages of 5%. This fact was an additional evidence to confirm the reversed phase interaction mechanism between the analytes and the magnetic material. The volume of the eluent was also studied between 100 μL and 500 μL. Recoveries obtained from the analytes with eluent volumes lower than 100 μL where between 50 and 60% for all the analytes. 200 μL of methanol were selected as eluent volume as recoveries for acetylsalicylic acid, acetoaminophen, diclofenac and ibuprofen were 87 ± 5, 89 ± 6, 93 ± 4, 90 ± 4% (n = 6), respectively. No improvement on the extraction efficiency was observed with higher volumes of eluent.

3.2.3. Volume of sample and amount of magnetic sorbent

Volumes of water between 1 and 200 mL were studied in order to reach the maximum preconcentration factor using 30 mg of magnetic sorbent. The results showed that the recoveries were not affected by the volume of the sample when an amount of water containing a mixture of acetylsalicylic acid, acetoaminophen, diclofenac and ibuprofen (0.5 mg/L) was analysed. Higher volumes could not be processed as the magnetism of the sorbent was decreased due to the high dispersion of the sorbent in the aqueous media. 20 mL was selected as optimal achieving preconcentration factor of 100. The amount of magnetic sorbent was also studied. Table 3 shows the recoveries obtained for the analytes as function of the amount of magnetic sorbent. As can be seen, similar and quantitative recovery values were obtained with 30 and 60 mg. Thus, 30 mg was selected as optimal.

3.2.4. Extraction time

Fig. 4 shows the recovery values as function of the extraction time for each analyte for a mixture of the target analytes at 0.5 mg/L. As can be seen, 10 min provided quantitative recoveries for acetoaminophen, diclofenac and ibuprofen. An increase on the extraction time for acetylsalycilic acid provided better recoveries since it is the more polar compound. Still, we selected 10 min as optimal extraction time since quantitative recoveries (from 86 to 98%) were obtained for all the analytes.

3.2.5. Reusability

Finally, we evaluated the reusability of the magnetic sorbent in different water river samples. The recoveries of acetylsalicylic acid, acetoaminophen, diclofenac and ibuprofen reminded constant after 20 uses of the magnetic support without any treatment. After these uses we observed a lost on the extraction efficiency, with recoveries decreasing down to 60%. This phenomenon was first observed for the most polar compounds. Probably after these uses, CTAB concentration in the magnetic material was altered and so the extracting capacity.

Table 3
Recoveries (%) ± standard deviations obtained in the extraction of analytes with variables amounts of Fe_3O_4/SiO_2 magnetic sorbent.

	Amount of Fe_3O_4/SiO_2 magnetic sorbent (mg)		
	10	30	60
Acetylsalycilic acid	86 ± 4	86 ± 5	95 ± 4
Acetoaminophen	62 ± 5	91 ± 3	91 ± 4
Diclofenac	63 ± 7	90 ± 6	89 ± 5
Ibuprofen	16 ± 3	90 ± 2	94 ± 3

Table 4
Analytical parameters obtained with the proposed method.

	$y=(a\pm s_a)+(b\pm s_b)\times 10^{-3}x$			LOD (ng/L)	RSD (%)			
					5 μg/L		0.5 μg/L	
	$a\pm s_a$	$b\pm s_b$ (μg/L)	R^2		Interday	Intraday	Interday	Intraday
Acetylsalycilic acid	120 ± 60	380 ± 9	0.999	50	7	11	9	12
Acetoaminophen	40 ± 20	47 ± 3	0.997	150	10	14	11	15
Diclofenac	−2400 ± 760	1200 ± 110	0.991	50	6	13	8	15
Ibuprofen	−2 ± 10	880 ± 90	0.990	40	10	12	12	14

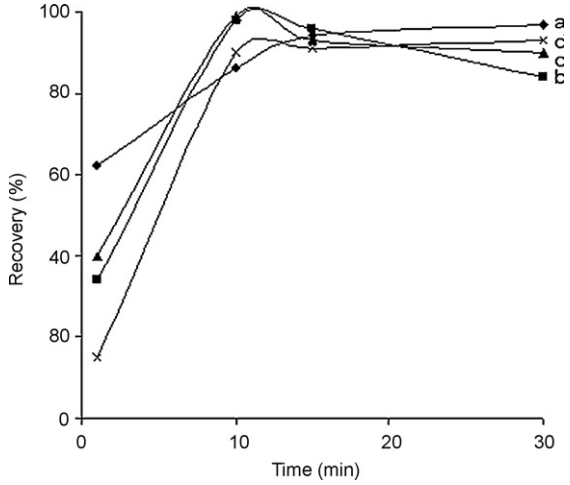

Fig. 4. %Recovery for the target analytes (0.5 mg/L) as function of the extraction time: (a) acetylsalycilic acid, (b) acetaminophen, (c) diclofenac and (d) ibuprofen.

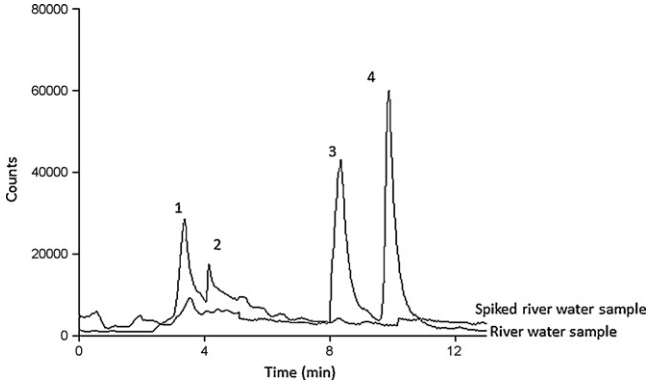

Fig. 5. Chromatograms obtained a water sample 4 and spiked water sample 4 with a mixture of the target analytes (2.5 μg/L). 1: acetylsalicylic acid, 2: acetaminophen, 3: diclofenac and 4: ibuprofen.

3.3. Analytical parameters

Analytical parameters were established under the optimum conditions with MS detection in order to apply the proposed methodology to environmental water samples. Table 4 depicted some figures of merit of the proposed method. Good linearity was observed for all the analytes in the working interval, 1–10 μg/L. Detection limits were obtained experimentally by injecting successive dilutions of a mixture of the analytes. As can be seen, satisfactory detection limits, ng/L, were obtained for the analysis of the target analytes in environmental waters. Precision was evaluated by processing a mixture of the target analytes at different concentration level (2 and 5 μg/L) Table 4 shows the results obtained expressed as inter- and intraday relative standard deviation (%RSD).

3.4. Analysis of water samples

Several water samples from different wastewater treatment plants were analysed on the basis of the impossibility of these plants to completely remove pharmaceuticals from industrial and urban influents and taking into account that the concentrations of these species in the analysed water samples [32].

The evaluation of matrix effect was carried out A recovery study was also carried out. For this aim, water samples were spiked with a mixture of the four analytes (2.5 μg/L). Table 5 shows the recoveries obtained for each analytes in each analysed water sample. Quantitative recoveries (between 87 and 100%) and relative standard deviation between 6 and 11% ($n=3$) were obtained, then, matrix effects were absent. Standard addition method was also applied for sample 1. The slopes of the standard addition method calibration curves were $(400\pm10)\times10^3$, $(48\pm5)\times10^3$, $(1300\pm140)\times10^3$ and $(810\pm100)\times10^3$ concentration expressed in μg/L (R^2 between 0.9985 and 0.9991) for acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen, respectively. The comparison of these slopes with the slopes of the calibration curves with standards for the abovementioned analytes was performed by means of a t-test. Sadistically similar results were obtained for both sloped at 95% confidence level ($t_{0.05,\ 6}=2{,}47$; $t_{calculated}=1{,}77$, 0,18, 2,27 and 1,14 for acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen, respectively, and then matrix effects were absent. The same conclusions were obtained for the other water samples analysed in this work. Therefore, external calibration could be used to quantify these analytes in the analysed samples.

Fig. 5 compares a water sample with the same water sample spiked with the analytes. Table 5 shows the results obtained after

Table 5
Concentration and recoveries obtained for the analysed river water samples.

	Acetylsalycilic acid		Acetoaminophen		Diclofenac		Ibuprofen	
	Mean ± s	R (%)	Mean ± s	R (%)	Mean ± s	R (%)	Mean ± s	R (%)
Sample 1	–	98 ± 8	–	87 ± 7	–	93 ± 5	–	85 ± 4
Sample 2	0.60 ± 0.05	91 ± 8	3.1 ± 0.2	86 ± 7	0.17 ± 0.02	83 ± 10	–	90 ± 4
Sample 3	–	88 ± 5	–	88 ± 7	<lod	89 ± 5	<lod	90 ± 7
Sample 4	0.62 ± 0.06	90 ± 8	–	93 ± 6	–	85 ± 6	<lod	91 ± 6
Sample 5	0.90 ± 0.05	96 ± 6	1.7 ± 0.1	90 ± 5	<lod	94 ± 7	<lod	93 ± 5
Sample 6	–	91 ± 8	–	95 ± 6	–	91 ± 4	0.12 ± 0.01	86 ± 7

–: not detected, <lod: detected below the detection limit. Concentration expressed in μg/L.

Table 6
Characteristics of different recently proposed procedures for the analysis of NSAIDs in environmental water samples.

Sample	Analytes	Pretreatment	Separation/detection technique	LOD (ng/L)	Ref.
Wastewater	Salycilic acid	*SPE* Conditioning (6 mL hexane, 6 mL acetone, 6 mL water) Sample: 1 L Elution (2 mL MeOH, 2 mL acetone), evaporation to 100 μL	LC/MS	15	[2]
	Ketoprofen			28	
	Naproxen			29	
	Diclofenac			5	
	Ibuprofen			43	
	Gemfibrozil			56	
Wastewater	Acetylsalycilic acid	*SBSE* Retention/extraction (25 mL sample 6 h) Separation (clean tweezers) Desorption (5 mL MeOH, ultrasounds) Evaporation to 200 μL	HPLC/DAD	0.8[a]	[33]
River and sea water	Ibuprofen			0.4[a]	
	Diclofenac			0.7[a]	
	Naproxen			1.1[a]	
	Mefenic acid			1.3[a]	
	Gemfibrozil			0.7[a]	
Wastewater	Ibuprofen	*L-L-L ME* Two LLME Extraction with hollow fibers (40 min) Desorption in the acceptor phase Injection 2 μL	HPLC/DAD	100	[34]
	2-(4-Chlorophenoxy)-2-methylpropionic acid			15	
Wastewater	Acetaminophen	*MSPD* (SiO_2–Fe_3O_4) Extraction (1 L of sample + 1 mL Triton X-100, Ultrasonic bath 10 min) Isolation: magnet Desorption (1 mL MeOH, after clean up with 1 mL water) Direct injection	HPLC/DAD	1[a]	[24]
	Naproxen			2[a]	
	Diclofenac			1[a]	
	Ibuprofen			1[a]	
River water	Acetylsalycilic acid	*MSPD* (Fe_3O_4(CTAB)/SiO_2) Extraction (20 mL water) Isolation (magnet) Desorption (200 μL MeOH) Direct injection	Capillary-LC/MS	50	Proposed procedure
	Acetaminophen			150	
	Diclofenac			50	
	Ibuprofen			40	

[a] Unit: μg/L.

analysis of each sample. We found acetylsalicylic acid in three of the samples. Ibuprofen and acetaminophen were found in two samples; in addition the content of acetaminophen was clearly higher than the content of the other analytes. Diclofenac was only found in one sample. The target analytes are commonly consumed by population, especially acetaminophen. Water samples 2, 4 and 5 correspond to three effluents of three water treatment plant in river Turía. The population-equivalents (PE) in these water treatment plants were 213.510, 243.144 and 62.340 for samples 2, 4 and 5, respectively. Those data revealed the high population pressure of these areas and so the contents of the target analytes. The PE for water samples 1, 3 and 6 were 78, 666 and 1435, respectively. Thus, low content of the target analytes were obtained in these water samples. The analytes were not detected in the same samples if UV detection (230 nm) was done, as the detection limits were 3, 8, 2 and 5 μg/L for acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen, respectively.

4. Conclusions

In this work, we have optimised the synthesis of a magnetic material based on Fe_3O_4 NPs supported in a SiO_2 gel. The magnetic adsorbent has been developed by a polarity controlled procedure by means of CTAB addition in the synthetic media. The presence of CTAB in the synthetic route has two functions: to transfer Fe_3O_4 NPs to aqueous media and to form apolar sites into the magnetic material that allowed the chemisorption of organic compounds in the adsorbent. Different extraction and preconcentration techniques have been proposed for the analysis of NSAIDs in environmental waters. Table 6 compares the results obtained with different techniques. Although all these procedures show suitable results, they imply long time consuming pretreatment procedures, and not always with adequate sensitivity to the analysis of these compounds. In addition, the magnetic material previously described, requires the addition of a surfactant to help the adsorption. Such a feature would probably difficult a MS analysis if necessary. The main advantages of the magnetic sorbent proposed in this work are the extraction efficiency without the necessity of addition of other compounds to help to the adsorption (i.e. surfactants), its high adsorption capacity with low amount of the extracting phase, the easy preparation and the reusability of the material (at least 20 extraction can be performed before changing the solid sorbent).

The use of the proposed magnetic material as preconcentration phase shows that the material works as an efficient and selective

preconcentration sorbent for different pharmaceuticals in environmental water samples with a preconcentration factor of 100. The extraction procedure has proved to be simple and rapid since, in addition, clean up was not necessary. The combination of this magnetic solid-phase extraction procedure with capillary LC–MS detection permitted the detection of the target analytes at low ng/L (50–150 ng/L), with RSD values between 6 and 15%. This procedure can be considered matrix-independent as recoveries for spiked water samples were between 85 and 98%. This characteristic allowed the detection and quantification of acetylsalicylic acid, acetaminophen, diclofenac and ibuprofen in different water samples from different water treatment plants.

Acknowledgements

The authors are grateful to the Spanish Ministerio de Ciencia Innovación (projects CTQ 2008-01329/BQU, CTQ 2008-06720, MAT2007-51584 and CSD2007-00010) and to the Generalidad Valenciana (Prometeo Program). Y.M.M expresses her grateful for a JdC research contract.

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