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Determination of non-steroidal anti-inflammatory drugs in sewage sludge by direct hollow fiber supported liquid membrane extraction and liquid chromatography–mass spectrometry

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ABSTRACT

In this study, a three-phase hollow fiber liquid-phase microextraction (HF-LPME) method combined with liquid chromatography–mass spectrometry was developed for direct determination of four non-steroidal anti-inflammatory drugs (ketoprofen, naproxen, diclofenac and ibuprofen) in sewage sludge. The drugs were extracted from non-spiked and spiked slurry samples with different amounts of sludge into an organic phase and then back-extracted into an aqueous phase held in the lumen of the hollow fiber. High enrichment factors ranging from 2761 to 3254 in pure water were achieved. In sludge samples, repeatability and inter-day precision were tested with relative standard deviation values between 10–18% and 7–15%, respectively. Average concentrations of 29 ± 9, 138 ± 2, 39 ± 5 and 122 ± 7 ng/g were determined in dried sludge from Källby sewage treatment plant (Sweden) for ketoprofen, naproxen, diclofenac and ibuprofen, respectively.

1. Introduction

Pharmaceutically active compounds (PhACs) are considered contaminants of emerging concern [1–8]. One of the most consumed groups of PhACs world-wide are non-steroidal anti-inflammatory drugs (NSAIDs) such as ketoprofen, naproxen, diclofenac and ibuprofen, which are used in humans and animals all over the world [5,7]. There is a big concern about their environmental impact because little is known about their possible negative effects and they are continuously introduced into the environment [4,9]. Nowadays, it is well known that one of the most important routes of PhACs into the environment is sewage treatment plants (STPs), either through effluent wastewater or sewage sludge. Some works have studied the occurrence of NSAIDs in wastewater showing that these compounds are not completely removed in STPs [1,3,6,7,9]. In biological treatment, some authors have reported a removal of these compounds at levels ranging from 20 to 90% [7,10]. Two processes can be responsible for this reduction: sorption onto sludge resulting in distribution between solid and aqueous phases [3,7,11–13] or biodegradation [7,14–16].

Sewage sludge is the main solid produced in sewage treatment plants where millions of tons are generated every year. The European Union (EU) promotes the use of sewage sludge as a fertilizer on agricultural land. In 2000 EU published a third draft of a future sludge directive where concentration limit values for some organic contaminants such as organohalogens, surfactants (LAS), phthalates, polyaromatic hydrocarbons, polychlorinated biphenyls, nonylphenol and dioxins were established [17]. Therefore it is important to know the occurrence of contaminants in sewage sludge [1,9,13,17–21]. In some works NSAIDs have been detected in sewage sludge, showing the presence of these compounds at levels of ng/g [4,9,11,22].

Most of the studies on the fate of pharmaceuticals in STPs are focused on liquid samples from sewage treatment plant because of the matrix complexity of sludge. A high number of possible interferences can be co-extracted, therefore it is necessary to remove them applying efficient clean-up techniques. Also, the enrichment of the analytes is an important step since they are detected at trace levels of ng/g in sewage sludge [9,11,18,22]. Several methodologies such as ultrasonic solvent extraction (USE), microwave assisted extraction (MAE) and pressurized liquid extraction (PLE)

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have been applied for the extraction of PhACs from sludge samples. In some cases, these techniques have been combined with solid phase extraction (SPE) for clean-up and concentration enrichment [4,9,11,18,19,22].

An alternative technique for the extraction of organic micro-contaminats in water is hollow fiber liquid-phase microextraction (HF-LPME) which has been shown to provide good clean-up efficiency and high enrichment factors in many applications [23–25]. In addition, HF-LPME compared to other techniques minimizes organic solvent consumption, gives an efficient clean-up and selectivity, needs short analysis time and has a low cost. Using HF-LPME instead of SPE cleaner chromatograms can be obtained [5,26]. There are two different modes of HF-LPME, two-phase and three-phase HF-LPME. In three-phase HF-LPME, which is applied in this work, an organic solvent is immobilized in the pores of the hollow fiber wall and an aqueous phase (acceptor phase) is held in the lumen [23–25]. The analytes are extracted from the aqueous sample through the organic solvent and into the acceptor phase. This is especially useful for acids or bases. The NSAID analytes are acidic compounds and can thus be extracted by applying a pH gradient. Using an acidic sample phase and a basic acceptor phase the analytes can pass through the membrane in protonated, uncharged form to the acceptor phase where acidic compounds are trapped as ions. As the analytes end up in an aqueous solution, liquid chromatography can be applied for the analysis. There are several applications of the determination of NSAIDs and other drugs in wastewater using this technique [5,27–31]. To the best of our knowledge, the use of HF-LPME for the direct determination of NSAIDs in sewage sludge has not been reported. An application of HF-LPME for the determination of SSRIs (selective serotonin reuptake inhibitors) in sewage sludge, by extraction and analysis of an aqueous extract of the sludge was recently published [32]. The objective of the present study was to develop and theoretically describe a simple method based on direct three-phase HF-LPME of a sludge slurry, combined with LC–MS for determination of some NSAIDs in sewage sludge.

2. Material and methods

2.1. Chemicals and standards

Methanol, analytical reagent grade, was obtained from Fisher Scientific (Pittsburgh, PA, USA). Ammonium carbonate (containing 30–33% NH_3), dihexylether (DHE) and sulphuric acid (95–97% pure) were supplied by Fluka (Buchs, Switzerland). Ketoprofen (KTP), naproxen (NPX), ibuprofen (IBP) and diclofenac sodium salt (DCF) were obtained from Sigma Aldrich Inc (St. Louis, MO, USA). Glacial acetic acid, ammonium acetate and formic acid (98–100% pure) were purchased from Merck (Darmstadt, Germany). Reagent water was obtained from a MilliQ water purification system (Millipore, Billerica, MA, USA).

Individual stock standard solutions containing 100 mg/L of ketoprofen, naproxen, diclofenac and ibuprofen were prepared in methanol. Working solutions of ibuprofen alone and a mixture of all four NSAIDs studied were prepared by appropriate dilution of individual stock solutions in reagent water. The standards for calibration curves were prepared by diluting individual stocks in 0.1 M ammonium carbonate. The solutions were stored under refrigeration at 4 °C in darkness. Acceptor buffer solution (0.1 M $(NH_4)_2CO_3$) was prepared by dissolving appropriate amount of the salt in reagent water. This buffer was chosen as an acceptor phase because it is a volatile buffer suitable for ESI–MS.

The extraction was performed by Q3/2 Accurel polypropylene hollow fiber membranes with a thickness of 50 μm (0.1 μm pore size) and an internal diameter of 280 μm (Membrana, Wuppertal, Germany).

The dry weight of the sludge was determined by weighing and drying at room temperature for several days.

2.2. Sampling site and sampling procedure

Källby STP is situated in the city of Lund in southern Sweden and treats the sewage of a population of 84,000. The sewage water undergoes primary sedimentation, biological treatment with activated sludge and finally chemical precipitation of phosphate. The sludge from the biological and chemical treatment steps are returned to incoming water and sludge is only removed from the system during primary sedimentation. After dewatering the sludge is anaerobically digested under mesophilic conditions (37 °C) for 20–30 days whereafter it undergoes further dewatering, resulting in a final product with a dry substance content of approximately 25%. Källby STP produces approximately 5000 tons of sludge each year and since 2009 this sludge is used as a fertilizer in agriculture. In a previous study [33], it was shown that all four NSAIDs occur in incoming sewage water to Källby in concentrations ranging from 0.2 μg/L for diclofenac to 4 μg/L for ibuprofen. The removal efficiency was calculated to 22% for diclofenac, 65% for ketoprofen, 93% for naproxen and 96% for ibuprofen. However, since no analysis of sludge was performed, it was not determined to what extent the removal of the substances is due to adsorption to sludge.

Sampling of the final sludge was performed in October 2009. The samples were collected in plastic bottles and transported to the laboratory. The samples were stored refrigerated in closed bottles at 4 °C until analysis.

2.3. Hollow fiber liquid-phase microextraction (HF-LPME) procedure

Before the membrane extraction an amount of homogeneous sewage sludge (0.5, 1 or 1.5 g) was filled into 50 mL of reagent water and stirred for 17 h (overnight) at 660 rpm to reach equilibrium. Afterwards, some of the slurry samples were spiked at three levels (0.5, 0.8 and 1 ng/mL) and the spiked and non-spiked samples were subjected to the extraction procedure. All experiments were performed with the same sludge with a dry weight of 29.2%.

Hollow fiber liquid-phase microextraction was based on previous work with some modifications [5]. A fiber length of 18 cm was selected to provide a volume of 10 μL of acceptor phase consisting of 0.1 M of ammonium carbonate at pH 9. After cutting the fiber, one of the ends was connected to a syringe (BDM Micro-Fine, Sweden) with needle diameter of 0.3 mm, holding 0.5 mL of acceptor phase and the lumen of hollow fiber was filled with acceptor phase. Next, the fiber was dipped into DHE for 1 min to impregnate the fiber pores and the excess of organic solvent in the lumen was rinsed with 0.3 mL of the remaining acceptor phase in the syringe. Then, the membrane was held by a metal wire and the two ends were folded with a piece of aluminum foil to seal the ends. Excess organic solvent was removed by the immersion of the fiber in reagent water for 30 s and the fiber was immersed into 50 mL of the donor solution adjusted to pH 1.5 with sulphuric acid in glass bottle covered with aluminum foil to prevent photodegradation.

Extraction experiments were carried out using a magnetic stirrer (RO10 power, IKA-Werke, Staufen, Germany) at 660 rpm for several hours and after the extraction the acceptor solution was collected in vials by pushing air through the fiber with a syringe. The final volume of the acceptor phase was about 10 μL and it was directly analyzed by liquid chromatography. In a few cases the signal exceeded the upper limit of the calibration curve, so the acceptor solutions obtained were diluted with 0.1 M $(NH_4)_2CO_3$ prior to analysis.

To compare experiments both enrichment factor (*Ee*) and extraction efficiency (*E*) were used. These are defined as in Eqs.

(1) and (2), respectively:

$$Ee = \frac{C_{Ae}}{C_{Di}} \quad (1)$$

where C_{Ae} is the concentration of a compound in the acceptor solution at equilibrium and C_{Di} is the concentration in the donor solution at the beginning of the extraction.

$$E = \frac{m_{Ae}}{m_{Di}} \times 100\% \quad (2)$$

where m_{Ae} is the amount in acceptor solution at equilibrium and m_{Di} is the amount added in the donor solution.

2.4. LC–ESI–MS analysis

For the determination of NSAIDs in sludge, a LC system composed by two Waters 515 pumps (Waters, Milford, MA, USA), a vacuum degasser, a Triathlon autosampler (Spark–Holland, Emmen, Netherlands), an ODS-2 hypersil (5 μm, 100 × 2.1 mm, (Thermo Scientific, Waltham, MA, USA) column, a C_8 precolumn (Phenomenex, Torrance, CA, USA) and a single quadrupole mass spectrometer (Waters Micromass ZMD) was used, controlled by the software MassLynx NT, ver. 4.2 (Micromass). Chromatographic separation of the four analytes was achieved by an isocratic elution using a mobile phase of 65% of MeOH and 35% of 10 mM ammonium acetate adjusted to pH 4 with acetic acid in reagent water at a flow rate of 0.4 mL/min. The injection was made in "pick-up"-mode with 5 μL of sample followed by 10 μL of mobile phase.

Data acquisition was performed in negative ion mode and MS parameters for the anlaysis were the following: capillary voltage 3.08 kV, cone voltage 9 V, ESI source block temperature 150 °C, desolvation temperature 325 °C, desolvation gas flow 535 L/h. Selective ion monitoring was used to detect ions with m/z ratios of 253, 229, 294 and 205, which correspond to the pseudo-molecular ions of ketoprofen, naproxen, diclofenac and ibuprofen, respectively.

3. Theoretical basis

In three-phase HF-LPME the analytes are extracted from the aqueous sample or donor solution, through the organic solvent to the acceptor phase present inside the lumen of the hollow fiber. After some time, equilibrium of the compound between the acceptor solutions, organic solvent and donor solution is achieved and can be written as:

$$K_{AD} = \frac{C_{Ae}}{C_{De}} = \frac{m_{Ae}.v_D}{m_{De}.v_A} \quad (3)$$

where K_{AD} is the acceptor–donor partition coefficient for the compound, which is determined by the conditions in the donor and acceptor phases [34], C_{De} is the concentration in donor solution at the end of the extraction procedure, m_{De} is the amount in the donor solution at equilibrium, v_D is the volume of the donor solution and v_A is the volume of the acceptor phase.

Moreover, in slurry samples under equilibrium conditions the concentration in the solution is assumed to be proportional to the concentration in the sludge (Eq. (4)).

$$K_{SD} = \frac{C_{Se}}{C_{De}} = \frac{m_{Se}.v_D}{m_{De}.w_S} \quad (4)$$

where K_{SD} is the sludge-donor partition coefficient, C_{Se} is the concentration in the sludge at equilibrium, m_{Se} is the amount in the sludge at equilibrium and w_S is the total amount of sludge. It has to be considered that K_{SD} is not the sludge-water distribution coefficient which is relevant in the environment, since the charge of the NSAIDs as well as ionizable groups in the sludge are pH dependant, so the adsorption pattern observed at pH 2 might not be applicable for environmental or STP conditions where pH is usually around 7.

Table 1
Linear dynamic range, coefficient of determination (R^2), repeatability ($n = 3$) and inter-day precision ($n = 3$) of NSAIDs in LC–MS method.

	R^2	Repeatability (%)	Inter-day precision (%)
Ketoprofen	0.991	1.9	17
Naproxen	0.994	2.5	14
Diclofenac	0.992	0.5	19
Ibuprofen	0.993	7	13

Moreover, at pH below 2, a change in the properties of sludge such as color, smell and physical appearance is observed [11].

In this work, a mass balance between the initial and final amount of each compound in the whole system is used for determination of the initial concentration of the compound in sewage sludge:

$$m_{Si} + m_{Di} = m_{Se} + m_{De} + m_{Ae} + m_{Me} \quad (5)$$

where m_{Si} is the initial amount of the compound in the sludge and m_{Me} signifies the amount of the compound in the membrane liquid.

According to Eqs. (3) and (4), m_{Ae}, m_{De}, m_{Se} and m_{Me} can be related as:

$$m_{Ae} = C_{Ae} \cdot v_A \quad (6)$$

$$m_{De} = \frac{m_{Ae} \cdot v_D}{K_{AD} \cdot v_A} \quad (7)$$

$$m_{Se} = \frac{m_{De} \cdot w_S \cdot K_{SD}}{v_D} \quad (8)$$

$$m_{Me} = \frac{m_{De} \cdot v_M \cdot K_{MD}}{v_D} \quad (9)$$

where K_{MD} is the partition coefficient between the membrane liquid and the water sample (donor) in analogy with Eq. (4) and v_M is the volume of the membrane liquid.

Combined with Eq. (5) we get:

$$m_{Si} + m_{Di} = C_{Ae} \cdot v_A \cdot \left(1 + \frac{K_{SD} \cdot w_S}{K_{AD} \cdot v_A} + \frac{v_D}{K_{AD} \cdot v_A} + \frac{K_{MD} \cdot v_M}{K_{AD} \cdot v_A}\right) \quad (10)$$

which can be written as:

$$C_{Ae} = \frac{m_{Di}}{A} + \frac{m_{Si}}{A} \quad (11)$$

$$A = \left(v_A + \frac{K_{SD} \cdot w_S + v_D + K_{MD} \cdot v_M}{K_{AD}}\right) \quad (12)$$

Thus, the initial amount of the compound in the sludge can be predicted if Eq. (11) is used to plot a calibration curve with the spiked m_{Di} as x and the measured C_{Ae} as y. Then the amount of the compound in the sludge (m_{Si}) can be obtained as the intercept divided by the slope of the line.

From the observed value of the slope ($1/A$) it should be possible to calculate K_{AD}, K_{MD} and K_{SD}. However, this demands the knowledge of the conditions in the membrane phase. This issue will be addressed in a later work.

4. Results and discussion

4.1. LC–MS method development

For chromatographic analysis by LC–MS, linearity was assessed by using standard solutions ranging from 0.15 to 0.8 mg/L with an upper limit of 1 mg/L. Calibration curves were constructed for each compound with R^2 >0.99, see Table 1. A chromatogram of reagent water spiked at 0.4 mg/L is shown in Fig. 1. LODs and LOQs were calculated as 3 and 10 times the background noise with values about 10 and 33 μg/L, respectively for ketoprofen, naproxen, diclofenac and ibuprofen. The repeatability and inter-day precision for each compound are shown in Table 1.

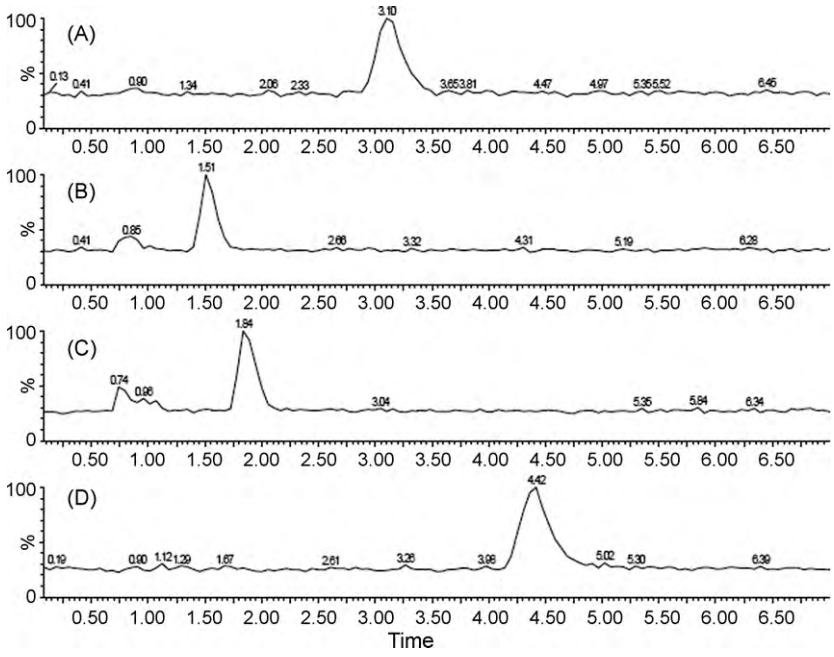

Fig. 1. Single ion monitoring (SIM) chromatograms obtained by LC–MS from reagent water spiked at 0.4 mg/L. (A) m/z = 294 (diclofenac), (B) m/z = 253 (ketoprofen), (C) m/z = 229 (naproxen) and (D) m/z = 205 (ibuprofen).

4.2. Extraction of ibuprofen alone

4.2.1. Extraction time

In order to test the influence of the extraction time, reagent water spiked at 1 μg/L of ibuprofen and sludge slurry samples with 1% of sludge spiked at 1 μg/L of ibuprofen were extracted during different times between 1 and 8 h. As can be seen in Fig. 2, the enrichment factor increased from 1 to 2 h while no increase was observed afterwards indicating that equilibrium was attained. After 5 h the enrichment decreases, as the stability of the extraction system deteriorates. This could be due to loss of organic membrane liquid or to pH changes in the acceptor. The extraction time chosen for further experiments was 3 h with average enrichment factors of 3052 and 1363 times for reagent water and sludge slurry, respectively. The decrease of the enrichment factor in sludge slurry is supposed to be due to sorption of the analyte by the sludge particles.

In reagent water the average extraction efficiency was 67% and for the acceptor–donor partition coefficient (K_{AD}) a value of 7821 was obtained. This value was calculated from Eq. (3) assuming that the influence of the membrane liquid can be neglected.

4.2.2. Analytical performance

Under the conditions mentioned, the performance of HF-LPME extraction was evaluated with reagent water spiked at three different levels (0.5, 0.8 and 1 μg/L) with an extraction time of 3 h. Good linearity (R^2 = 0.9939) was obtained with a repeatability (n = 2) and inter-day precision (n = 3) of 3% and 5%, respectively, while for 1% slurry samples values of 3% and 10%, respectively, were obtained.

4.2.3. Concentration in sludge

The developed method was applied for the determination of the concentration of ibuprofen in sewage sludge. For this purpose, different amounts of the analyte were added to slurry samples with three different quantities of sludge (1, 2 and 3%, corresponding to 0.5, 1.0 and 1.5 g wet weight, respectively). The results obtained can be observed in Fig. 3, showing that when the amount of sludge increased, a decrease of concentration in acceptor phase was found. It can be observed that for reagent water (0% sludge) the extraction efficiency was higher than for sludge. For each amount of sludge a linear regression between the amount spiked and the concentration obtained in the acceptor can be found as expected from Eq. (11).

In Table 2, coefficients of determination are presented with values higher than 0.88. Also, the values of the slope and intercept are shown with an intercept close to 0 for reagent water and practically equal intercepts for the sludge samples. By applying Eq. (11), the initial amount of ibuprofen was calculated for each amount of

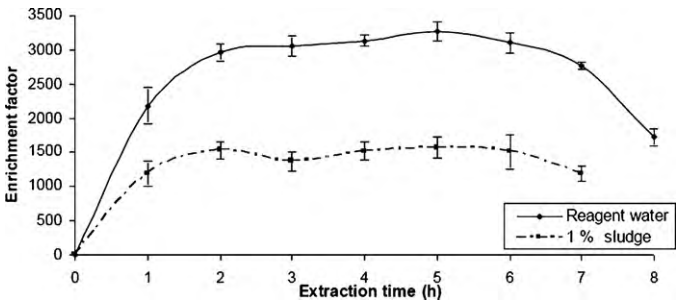

Fig. 2. Extraction time profiles for ibuprofen in spiked reagent water and sludge slurry samples with 1% of sludge at a concentration of 1 μg/L. Standard deviations (n = 2) are marked.

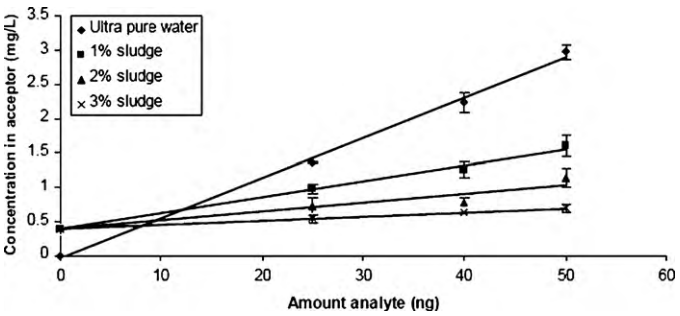

Fig. 3. Concentration of analyte (ibuprofen) obtained in the acceptor phase as a function of the amount of analyte added in the slurry sample for different quantities of sludge. Standard deviations (n = 2) are marked.

Table 2
Coefficient of determination (R^2), slope and intercept for the regression lines in Fig. 3, m_{Si}, C_{Si} and average C_{Si} with standard deviation (RSD).

Sludge (%)	R^2	Slope	Intercept	m_{Si} (ng)	C_{Si} (ng/g)	Average C_{Si} (ng/g)
0	0.994	0.0598	−0.055			
1	0.992	0.0233	0.3922	17	34	36 ± 7 (20%)
2	0.884	0.0129	0.3923	30	30	
3	0.999	0.0060	0.3971	66	44	

Table 3
Average enrichment factor (*Ee*), extraction efficiency (*E*) and acceptor–donor partition coefficient (K_{AD}) for NSAIDs extracted from reagent water ($n = 2$).

	Ee	*E* (RSD) (%)	K_{AD}
Ketoprofen	3158	61 (8.5%)	8569
Naproxen	2761	53 (10.1%)	6164
Diclofenac	3254	62 (9.7%)	9318
Ibuprofen	2989	57 (8.7%)	7433

sludge added, giving three values and the average concentration in wet sludge was 36 ng/g with a relative standard deviation of 20%.

4.3. Extraction of four NSAIDs

4.3.1. Extraction time

Fig. 4 shows the influence of the extraction time on the enrichment factor for all NSAIDs chosen. The extraction was carried out with reagent water spiked at 1 μg/L. The analysis was made with LC–MS as described above. Optimum enrichment factors were obtained after 3 h for naproxen, diclofenac and ibuprofen while for ketoprofen the maximum value was achieved after 5 h. However, during prolonged extraction time a decrease of the stability of the system was observed, consequently an extraction time of 4 h was selected.

In spiked reagent water the average *Ee* values for all studied compounds ranged from 2761 to 3158 (Table 3). In Table 3 the extraction efficiency is shown with values between 53 and 62%. Acceptor–donor partition coefficients are also shown. These are calculated from Eq. (3) assuming that the influence of the membrane liquid can be neglected.

4.3.2. Analytical performance

To evaluate the hollow fiber technique for ketoprofen, naproxen, diclofenac and ibuprofen after 4 h of extraction, repeatability and inter-day precision in reagent water and slurry samples at 1% of sludge were tested (Table 4). Values for repeatability and inter-day precision were 2.5–12 and 6–12% for reagent water and 10–18% and 7–16% for sludge slurry at 1%, respectively.

Table 4
Method repeatability and inter-day precision ($n = 2$) as standard deviations for reagent water and slurry spiked at 1 μg/L.

	Repeatability (%)		Inter-day precision (%)	
	Reagent water	1% sludge	Reagent water	1% sludge
Ketoprofen	2.5	14.0	11.7	6.8
Naproxen	7.1	17.7	7.9	9.2
Diclofenac	12	9.7	8.7	15.5
Ibuprofen	5.3	10.3	5.8	10.7

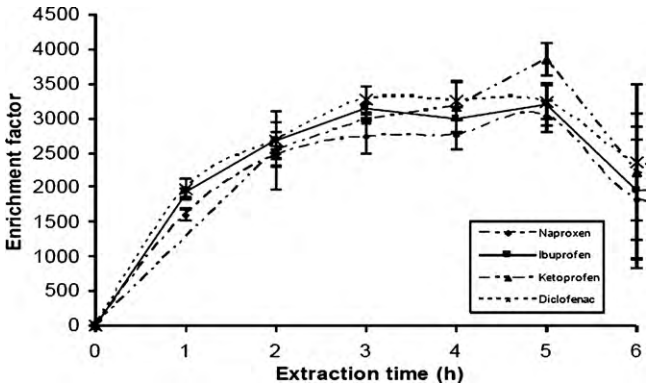

Fig. 4. Extraction time profiles for spiked reagent water at analyte concentrations of 1 μg/L. Standard deviations ($n = 2$) are marked.

4.3.3. Concentration in sludge

Similar correlations as shown in Fig. 3 were obtained with different amounts of sludge at two different spike levels for the four NSAIDs. In non-spiked samples ketoprofen was not detected, therefore a straight line for that compound was obtained using only 2 points. For the other compounds R^2 was better than 0.965. The relative standard deviations of the concentrations in acceptor phase range from 2 to 15%, 12 to 18%, 2 to 15% and 6 to 14% for ketoprofen, naproxen, diclofenac and ibuprofen, respectively.

The average concentrations detected in sludge are given in Table 5. For naproxen in slurry samples with 2% sludge a technical problem with the LC–MS occurred, for these reasons corresponding values are not shown in Table 5. It should be noted that the result for ibuprofen is very similar to the one obtained when ibuprofen was determined without other NSAIDS (see Section 4.2.3). Finally, the concentrations of these compounds in dried sewage sludge are calculated.

Earlier reported data regarding occurrence of NSAIDs in digested sludge from other Swedish STPs [35] show concentrations in the range: 4–77 ng/g d.w. for diclofenac, 4–560 ng/g d.w. for ibuprofen, 5–580 ng/g d.w. for ketoprofen and 3–350 ng/g d.w. for naproxen. Other studies [4,9,11,18,22] show concentrations in the same

Table 5
m_{Si}, C_{Si} and average C_{Si} with standard deviation of NSAIDs found in wet sewage sludge ($n = 3$, for naproxen $n = 2$).

Substance	Sludge (%)	m_{Si} (ng)	C_{Si} (ng/g)	Average C_{Si} (ng/g)	Concentration in dry sludge (ng/g d.w.)
Ketoprofen	1	5.7	11.5	9 ± 3 (30%)	29 ± 9 (30%)
	2	6.7	6.7		
	3	11.3	7.5		
Naproxen	1	20	40	40.4 ± 0.6 (1.4%)	138 ± 2 (1.4%)
	3	61	40.8		
Diclofenac	1	5.1	10.2	12 ± 1 (11.5%)	39 ± 5 (11.5%)
	2	12.9	12.9		
	3	16.9	11.3		
Ibuprofen	1	16.9	33.7	36 ± 2 (5.6%)	122 ± 7 (5.6%)
	2	37.7	37.7		
	3	53.3	35.5		

ranges. The values obtained in this study lie well within these ranges, however it has to be noted that the ranges of these literature values are very wide. This could however be attributed to differences in the treatment processes at the different STPs investigated or perhaps in the analytical methods applied. It definitely underlines the need for further investigations of the pharmaceutical content of sludge, a process in which the simple method developed in this study could aid. Several tonnes of sewage sludge are today spread on farmland each year and precise and accurate measurements of its pharmaceutical content is a crucial parameter in conducting high quality risk assessments of this use.

5. Conclusions

A new and direct method for the determination of some NSAIDS in sewage sludge was developed. Hollow fiber liquid-phase microextraction was applied successfully as an extraction and clean-up technique for acidic compounds. High enrichment factors, about 3000 times, were obtained for all analytes in reagent water.

The developed method allows the application of water for the extraction of the analytes from sewage sludge and the quantification of ketoprofen, naproxen, diclofenac and ibuprofen using an equilibrium system. Different amounts of sludge were used and the same concentration was found in all cases. Concentrations about 29, 39, 122 and 138 ng/g d.w. were measured for ketoprofen, diclofenac, ibuprofen and naproxen, respectively.

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