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Simultaneous quantification of neutral and acidic pharmaceuticals and pesticides at the low-ng/l level in surface and waste water

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Abstract

A new analytical method is presented that allows simultaneous determination of neutral and acidic pharmaceuticals and pesticides in natural waters. The compounds investigated include frequently used pharmaceuticals, i.e., the anti-epileptic carbamazepine, four analgesic/anti-flammatory drugs (ibuprofen, diclofenac, ketoprofen and naproxen) and the lipid regulator clofibric acid and important pesticides including triazines, acetamides and phenoxy acids. Sample enrichment was achieved in one step with a newly developed solid-phase extraction procedure using the Waters Oasis HLB sorbent. The neutral compounds were analyzed by GC–MS in a first step, and then the acidic compounds after derivatization with diazomethane. Relative recoveries using isotope labeled internal standards were between 71 and 118% and the detection limits were in the range of 1 to 10 ng/l in drinking water, surface water and waste water treatment plant effluents (precision: 1–15%). The developed analytical method proved to be very durable during a 3-month field study and the target analytes were detected in concentrations of 5–3500 ng/l in waste water treatment plant effluents, river water and lake water.

Keywords: Water analysis; Environmental analysis; Pharmaceuticals; Pesticides; Carbamazepine; Profens; Naproxen; Diclofenac; Clofibric acid

1. Introduction

Pharmaceuticals are used for humans and animals (e.g., live stock production) and pesticides are used in agriculture and as material protection agents in textiles and coatings, etc. Therefore, both compound classes may enter the aquatic environment through waste water effluents and/or, e.g., surface run-off and are found in waste water, surface waters and drinking water. Due to their biological activity they are of great environmental concern [1–7] and the concentrations, and the fate and behavior (e.g., transport and degradation processes) of these chemicals in natural waters must be known and quantified. To quantitatively evaluate the fate of these chemicals for a proper risk assessment and to monitor the drinking water quality, a trace analytical method at the low-ng/l level with high precision is a prerequisite. Our aim was to develop an analytical method, which allows the simultaneous quantification of pharmaceuticals and pesticides in natural waters and waste water at the low-ng/l level. A single method of analysis for these various compound classes would have several advantages, such

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as a shorter overall analysis time, reduced field sampling and cost reduction for drinking water suppliers and other institutions concerned with the quality of the aqueous environment.

To date, many multi-residue analytical methods for determination of pollutants in an aqueous environment have been described in the literature [1,8–12]. Previously, we described the quantification of a wide range of neutral and acidic pesticides with gas chromatography–mass spectrometry (GC–MS) after their sequential elution from graphitized carbon black and derivatization of the acidic fraction with diazomethane [8]. Ternes and co-workers published various analytical methods with both GC–MS(–MS) and LC–MS(–MS) in combination with either polymer-based or octadecylsilica solid-phase extraction (SPE) sorbents for the analysis of pharmaceutical compounds [5,9,10]. However, the analytical methods described above exclusively focus on either pesticides, pharmaceuticals or their sub-classes.

In addition, these methods require separate and time-consuming sample pre-treatment for neutral and acidic compounds. Many frequently used pharmaceuticals and pesticides show rather similar physico–chemical properties and are present in the same sample allowing their simultaneous sample pre-treatment and analysis.

To develop a multi-residue analytical method for neutral and acidic pharmaceuticals and pesticides we have selected a representative set of commonly used compounds including the pharmaceuticals carbamazepine (anti-epileptic), the commonly used analgesic/anti-flammatory drugs ibuprofen, diclofenac, ketoprofen and naproxen and the lipid regulator clofibric acid, the widely used pesticides atrazine, simazine, terbutylazine, terbutryne, metolachlor, dimethenamide, tebutam, 2,4-D, (2-methyl-4-chlorophenoxy)acetic acid (MCPA), triclopyr and mecoprop, and irgarol, an anti-fouling agent for ship hulls and construction materials (for structures see Fig. 1). Note that the pharmaceutical clofibric acid is the active metabolite of clofibrate (and two other lipid regulators etofibrate and theofibrate), formed after hydrolyzation of the ester group shortly after ingestion [2,4].

The neutral and acidic target compounds (see Fig. 1) can be enriched on solid phases exhibiting Van der Waals and H-donor–H-acceptor interactions [13,14]. An example of such a material is graphitized carbon [8,13–15], however, its bad wet-ability is a drawback especially in trace routine analysis. Recently, the Oasis HLB sorbent (a polystyrene–divinylbenzene–*N*-vinylpyrrolidone terpolymer) with hydrophilic and lipophilic characteristics has been introduced [13,16]. The excellent wetting properties of the Oasis sorbent are provided by the hydrophilic *N*-vinylpyrrolidine monomer. ''Running dry'' of the cartridge has no negative effect on the analyte recovery, because the Oasis sorbent is instantly ''water wettable'' [17]. The lipophilic polystyrene–divinylbenzene provides the Van der Waals and the H-donor–H-acceptor interactions to trap the target compounds. After enrichment, the neutral compounds can directly be analyzed by GC–MS. After these measurements the acidic compounds can be derivatized with diazomethane.

Also, to achieve the required analytical performance for studying the fate and the mass fluxes of the target compounds into the environment, i.e., through waste water effluents and/or surface run-off into surface waters of the compounds, quantitatively, we have used several isotope labeled internal standards, i.e., [$^{2}H_{5}$]atrazine (atrazine-d_5), [$^{13}C_{6}$]metolachlor, [$^{2}H_{3}$]dimethenamide (dimethenamide-d_3), [$^{2}H_{3}$]mecoprop (mecoprop-d_3), [$^{2}H_{3}$]MCPA (d_3-MCPA) and for carbamazepine the structurally similar compound dihydrocarbamazepine.

In this paper, we present a new analytical method with SPE–GC–MS for the quantification of regularly used neutral and acidic pharmaceuticals and pesticides in various water matrices. Special attention was paid to the durability of the SPE method for routine trace analysis of the analytes in natural waters and waste water. The method was employed in a 3-month field study for the determination of these compounds in lake water, river water and waste water treatment plant effluents. The excellent performance of the analytical method even at low-ng/l concentrations showed that this method is a powerful tool for multi-residue analysis of pharmaceuticals and pesticides.

2. Experimental

2.1. Chemicals and materials

Carbamazepine, clofibric acid, ibuprofen, keto-

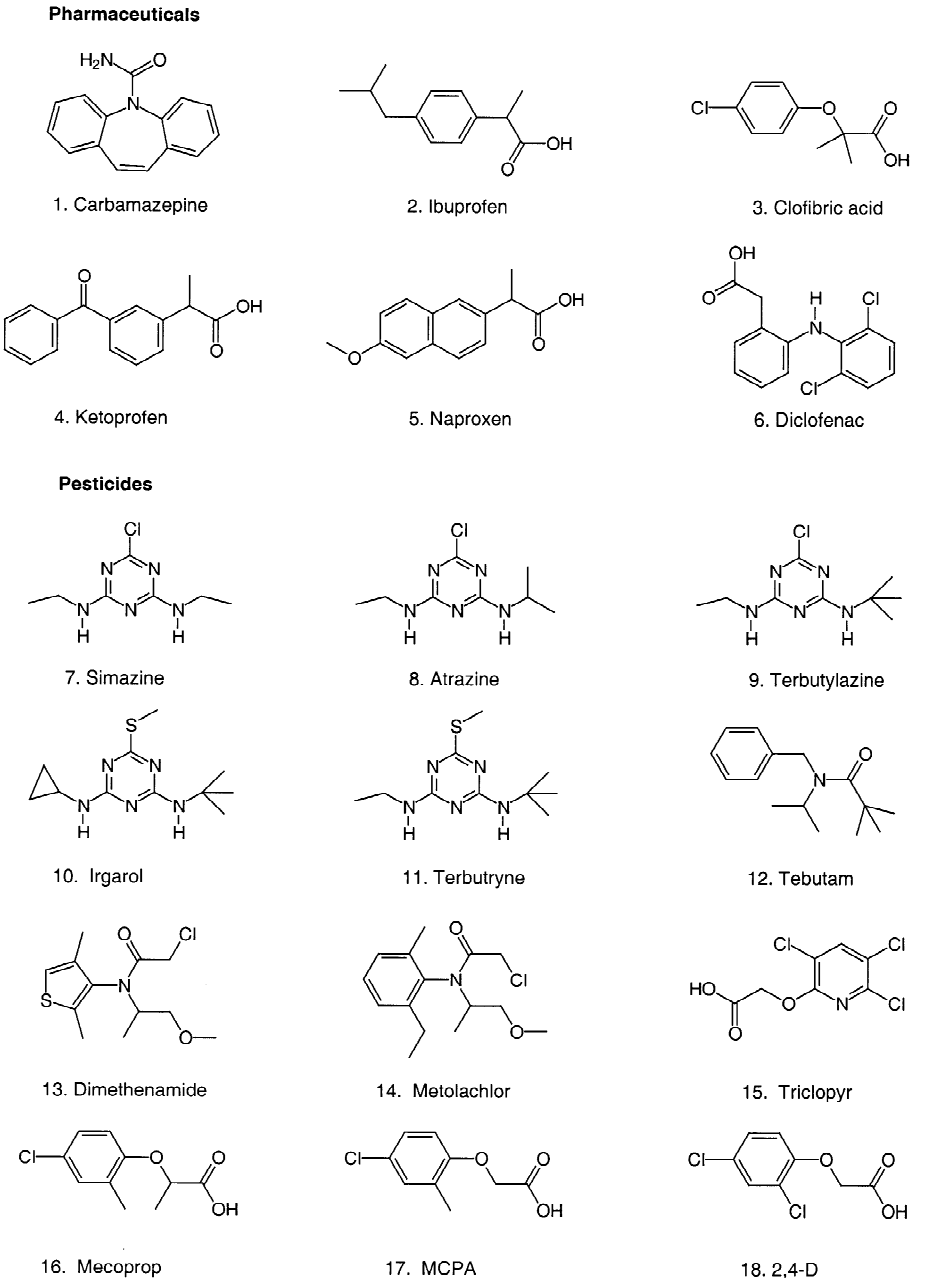

Fig. 1. Structures of the investigated compounds: neutral pharmaceuticals (1) and acidic pharmaceuticals (2–6), neutral pesticides (7–14) and acidic pesticides (15–18).

profen and diclofenac were all purchased from Sigma–Aldrich (Steinheim, Germany). Naproxen was obtained from Fluka (Buchs, Switzerland). Dimethenamide was obtained from Sandoz Agro (Basel, Switzerland) and Irgarol from Ciba (Basel, Switzerland). All other pesticides were obtained from Riedel-de Haën (Seelze, Germany). Dihydrocarbamazepine was obtained from Alltech Applied Science Labs. (State College, PA, USA). Ring labeled [$^{13}C_6$]metolachlor and atrazine-d_5 were

obtained from Cambridge Isotope Labs. (Andover, MA, USA). Mecoprop-d_3 and MCPA-d_3 were obtained from Dr. Ehrensdorfer Lab. (Augsburg, Germany). Dimethenamide-d_3 was kindly supplied by Monsanto Europe (Louvain-la-Neuve, Belgium). Ethyl acetate (EtOAc), methanol (MeOH) and dichloromethane (CH_2Cl_2) were all of HPLC grade (Fluka). Other common chemicals were purchased from Merck (Darmstadt, Germany). Nitrogen and helium gas were supplied by Carbagas (Rümlang, Switzerland).

2.2. Sampling and sample preparation

Water samples were collected from Lake Greifen (Greifensee), its main tributaries Aa and Aabach and the waste water treatment plant (WWTP) effluents of the communities of Maur, Uster and Mönchaltdorf (Switzerland). Lake Greifen water samples were collected using a Niskin bottle (General Oceanics, Miami, FL, USA), a cylindric, metallic box which allows collection of representative water samples at various depths. The water samples were then transferred into 1-l glass bottles. After collection, the water samples were immediately filtered in the laboratory with the high-pressure filtration equipment MD142-5-3 (Schleicher & Schuell) using regenerated cellulose filters RC 55 (pore size 0.45 μm, diameter 142 mm; Schleicher & Schuell). In most cases collection and filtration of the water samples and sample enrichment could not be completed at the same day. In that case the filtered water samples were kept in the dark overnight at 4°C and sample enrichment was carried out the next day.

Before SPE water samples were allowed to reach room temperature and the pH was adjusted to pH 3 to enhance trapping of the acidic compounds on the SPE sorbent. Finally the water samples were spiked with a mixture of internal standards. For recovery studies and/or internal calibration, Nanopure, surface water (Lake Greifensee) and waste water samples were spiked additionally with a standard mixture of the investigated compounds. Samples were shaken vigorously after spiking.

2.3. Solid-phase extraction

Commercially available 3-ml SPE cartridges with 60 mg Waters Oasis HLB sorbent (Waters, Bergen op Zoom, The Netherlands) were used as received. SPE was performed using a 12-fold vacuum extraction box (Supelco, Bellefonte, PA, USA).

The SPE cartridges were conditioned subsequently with 2 ml elution solvent, 2 ml MeOH and 3 ml Nanopure water. Extraction of the 1-l samples was carried out under vacuum at a flow-rate of approx. 15 ml/min. After sample loading, the cartridge was washed with 1 ml MeOH–water (10:90, v/v) and subsequently air-dried for 30–60 min. The analytes were eluted with 6 ml of EtOAc–acetone (50:50, v/v). The eluates were collected in 7.5-ml conical glass vessels (Supelco). The elution volume was then reduced under a stream of nitrogen to about 300 μl. In order to control the water content of the eluate, 50 μl hexane was added to the eluate. If small amounts of water were still present in the eluate, observable by becoming a turbid solution, sodiumsulfate was added to dry the eluate additionally. Then the eluate was transferred carefully into another conical vessel in order to eliminate the Na_2SO_4 from the eluate. Note that if the Na_2SO_4 is not removed adequately from the eluate, this may lead to plugging of the needle during injection of the sample into the GC system. The eluate was further concentrated by nitrogen gas flow to a final volume of approximately 150 μl. Finally, the extract was transferred into a GC vial (500 μl; Supelco).

2.4. Derivatization of the acidic compounds

The acidic compounds were derivatized by adding about 800 μl diazomethane to the eluate. *Caution: Diazomethane is carcinogenic and explosive, all handling of diazomethane should be done with great care and inside a hood*. The analytes were allowed to react for 30 min and the volume was reduced to approx. 150–200 μl.

2.5. Analytical procedure

After elution from the cartridge and volume reduction of the elution solvent, the neutral compounds were determined by GC–MS in a first step. After these measurements, the acidic pharmaceuticals and pesticides were derivatized with diazomethane in the same extract and analyzed again by

GC–MS in a second step. Although it is possible to separate and determine both the neutral and acidic analytes in a single chromatographic run, simultaneous derivatization and analysis of both the neutral and acidic analytes is not advisable, because reduced recoveries were observed for several neutral substances. Note that it is also possible to split the extract into two equal fractions (which would lead to higher detection limits). One fraction can be analyzed directly for neutral compounds, the other fraction can be derivatized for GC–MS analysis of the acidic analytes.

2.6. Instruments

The GC–MS system consisted of a HRGC 8060, a MD 800 mass spectrometer and an auto-sampler A200S, all from Fisons Instruments (Beverly, MA, USA). Helium was used as carrier gas (flow 1.5 ml/min). A fused-silica column RTX-5MS (DB5 equivalent, 30 m×0.25 mm I.D., d_f=0.25 μm) was purchased from BGB Analytik (Anwil, Switzerland). A deactivated pre-column (2.5 m×0.32 mm I.D.) and transfer capillary (1.5 m×0.18 mm I.D.) were installed for protection of the analytical column. Injection was performed with a split/splitless injector at a temperature of 250°C. Splitless time was 1 min. Injection volume was 2 μl.

The GC oven was programmed as follows: 1 min at 90°C, first ramp 15°C/min to 150°C, 15 min at 150°C, second ramp 5°C/min to 200°C, 5 min at 200°C, third ramp 15°C/min to 290°C, 6 min at 290°C. The total analysis time for one GC run was approximately 47 min. The GC–MS interface temperature and ion source was kept at 290°C and 220°C, respectively.

The mass spectrometer was run in the positive electron impact mode at 70 eV. Single ion monitoring (SIM) was used to identify the compounds (m/z: see Table 1). Dwell times varied from 0.05 to 0.2 s depending on the selected monitored masses for each compound and the amount of compounds in each SIM window.

2.7. Recoveries and calibration

For the determination of absolute recoveries, the water samples were spiked with the analytes (100–200 ng/l) before the SPE and the internal standards were spiked into the SPE eluate just before GC–MS analysis (or just before derivatization for the acidic compounds). For relative recoveries, the water samples were spiked with both the analytes and internal standards before SPE. A calibration with standard solutions in EtOAc was used for quantification of the absolute and relative recoveries.

3. Results and discussion

3.1. SPE method development

The published standard SPE procedure with Oasis HLB sorbent consists of the conditioning of the sorbent with 1 ml methanol and 1 ml water, the sample loading, the washing of the cartridge with 1 ml water–MeOH (95:5, v/v) and finally the elution with 1 ml MeOH [16,17]. Preliminary experiments with this standard procedure using MeOH as an elution solvent showed absolute recoveries much less than 100% for a few of the compounds, i.e., ketoprofen, diclofenac and carbamazepine. Therefore, solvents with a higher elution strength, i.e., solvent mixtures of EtOAc–MeOH and EtOAc–acetone were evaluated. The results of these experiments revealed satisfactory absolute recoveries for all compounds (all above 60%) except for carbamazepine (recoveries between 45 and 65%). The EtOAc–acetone (50:50) elution solvent mixture revealed the best recoveries for all compounds. Other considerations favoring the choice for the EtOAc–acetone (50:50) solvent were the low toxicity of both solvents and the easy removal of acetone by nitrogen flow when reducing the elution volume for further sample concentration.

In a second series of experiments the methanol content in the wash solvent was optimized to obtain maximum benefit from ‘‘solvent’’ drying without eluting the analytes during the washing step. We found that percentages of up to 20% MeOH in the washing solvent do not affect analyte recoveries. Even the quite polar lipid regulator clofibric acid and the herbicide mecoprop were completely retained. Significant analyte loss occurred for all analytes,

Table 1
Absolute and relative recoveries (standard deviations in % are given in parentheses) and GC–MS parameters (retention times, monitored masses and used internal standards) for pharmaceuticals and pesticides[a]

Analyte	Retention time (min)	*m/z* for SIM[b]	Internal standard	Absolute recovery (%)			Relative recovery (%)		
				Nanopure (n=4)	Lake Greifensee (n=4)	WWTP (n=4)	Nanopure (n=4)	Lake Greifensee (n=4)	WWTP (n=4)
Pharmaceuticals									
Neutral compounds									
Carbamazepine	45.3	193, *236*	DHC[c]	65 (9)	57 (15)	46 (5)	88 (5)	80 (2)	115 (9)
Acidic compound									
Clofibric acid	8.6	128, *228*	Mecoprop-d_3	88 (5)	91 (7)	100 (2)	105 (2)	103 (4)	97 (1)
Ibuprofen	9.2	177, *220*	Mecoprop-d_3	95 (5)	89 (9)	97 (2)	112 (7)	99 (3)	89 (2)
Naproxen	34.8	*185*, 244	Mecoprop-d_3	102 (8)	78 (3)	90 (7)	112 (10)	85 (6)	91 (3)
Ketoprofen	39.9	209, *268*	Mecoprop-d_3	98 (7)	65 (4)	78 (5)	108 (9)	71 (7)	79 (5)
Diclofenac	42.2	*214*, 309	Mecoprop-d_3	89 (6)	80 (1)	68 (4)	110 (6)	93 (7)	102 (13)
Pesticides									
Neutral compounds									
Simazine	19.0	186, *201*	Atrazine-d_5	89 (2)	88 (8)	101 (3)	88 (7)	98 (6)	98 (4)
Atrazine	19.4	*200*, 215	Atrazine-d_5	75 (5)	70 (3)	78 (6)	85 (3)	83 (1)	91 (11)
Terbutylazine	20.2	*214*, 229	Atrazine-d_5	67 (2)	60 (7)	71 (2)	84 (2)	89 (4)	100 (3)
Terbutryne	29.5	*226*, 241	Atrazine-d_5	89 (6)	79 (14)	95 (8)	104 (2)	104 (7)	100 (4)
Irgarol	37.5	*238*, 253	Atrazine-d_5	77 (9)	78 (15)	89 (9)	118 (3)	112 (6)	117 (5)
Dimethenamide	26.9	154, *230*	Dimethenamide-d_3	97 (3)	86 (14)	95 (3)	99 (2)	94 (1)	88 (1)
Metolachlor	32.5	162, *238*	[$^{13}C_6$]Metolachlor	86 (2)	91 (4)	100 (2)	99 (1)	100 (1)	98 (1)
Tebutam	15.2	190, *233*	[$^{13}C_6$]Metolachlor	79 (6)	90 (4)	109 (5)	98 (2)	95 (4)	102 (3)
Acidic compounds									
Mecoprop	10.0	*228*, 230	Mecoprop-d_3	91 (6)	92 (3)	99 (2)	102 (5)	92 (3)	94 (2)
MCPA	10.6	*214*, 216	MCPA-d_3	74 (7)	78 (1)	86 (4)	96 (6)	88 (3)	85 (2)
2,4-D	12.2	*234*, 236	Mecoprop-d_3	82 (14)	97 (6)	104 (6)	101 (7)	99 (4)	96 (2)
Trichlopyr	15.5	210, *269*	Mecoprop-d_3	82 (9)	79 (4)	82 (5)	99 (1)	82 (8)	79 (3)

[a] Spike level for absolute and relative recovery experiments was 100 ng/l.
[b] Quantifier ion in italic.
[c] Dihydrocarbamazepine.

however, when the MeOH content was increased to 50%. Although the results suggested that the MeOH content can be increased to 20%, we considered it preferable to create a safety margin because changing conditions in natural waters, i.e., varying dissolved organic matter (DOM) content could reduce the retention of the compounds. In all subsequent experiments a MeOH percentage of 10% was used for washing the cartridges. The final SPE method used in this work is shown in Fig. 2.

3.2. Absolute and relative recoveries

With the optimized SPE method, absolute and relative recoveries were determined in Nanopure water, surface water and waste water treatment plant effluents. The water samples were spiked with the analytes at 100 ng/l. The internal standards were spiked either before SPE (relative recovery) or after elution and just before derivatization (absolute recovery). For all three types of water samples,

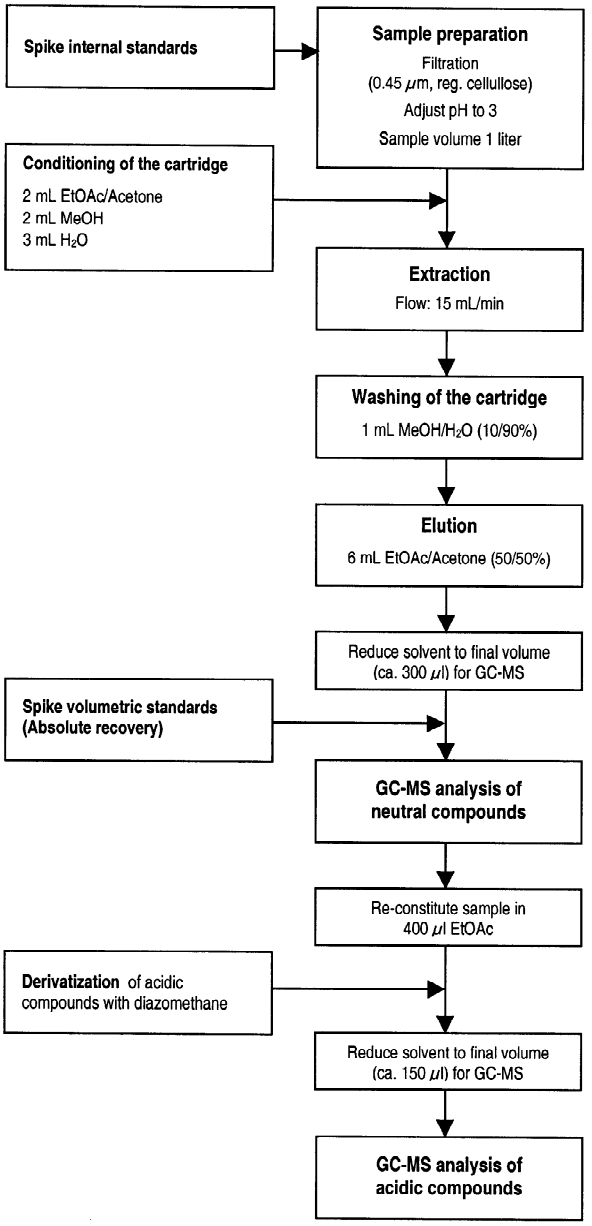

Fig. 2. Schematic representation of the solid-phase extraction procedure with the Oasis HLB sorbent.

fortified and unfortified water samples were enriched. The concentration in the unfortified water samples were subtracted to determine recoveries.

The results of these experiments are summarized in Table 1. For both the neutral and acidic compounds, absolute recoveries ranged from 46 to 109%. Relative recoveries ranged from 71 to 118% for both neutral and acidic pharmaceuticals and pesticides in all three types of water samples.

3.3. Internal standards, calibration, GC–MS performance and detection limits

Deuterated or ^{13}C ring-labeled compounds were used as internal standards for all analytes except for carbamazepine. Some preliminary experiments with carbamazepine showed that this compound is partly degraded in the injector to iminostilbene. However, dihydrocarbamazepine was added as an internal standard to compensate losses since dihydrocarbamazepine shows an equivalent degradation process as carbamazepine [10]. Note also that as long as the injector temperature was kept constant the degradation process in the injector was found to be reproducible. Typically, 75 ng of the labeled standards and 100 ng dihydrocarbamazepine were added as internal standards. Note that only the carbamazepine peak was integrated and compared to dihydrocarbamazepine for quantification of carbamazepine; the iminostilbene peak was not considered.

Both external and internal calibration were applied for quantification. For external calibration spike solutions of the analytes of interest and internal standards were added to EtOAc. For internal calibration, 1 l of Nanopure water was extracted and analyzed with the analytical method described. Calibrations were found to be linear ($0.977<r^2<0.999$) within the 10–4000 ng/l range. The retention times, the monitored quantification and identification masses for the various analytes including the isotope labeled standards are shown in Table 1.

In Fig. 3 the SIM traces of masses used for compound quantification are shown separately for the neutral and acidic fraction of a unfortified lake water sample. For identification of each analyte (at least) two compound specific ions were recorded in SIM mode: analytes were identified positively in case identical retention times and mass ratios similar to the mass ratios retrieved through calibration (allowing a variation of ±15%) were obtained. In general, the SIM mass trace showing highest sensitivity, no disturbance and low background noise

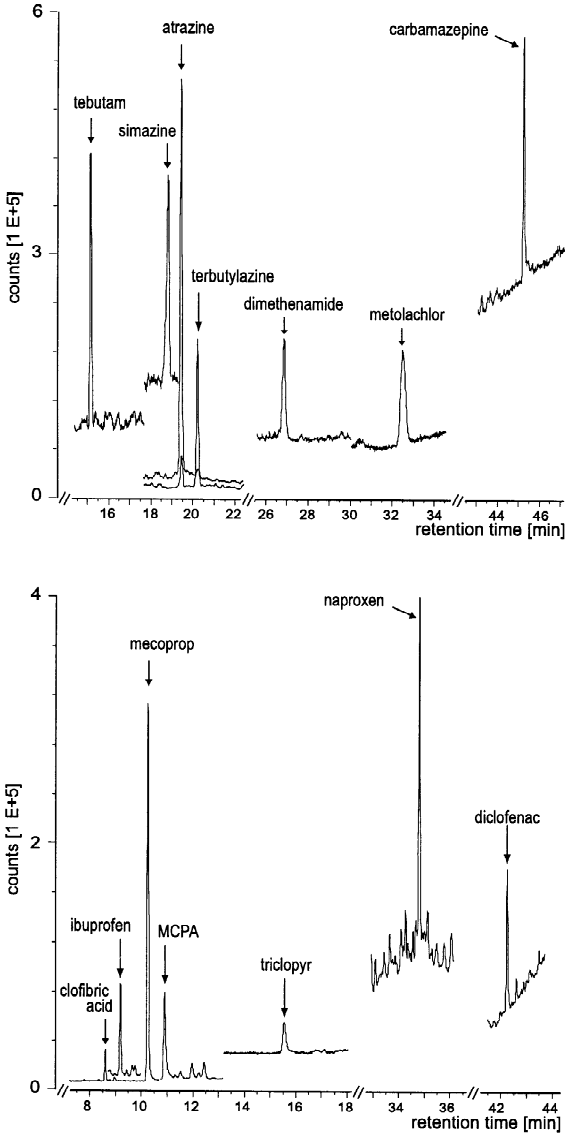

Fig. 3. Chromatograms (single ion monitored traces) of the quantification ions for several compounds in unfortified Lake Greifen water at the depth of 10 m, October 1999. Concentrations of the detected analytes in the neutral fraction (upper plot): tebutam 24 ng/l, simazine 21 ng/l, atrazine 61 ng/l (scale reduced by a factor of 5), terbutylazine 16 ng/l (scale reduced by a factor of 5), dimethenamide 5 ng/l, metolachlor 5 ng/l, carbamazepine 58 ng/l. Concentrations of the detected analytes in the acidic fraction (lower plot): clofibric acid 8 ng/l, ibuprofen 8 ng/l, mecoprop 37 ng/l, MCPA 11 ng/l, triclopyr 5 ng/l (scale increased by a factor of 5), naproxen 7 ng/l, diclofenac 7 ng/l.

was used for quantification. It can be seen from Fig. 3 that good signal-to-noise ratios and rather undisturbed mass traces were obtained at low concentration levels (illustrating the good performance of the GC–MS system).

Note that the broad peak shape for metolachlor in comparison to the other analytes originates from the incomplete separation of the diastereomers of metolachlor [18].

Method detection limits (MDLs) were determined in both Nanopure and surface water. In Nanopure water MDLs were between 0.9 and 3.6 ng/l for all analytes except for carbamazepine (6.5 ng/l). In the surface water MDLs varied from 0.3 to 4.5 ng/l for the majority of the compounds. Higher MDLs were encountered for carbamazepine (8.7 ng/l). Note that the MDL values were established by determining relative standard deviations of several identical samples. Therefore, occasionally the MDL values in surface water were higher than in Nanopure water, because the calculated MDL value is affected by both matrix effects and the variability in the total sample work up.

3.4. Performance of the new SPE–GC–MS method for the simultaneous quantification of neutral and acidic pesticides and pharmaceuticals during a field study

The target compounds were quantified in the effluents of WWTPs, in river water and in lake water (Lake Greifen; at various depths above the deepest point). The compounds were detected at concentrations varying from 4 up to 3500 ng/l (for results see Table 2). Fig. 4 shows the concentration of selected compounds in the water column of Lake Greifen (pharmaceuticals in Fig. 4a and pesticides in Fig. 4b in Lake Greifen, 12 October, 1999). Due to the sharp density gradient at ca. 8 m, the upper lake compartment (epilimnion) and the lower compartment (hypolimnion) can be theoretically regarded as separated but well mixed boxes [19,20].

Therefore, the samples taken at different depths within the epilimnion and within the hypolimnion represent the same water. If no fast transport or degradation process affects the analytes and assuming constant input, the concentration will be the same within the epilimnion and hypolimnion, respectively.

Table 2
Concentration range (in ng/l) of various pharmaceuticals and pesticides in lake, river and water waste treatment plant (WWTP) effluent water

Compound	Lake (n=28)	River (n=17)	WWTP (n=24)
Pharmaceuticals			
Carbamazepine	35–60	30–250	100–800
Clofibric acid	5–10	n.d.–25	n.d.–60
Ibuprofen	5–15	n.d.–80	5–1500
Naproxen	n.d.–10	10–400	100–3500
Ketoprofen	n.d.	n.d.–5[a]	n.d.–200
Diclofenac	n.d.–10	20–150	100–700
Pesticides			
Simazine	10–40	10–100	20–200
Atrazine	50–140	10–80	10–90
Terbutylazine	10–20	5–40	10–60
Terbutryne	n.d.–5	n.d.–10	n.d.–15
Irgarol	n.d.–5	n.d.	n.d.–15[b]
Dimethenamide	4–10	n.d.–20	n.d.–5
Metolachlor	4–10	n.d.–15	n.d.–10
Tebutam	10–30	5–300	10–1000
Mecoprop	30–50	10–300	20–400
MCPA	10–25	n.d.–60	n.d.–100
2,4-D	n.d.–10	n.d.–50	n.d.–20
Triclopyr	n.d.–5	n.d.–25	n.d.–10

[a] Sporadic occurrence (less than four positive identifications out of 17 samples of river water).
[b] Sporadic occurrence (less than two positive identifications out of 24 samples of WWTPs).
n.d., Not detectable.

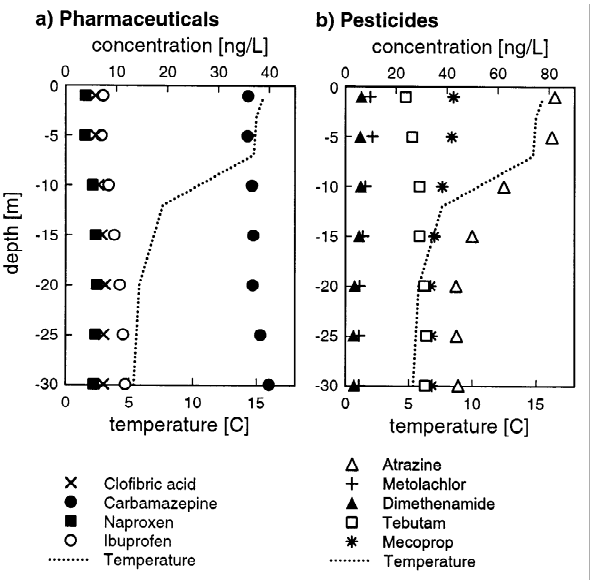

Fig. 4. Vertical concentration profiles of selected pharmaceuticals (a) and pesticides (b) over the deepest point in Lake Greifen in October 1999.

In fact, Fig. 4 confirms the excellent overall performance of the analytical method even at low concentrations in natural waters. Fig. 4 shows that pesticide concentrations (especially atrazine) are higher in the epilimnion than in the hypolimnion reflecting the seasonal input [19,20]. In contrast to the pesticides, the concentrations of the pharmaceuticals in the epilimnion are generally lower than in the hypolimnion. Assuming a constant input, it could be speculated, that these pharmaceutical compounds are degraded in the epilimnion of the lake.

We are currently quantitatively evaluating the fate of some of the discussed compounds in Lake Greifen using these field measurements and model calculations. The focus is to which degree degradation of especially the pharmaceutical compounds in aqueous environments occurs.

In summary, the results in Table 2 and Fig. 4 prove that the newly developed analytical method is an excellent tool for the simultaneous determination of neutral and acidic pharmaceuticals and pesticides in natural waters and waste water treatment plant effluents even at very low concentrations. Furthermore, during this field study the analytical method showed a rugged performance and straightforward, easy handling.

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