Journal of Environmental Science and Health Part B (2010) **45**, 682–693

ISSN: 0360-1234 (Print); 1532-4109 (Online)
DOI: 10.1080/03601234.2010.502446

Taylor & Francis
Taylor & Francis Group

Rapid resolution liquid chromatography-tandem mass spectrometry method for the determination of endocrine disrupting chemicals (EDCs), pharmaceuticals and personal care products (PPCPs) in wastewater irrigated soils

FENG CHEN, GUANG-GUO YING, JI-FENG YANG, JIAN-LIANG ZHAO and LI WANG

State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou, China

A multiresidue analytical method was developed for the determination of 9 endocrine disrupting chemicals (EDCs) and 19 pharmaceuticals and personal care products (PPCPs) including acidic and neutral pharmaceuticals in water and soil samples using rapid resolution liquid chromatography-tandem mass spectrometry (RRLC-MS/MS). Solid phase extraction (SPE), and ultrasonic extraction combined with silica gel purification were applied as pretreatment methods for water and soil samples, respectively. The extracts of the EDCs and PPCPs in water and soil samples were then analyzed by RRLC-MS/MS in electrospray ionization (ESI) mode in three independent runs. The chromatographic mobile phases consisted of Milli-Q water and acetonitrile for EDCs and neutral pharmaceuticals, and Milli-Q water containing 0.01 % acetic acid (v/v) and acetonitrile: methanol (1:1, v/v) for acidic pharmaceuticals at a flow rate of 0.3 mL/min. Most of the target compounds exhibited signal suppression due to matrix effects. Measures taken to reduce matrix effects included use of isotope-labeled internal standards, and application of matrix-match calibration curves in the RRLC-MS/MS analyses. The limits of quantitation ranged between 0.15 and 14.08 ng/L for water samples and between 0.06 and 10.64 ng/g for solid samples. The recoveries for the target analytes ranged from 62 to 208 % in water samples and 43 to 177 % in solid samples, with majority of the target compounds having recoveries ranging between 70–120 %. Precision, expressed as the relative standard deviation (RSD), was obtained less than 7.6 and 20.5 % for repeatability and reproducibility, respectively. The established method was successfully applied to the water and soil samples from four irrigated plots in Guangzhou. Six compounds namely bisphenol-A, 4-nonylphenol, triclosan, triclocarban, salicylic acid and clofibric acid were detected in the soils.

Keywords: Endocrine disrupting chemicals; pharmaceuticals; soil; liquid chromatography-mass spectrometry.

Introduction

In the last decade, endocrine disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs) have become emerging contaminants, which attracted an increasing attention in the scientific community and general public. Some EDCs have been reported to be ubiquitous in the environment[1,2] and may cause detrimental effects on organisms even at very low concentrations.[3] Chronic exposure to EDCs may result in hormone-related diseases and a decrease in sperm count and quality.[4,5,6] In addition, exposure to EDCs increases the risk of breast cancer.[7] Pharmaceuticals and personal care products (PPCPs) are chemicals used both for humans and animals for the disease treatment and prevention as well as daily personal care. After consumption, these bioactive compounds and their metabolites are discharged to aquatic environments via untreated and treated sewage from sewage treatment plants. Previous studies have reported the presence of wastewater associated EDCs and PPCPs in the environment.[2,8–17] These EDCs and PPCPs usually present as mixtures in the environment may pose potential risks to ecosystem and human health, even at trace levels.[18] Therefore, multiresidue analytical methods are required to detect these substances in the environment.

Gas chromatography-mass spectrometry (GC-MS)[19–22] and liquid chromatography-tandem mass spectrometry (LC-MS/MS)[23–29] are the two most commonly used techniques for determination of trace organic contaminants. Since most of the EDCs and PPCPs contain polar

Address correspondence to Guang-Guo Ying, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences; E-mail: guang-guo.ying@gig.ac.cn; guangguo.ying@gmail.com
Received April 2, 2010.

functional groups, they are often not amenable to GC-MS without derivatization. Thus in recent years LC-MS/MS with soft ionization has become a preferred choice for the analysis of these compounds in water.[30–33] Environmental samples have complex matrices; matrix interferences could lead to signal suppression or enhancement during LC-MS/MS.[25,29,30,34–39] Despite this, LC-MS/MS can be applied to determine trace levels of EDCs and PPCPs in the environmental samples after proper extraction and purification procedures. However, analytical methods available in the literature were developed mainly for water samples. There is a need to have robust analytical methods for EDCs and PPCPs in soils and sediments.

Owing to the shortage of water resources in some parts of the world, wastewater (or wastewater-contaminated irrigation water) has been used for irrigation of crops in many countries.[40–42] Since these irrigation waters may contain a variety of contaminants including EDCs and PPCPs, there are potential ecological and human health risks associated with the application of wastewater on land.[43,44] Wastewaters and wastewater–contaminated surface waters have also been used in some parts of China to irrigate crops. This could lead to accumulation of contaminants in soils and contamination of food.[45,46]

The objective of the present study is to develop sensitive multiresidue methods for determination of selected 28 EDCs and PPCPs in irrigation waters and soils using rapid resolution liquid chromatography-tandem mass spectrometry (RRLC-MS/MS). The compounds included in the analysis were 2 natural estrogenic steroids estrone (E1) and 17β-estradiol (E2), 2 synthetic steroids 17α-ethynylestradiol (EE2) and diethylstilbestrol (DES), 3 industrial chemicals bisphenol A (BPA), 4-tert-octylphenol (4-t-OP) and 4-nonylphenol (4-NP), 2 antiseptic and disinfectant triclosan (TCS) and triclocarban (TCC), and 19 pharmaceuticals belonging to anti-inflammatory and antipyretic drugs, blood lipid regulator and anti-epileptic drugs as well as herbicides. The developed analytical methods were also applied to screen potential EDCs and PPCPs in irrigation waters and soils from Guangzhou, China.

Materials and methods

Chemicals and materials

Standards 4-NP, 4-*n*-NP, E2, TCS, EE2, TCC, salicylic acid, clofibric acid, bentazone, 2,4-D, MCPA, ibuprofen, fenoprofen, diclofenac, indometacin, mefenamic acid, gemfibrozil, tolfenamic acid, ketoprofen, naproxen, cyclophosphamide and carbamazepine were purchased from Dr. Ehrenstorfer GmbH (Germany). 4-*t*-OP, BPA and BPA-d16 were provided by Supelco (USA). AE1, DES, mecoprop and fenoprop were obtained from Riedel-de Haën (RDH, Germany); The compound $^{13}C_{12}$-TCS and E1-d4 were available from Cambridge Isotope Laboratories Incorporation (Massachusetts, USA). Meclofenamic acid, primidone and dihydrocarbamazepine were purchased from Sigma-Aldrich (USA), while E2-d4 was supplied by CDN Isotopes. Chemical information of the target compounds is shown in Tables 1 and 2. All the organic solvents used were of HPLC grade and purchased from Merck Corporation (Shanghai, China). Ultrapure water was produced by a Milli-Q system from Millipore (Watford, UK). Oasis HLB extraction cartridges (6 mL, 500 mg) were obtained from Waters Corporation (Milford, MA, USA). Sodium sulfate was baked at 400°C for 4 h and kept in a desiccator. Silica gel (100-200 mesh) was sequentially rinsed with methanol and dichloromethane for 24 h by a Soxhlet extractor. After baked at 160°C for 24 h, it was stored in a desiccator for later use.

Stock solutions at a concentration of 100 mg/L of each target compound and internal standard were prepared in methanol and stored in amber glass bottles at -18°C. Composite working solutions were made by mixing the individual standard solutions and diluting it with methanol when needed.

Sample collection and preparation

The clean water and soil samples used for recovery tests and controls were collected from Liuxi River reservoir area, which is located to the northeast of Guangzhou city, southern China. Water and soil samples were collected from four

Table 1. Details of the endocrine disrupting chemicals including abbreviation (Abbr.), CAS number (CAS no.), molecular formula, molecular weight (MW.), internal standard and use.

Compound	*Abbr.*	*CAS no.*	*Molecular formula*	*MW.*	*Internal standard*	*Use*
Bisphenol-A	BPA	80-05-7	$C_{15}H_{16}O_2$	228.29	Bisphenol-A d16	Industrial chemical
17-β-Estradiol	E2	50-28-2	$C_{18}H_{24}O_2$	272.38	Estradiol-d4	Natural estrogen
17α-ethinylestradiol	EE2	57-63-6	$C_{20}H_{24}O_2$	296.4	Estrone-d4	Synthetic estrogen
Estrone	E1	53-16-7	$C_{18}H_{22}O_2$	270.37	Estrone-d4	Natural estrogen
Diethylstilbestrol	DES	56-53-1	$C_{18}H_{20}O_2$	268.35	Estrone-d4	Synthetic estrogen
Triclocarban	TCC	101-20-2	$C_{13}H_9C_{13}N_2O$	315.58	Triclocarban-d7	Antiseptic and disinfectant
Triclosan	TCS	3380-34-5	$C_{12}H_7C_{13}O_2$	289.54	$^{13}C_{12}$-Triclosan	Antiseptic and disinfectant
4-tert-Octylphenol	4-*t*-OP	140-66-9	$C_{14}H_{22}O$	206.32	4-*n*-Nonylphenol	Industrial chemical
4-Nonylphenol	4- NP	84852-15-3	$C_{15}H_{24}O$	220.35	4-*n*-Nonylphenol	Industrial chemical

Table 2. Details of the pharmaceuticals and personale care products including CAS number (CAS no.), molecular formula, molecular weight (MW.), internal standard and use.

Compound	*CAS no.*	*Molecular formula*	*MW.*	*Internal standard*	*Use*
Salicylic acid	69-72-7	$C_7H_6O_3$	138.12	Mecoprop	Anti-inflammatory
Clofibric acid	882-09-7	$C_{10}H_{11}ClO_3$	214.65	Mecoprop	Blood lipid regulator
2,4-D	94-75-7	$C_8H_6Cl_2O_3$	221.04	Mecoprop	Herbicide
MCPA	94-74-6	$C_9H_9ClO_3$	200.62	Mecoprop	Herbicide
Ibuprofen	15687-27-1	$C_{13}H_{18}O_2$	206.28	Mecoprop	Anti-inflammatory and antipyretic
Bentazone	25057-89-0	$C_{10}H_{12}N_2O_3S$	240.28	Fenoprop	Herbicide
Fenoprofen	31879-05-7	$C_{15}H_{14}O_3$	242.27	Fenoprop	Anti-inflammatory and antipyretic
Diclofenac	15307-86-5	$C_{14}H_{11}C_{l2}NO_2$	296.15	Fenoprop	Anti-inflammatory
Indometacin	53-86-1	$C_{19}H_{16}ClNO_4$	357.79	Fenoprop	Anti-inflammatory and antipyretic
Meclofenamic Acid	644-62-2	$C_{14}H_{11}Cl_2NO_2$	296.15	Fenoprop	Anti-inflammatory and antipyretic
Mefenamic Acid	61-68-7	$C_{15}H_{15}NO_2$	241.29	Fenoprop	Anti-inflammatory and antipyretic
Gemfibrozil	25812-30-0	$C_{15}H_{22}O_3$	250.33	Fenoprop	Antihyperlipoproteinemic
Tolfenamic acid	13710-19-5	$C_{14}H_{12}ClNO_2$	261.7	Fenoprop	Anti-inflammatory and antipyretic
Ketoprofen	22071-15-4	$C_{16}H_{14}O_3$	254.28	Fenoprop	Anti-inflammatory and antipyretic
Naproxen	22204-53-1	$C_{14}H_{14}O_3$	230.26	Fenoprop	Anti-inflammatory and antipyretic
Paracetamol	103-90-2	$C_8H_9NO_2$	151.16	Dihydrocarbamazepine	antipyretic
Primidone	125-33-7	$C_{12}H_{14}N_2O_2$	218.25	Dihydrocarbamazepine	Anti-epileptic
Cyclophosphamide	50-18-0	$C_7H_{15}Cl_2N_2O_2P$	261.08	Dihydrocarbamazepine	Immunosuppressant and antitumor
Carbamazepine	298-46-4	$C_{15}H_{12}N_2O$	236.27	Dihydrocarbamazepine	Anti-epileptic

irrigation plots of Guangzhou (September 2008), and used for validation of the developed method. Detailed information of the sampling sites is given in Table 3. Except for site A irrigated with a lake water, the other three sites (B, C and D) have been irrigated with the river water. The rivers have been heavily contaminated with untreated wastewater from nearby towns. Soil samples from the irrigation plots were collected at the depths of 0–10 cm, 10–20 cm and 20–30 cm from five points in each selected plot (200 m × 200 m). Irrigation water samples were collected in 1 L pre-cleaned brown glass bottles, while soil samples were collected in 1 L glass jars. The water samples were immediately added with 50 mL of methanol and adjusted to pH 3.0 using 4 M H_2SO_4. All the samples were kept cool during the transport to the laboratory. Once in the laboratory, water samples were filtered though 0.7 μm glass fiber filters (Whatman GF/F, UK) to remove suspended particulate matter and extracted within a week, while solid samples were freeze-dried and passed through a 60 mesh standard sieve. The processed liquid and solid samples were stored at 4°C until analysis.

Extraction

Extraction of irrigation water samples

The collected water samples were extracted with solid phase extraction (SPE) in accordance with the previously reported method.[15,16,22] After the water samples were spiked with the internal standards (100 ng/L each), they were loaded onto Oasis HLB SPE cartridges, which were preconditioned with 10 mL of methanol and 10 mL of Milli-Q water. After the water samples were passed through the cartridges at a flow rate of approximately 10 mL/min, SPE cartridges were rinsed twice with 50 mL of Milli-Q water containing 5 % methanol (v/v). The cartridges were dried under vacuum for 2 h and then eluted with 4×3 mL of methanol followed by 3×2 mL of dichloromethane. The extracts were concentrated under a gentle stream of nitrogen gas, and then redissolved in 1 mL of methanol. Before being transferred to a 2 mL amber glass vial, the extracts were filtered through nylon membrane filters (13 mm × 0.22 μm, Anpu, Shanghai). The final extracts were stored at −18°C prior to analysis.

Table 3. Detailed information of the sampling sites in Guangzhou.

Water sample	*Soil sample*	*Plot type*	*Location*	*Coordinates*
WA	SA	Irrigation with lake water	Tianhe	23°10'N 113°23'E
WB	SB	Irrigation with river water (sewage effluent contaminated)	Haizhu	23°04'N 113°19'E
WC	SC	Irrigation with river water (sewage effluent contaminated)	Fangcun	23°03'N 113°15'E
WD	SD	Irrigation with river water (sewage effluent contaminated)	Huangpu	23°06'N 113°27'E

Table 4. Retention time (R_t), precursor and product ions (bold numbers are quantification ions), and optimized electrospray ionization tandem mass Spectrometry (ESI-MS/MS) Parameters for the endocrine disrupting chemicals, acidic pharmaceuticals and neutral pharmaceuticals.

Compounds	*R_t (min)*	*Precursor ion (m/z)*	*Products ions (m/z)*		*Fragmentor voltage (V)*	*Collision energy (V)*
Endocrine disrupting chemicals*						
BPA	5.25	227.1	**212.1**	133.1	127	13/21
E2	5.98	271	**183**	145	204	33/30
EE2	7.03	295	159	**145**	170	34/38
E1	7.74	269	**145.1**	143.1	148	33/57
DES	8.45	267	**251.1**	237.1	163	17/21
TCC	14.93	313	**160.1**	126.1	86	5/13
TCS	15.21	287	**35.1**		65	1
4-*t*-OP	16.11	205.3	**133.2**	117	111	21/45
4-NP	18.85	219.3	**133.2**		101	25
BPA-d16	5.10	241	**223.2**		142	13
E2-d4	5.92	275	**187**		219	25
E1-d4	7.68	273	**147.2**		168	37
TCC-d7	14.80	320	**163.1**		107	5
$^{13}C_{12}$-TCS	15.21	299	**35.1**		65	1
4-n-NP	20.81	219.2	**106**		96	10
Acidic pharmaceuticals						
Salicylic acid	2.45	137	**93.1**	65.2	87	9/29
Bentazone	3.32	239	197.1	**132.1**	124	13/21
2, 4-D	7.21	219	**161.1**	125.1	77	5/21
MCPA	8.33	199	**141.1**	105.2	87	5/25
Compounds	R_t(min)	Precursor ion (m/z)	Products ions (m/z)		Fragmentor (V)	Collision energy (V)
Clofibric acid	11.61	213	**127.1**	85.1	72	5/1
Ketoprofen	14.71	253	**209.2**		77	1
Naproxen	15.37	229	185.2	**169.1**	72	1/25
Fenoprofen	20.51	241	**197.2**	93.1	87	1/33
Diclofenac	21.91	294	**250**	214.1	82	1/9
Indometacin	22.32	356	**312.1**		97	1
Ibuprofen	22.53	205	**161.2**		70	1
Meclofenamic Acid	23.87	294	258.1	**214.1**	235	1/9
Mefenamic Acid	23.89	240	**196.2**	192.2	240	9/21
Gemfibrozil	24.49	249	127.2	**121.2**	87	1/5
Tolfenamic acid	24.68	260	**216.1**	35.2	112	5/17
Mecoprop	12.56	213	**141.1**		82	5
Fenoprop	15.56	267	**195**		82	1
Neutral pharmaceuticals						
Paracetamol	2.08	152	110.1	**65.1**	98	13/29
Primidone	3.87	219	**162**	91.1	98	5/25
Cyclophosphamide	5.92	261	**140**	63.1	136	21/41
Carbamazepine	8.02	237	**194.1**	193.4	136	17/33
10,11-dihydroCarbamazepine	8.31	239	**194.1**	180.1	174	21/45

*BPA: bisphenol-A; E2: estradiol; EE2; ethynylestradiol; E1: estrone; DES: Diethylstilbestrol; TCC: triclocarban; TCS: triclosan; 4-*t*-OP: 4-tert-octylphenol; 4-NP: 4-nonylphenols.

Extraction of soil samples

Freeze-dried solid samples (5 g each) were spiked with 100 ng of each standard, carefully mixed, and left in a fume cupboard to remove organic solvent. Then the samples were placed in a −4°C cold room overnight and extracted in the following day. Each sample was mixed with 10 mL of ethyl acetate: formic acid (50:1, v/v), sonicated for 15 min at room temperature, and then centrifuged at 1370g for 10 min. The above procedure was repeated twice, and the extracts were combined and dried under a gentle nitrogen stream. Purification of each extract was carried out by using a silica gel column (18 cm × 1 cm i.d.), which consisted of anhydrous sodium sulfate (about 0.5 cm, on top) and silica gel (1 g). Before loading the sample, the sorbent was conditioned with methanol (4 mL), ethyl acetate (4 mL) and *n*-hexane (6 mL) in series. The silica gel column was

eluted using 6 mL of *n*-hexane, and then 6 mL of ethyl acetate followed by 6 mL of methanol. The first 6 mL of eluate was discarded, and the following two elutes were collected in 10 mL of glass tubes. The fractions containing the target compounds were combined and concentrated under a gentle nitrogen stream and then redissolved in 1 mL of methanol. The final extracts were stored at −18°C after they were filtered through nylon membrane filters (13 mm × 0.22 μm, Anpu, Shanghai).

LC-MS/MS analysis

The target compounds were separated into three groups (EDCs, acidic and neutral pharmaceuticals) and analyzed by using Agilent 1200 rapid resolution liquid chromatograph coupled to Agilent G6460A triple quadrupole mass spectrometer. The chromatographic separation of each group was performed on an Agilent SB-C18 column (3.0 × 100 mm, 1.8 μm) with a RRLC in-line filter kit (4.6 mm, 0.2 μm filter) (Germany). The column temperature was maintained at 40°C. The chromatographic mobile phases were run at a flow rate of 0.3 mL/min. The mobile phase for analysis of the EDCs consisted of (A) Milli-Q water and (B) acetonitrile, with the gradient programmed as follows: 0 min, 40 % B; 15 min, 70 % B; and 20 min, 95 % B. The initial mobile phase was equilibrated for 8 min after each run. The mobile phase for analysis of acidic pharmaceuticals consisted of (A) Milli-Q water containing 0.01 % acetic acid (v/v) and (B) acetonitrile: methanol (1:1, v/v), with the gradient programmed as follows: 0 min, 40 % B; 15 min, 50 % B; and 20 min, 75 % B. The mobile phase for neutral pharmaceuticals consisted of (A) Milli-Q water and (B) acetonitrile, with the gradient programmed as follows: 0 min, 20 % B; 10 min, 60 % B; and 13 min, 90 % B.

The mass spectrometer was operated in electrospray ionization mode (ESI) with optimized parameters as follows: drying gas temperature 350°C and flow rate 8 mL/min, capillary voltage 3500 V, nebulizing gas pressure 50 psi, sheath gas temperature 350°C and flow rate 12 mL/min. The injection volume was 10 μL.

Results and discussion

RRLC-MS/MS analysis

According to their chemical structures, the target compounds were separated into three groups for RRLC-MS/MS analysis. The EDCs and acidic pharmaceuticals were analyzed by RRLC-MS/MS under ESI (−) mode, while the neutral pharmaceuticals were analyzed under ESI (+) mode. The MS/MS operating parameters for ionization and fragmentation were optimized by the Agilent software Optimizer in combination with manual infusion (Table 4). Similar fragmentation patterns for some of the target compounds under ESI (+) or ESI (−) have also been reported in previous studies.[47–50]

In order to have a better separation and sensitivity for the target compounds, different mobile phases (various organic solvents and buffers) were tested. For the EDCs

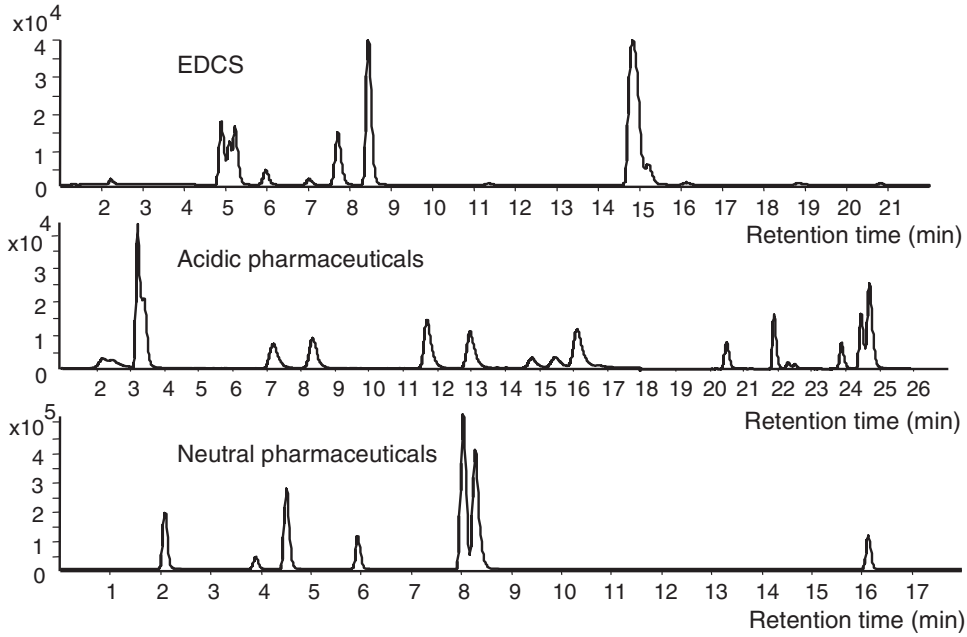

Fig. 1. Total ion chromatograms (TIC) of the target analytes by rapid resolution liquid chromatography-electrospray ionization(RRLC-ESI-MS/MS) at the concentration each of 100 ng/L. The retention time of each compound can be found in Figures 1–4. EDCs: endocrine disrupting chemicals.

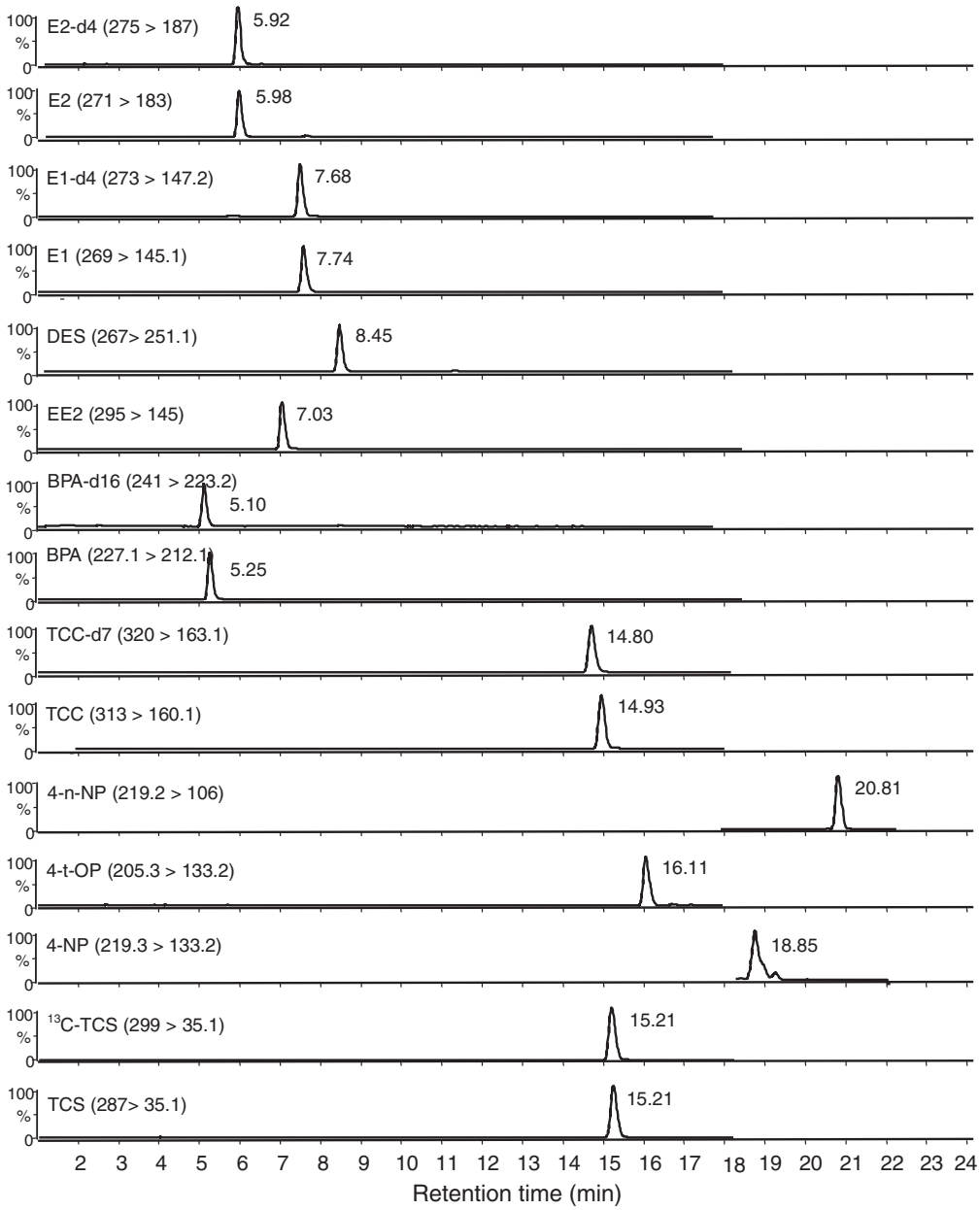

Fig. 2. Extracted ion chromatograms (XIC) of the quantitative ions for endocrine disrupting chemicals (EDCs) in neat solvent at the concentration each of 100 ng/L. BPA: bisphenol-A, E2: estradiol, EE2; ethynylestradiol, E1: estrone, DES: Diethylstilbestrol, TCC: triclocarban, TCS: triclosan, 4-*t*-OP: 4-tert-octylphenol, 4-NP: 4-nonylphenols.

and neutral pharmaceuticals, a mobile phase consisting of acetonitrile and Milli-Q water without any additive was found to produce the best peak shape and intensity. This is consistent with a previous analytical report on phenolic EDCs.[51] However, for the acidic pharmaceuticals, the best choice was the mobile phase containing 0.01 % acetic acid (v/v) in Milli-Q water. Better peak shape could be achieved for the target compounds with increasing concentration of acetic acid in the mobile phase, but higher concentration of acetic acid reduced the signal responses. On the contrary, addition of ammonium acetate could produce higher responses but poor peak shapes. As for the use of solvent mixture of acetonitrile: methanol (1:1, v/v) in the analysis of acidic pharmaceuticals, it did not influence the separation and intensity, but decreased the cost of analysis as methanol is much cheaper. With the high resolution capability of the RRLC and the gradient programs applied for the three groups of target compounds, good separation was achieved for all target compounds by RRLC-MS/MS (Figs. 1–4).

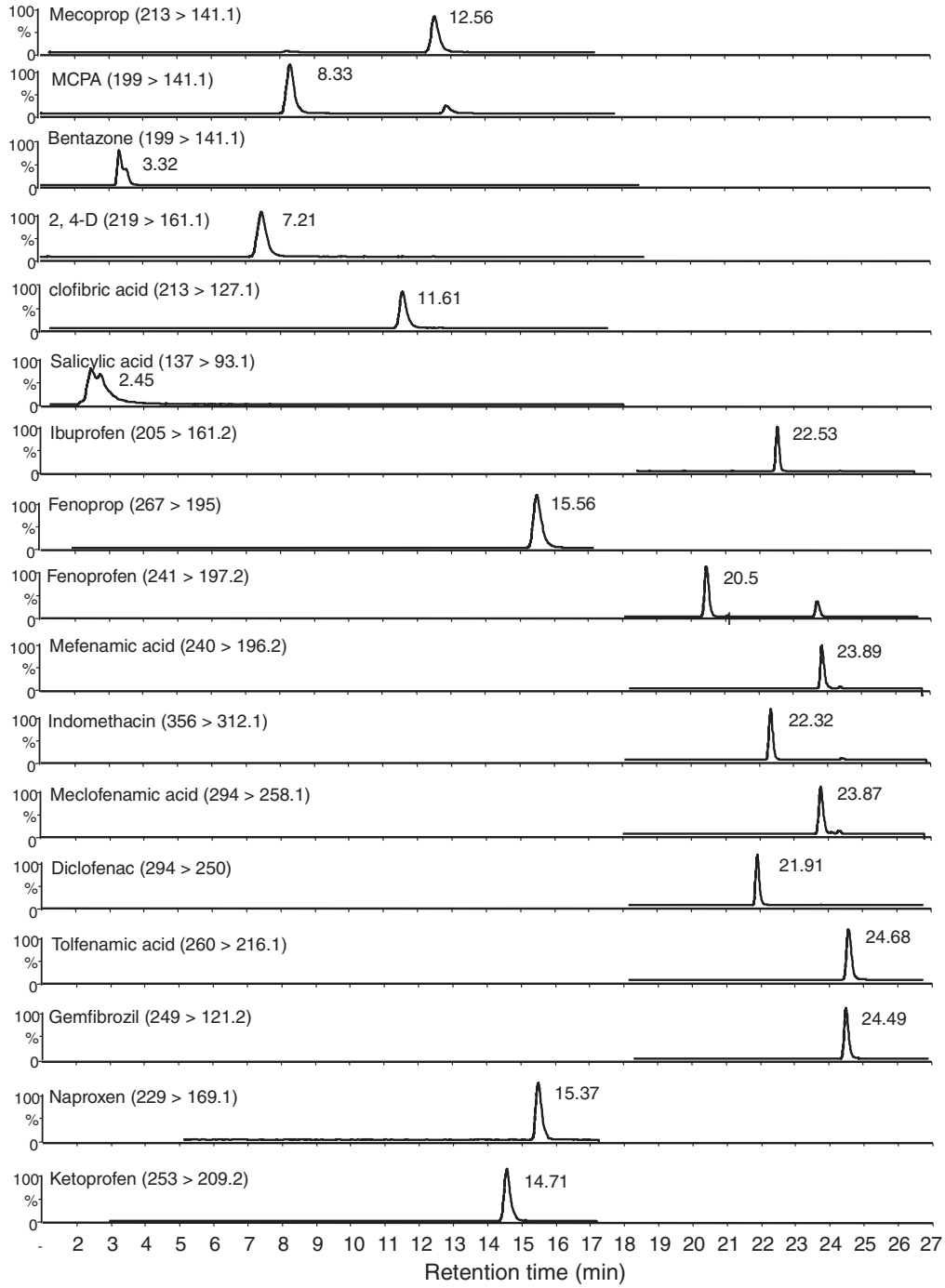

Fig. 3. Extracted ion chromatograms (XIC) of the quantitative ions for acidic pharmaceuticals in neat solvent at the concentration each of 100 ng/L.

Matrix effects

Matrix effects were observed in the RRLC-MS/MS of the target compounds. In fact, matrix effect is a widely perceived problem for mass spectrometry with electrospray ionization mode.[29,30,35,38] Since matrix effect-can lead to signal suppression or enhancement and is difficult to eliminat through cleanup procedures,[47] we took two measures to lessen the matrix effect: addition of appropriate internal standards into samples and application of matrix-matched calibration curves. These two strategies have been previously applied in LC-MS/MS analysis.[27,35,49,52] Matrix-matched calibration curves were prepared at concentrations of 1, 5, 10, 50, 100 and 200 ng/L for each target compound. The matrix effects, expressed as the ratio of the analyte signal in matrix to the analyte signal in solvent,[53]

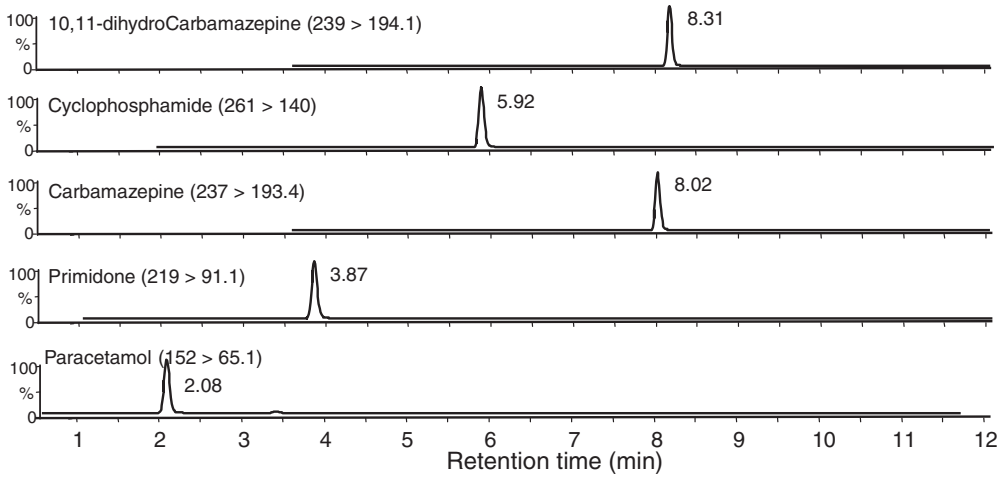

Fig. 4. Extracted ion chromatograms (XIC) of the quantitative ions for neutral pharmaceuticals in neat solvent at the concentration each of 100 ng/L.

were tested at the concentration of 100 ng/L for each compoundbreak (Table 5). The values of less or greater than 100 % indicate signal suppression or enhancement, respectively. Table 5 showed that most of the target compounds exhibited signal suppression, which is consistent with the previous studies.[35,50]

Method validation

The recovery test with four replicates ($n = 4$) was performed for each target compound by spiking at a concentration of 100 ng/L into water. Most of the target compounds had recoveries falling between 70 % and 120 %, except for EE2 (65 %), TCC (128 %), 4-NP (135 %), 4-t-OP (62 %), salicylic acid (64 %) and indometacin (68 %) (Table 5). Due to strong matrix effects, paracetamol had a very high recovery (208 %). Use of an isotope labeled compound may be necessary to reduce the matrix effect. For solid samples, most of the target compounds had desirable recoveries (70–120 %) except for cyclophosphamide, ibuprofen and tolfenamic acid (Table 5).

The LOD and LOQ were calculated according to previously reported methods.[49,54,55] The LOD and LOQ were calculated as the concentration with a signal-to-noise-ratio of 3 and 10, respectively, when water/solid samples spiked at low concentrations were analysed. For water samples, the spiked concentrations were 10 ng/L for E2, EE2, DES, 4-t-OP, meclofenamic acid and mefenamic acid and 1 ng/L for the rest of the compounds. For sediment samples, the spiked concentrations were 50 ng/g for E2, EE2, DES and 4-t-OP, and 10 ng/g for the rest of the target compounds. From Table 5, the LOD ranged from 0.05 to 4.23 ng/L in water, and 0.02 to 3.19 ng/g in sediments. Most of them were lower than 1 ng/L or 1 ng/g.

Regarding intra-day and inter-day precision, the repeatability and reproducibility, expressed as the relative standard deviation (RSD) of measured concentrations, were calculated based on the analysis of a standard mixture at a concentration of 100 μg/L for three times within one day and within three consecutive days, respectively. Repeatability for the target compounds varied from 0.2 to 7.6 %, while reproducibility ranged from 0.7 to 20.5 % (Table 5).

Method application

The analytical methods developed for the EDCs and PPCPs were applied to the determination of these compounds in irrigation waters and soil samples from four plots in Guangzhou. In these irrigation water samples, 7 out of 28 target compounds determined were found (Table 6). The four EDCs 4-t-OP, 4-NP, BPA and TCS were detected in all irrigation water samples from the four plots, while only three acidic pharmaceuticals (salicylic acid, ibuprofen and ketoprofen) were detected in the irrigation waters from one or two sites (WB and WD). Among all detected compounds in the irrigation water samples, 4-NP was found at the highest concentrations. The rest of target compounds not mentioned here were all below the limit of detection in the water samples collected in September 2008; however, that does not mean these compounds were not present in irrigation waters in other seasons during the year. The river waters used for irrigation have been heavily contaminated by sewage effluents. The target compounds determined in the present study have been reported in rivers with discharge of sewage effluents.[15,22]

In the soil samples collected from the four plots, six target compounds namely BPA, TCC, TCS, 4-NP, salicylic acid and clofibric acid were detected (Table 7). Among them, BPA, TCS, 4-NP and salicylic acid were also found in the irrigation water samples collected in September 2008, while TCC and clofibric acid were not detected in the water samples. However, TCC and clofibric acid have been widely reported in sewage effluents[56,57] and they have been found

Table 5. Linearity (correlation coefficient), repeatability and reproducibility (relative standard deviation [RSD] % for $n = 3$), recoveries (%) and method precision (RSD % for $n = 4$), matrix effect (%), limit of detection (LOD) and quantitation (LOQ) for each investigated compound.

				Water				*Soil*			
Compounds	*Linearity* (r^2)[a]	*Repeat-ability*	*Reprod-ucibility*	*Recovery % ± RSD*	*Matrix effect*	*LOD (ng/L)*	*LOQ (ng/L)*	*Recovey % ± RSD*	*Matrix effect*	*LOD (ng/g)*	*LOQ (ng/g)*
Endocrine disrupting chemicals [c]											
BPA	0.9999	2.6	18.2	78 ± 4	79	0.11	0.37	111 ± 2	113	1.02	3.40
E2	0.9996	1.6	7.8	104 ± 5	100	1.18	3.92	106 ± 2	101	0.49	1.63
EE2	0.9966	4.2	3.7	**65 ± 14** [b]	59	0.60	2.01	115 ± 7	107	0.83	2.77
E1	0.9994	4.1	1.8	98 ± 2	92	0.42	1.41	97 ± 5	90	0.60	1.99
DES	0.9979	3.1	6.3	119 ± 16	105	0.53	1.75	**56 ± 20**	53	1.62	5.41
TCC	0.9953	2.1	7.1	**128 ± 3**	121	0.24	0.79	108 ± 1	101	0.12	0.39
TCS	0.9988	0.9	8.9	97 ± 1	101	0.21	0.70	95 ± 3	99	0.47	1.58
4-*t*-OP	0.9972	7.1	13.0	**62 ± 14**	58	0.40	1.33	94 ± 15	94	1.29	4.29
4-NP	0.9940	0.5	6.6	**135 ± 2**	123	0.09	0.31	**124 ± 3**	114	0.49	1.63
Acidic pharmaceuticals											
Salicylic acid	0.9989	4.3	8.4	**64 ± 7**	62	0.34	1.15	108 ± 8	103	0.33	1.11
Bentazone	0.9964	3.9	2.1	86 ± 4	82	0.13	0.43	95 ± 4	92	0.06	0.20
2, 4-D	0.9993	2.0	1.1	90 ± 3	77	0.24	0.79	85 ± 4	72	0.53	1.78
MCPA	0.9986	2.4	0.7	90 ± 2	73	0.37	1.23	97 ± 3	78	0.19	0.63
Clofibric acid	0.9976	0.2	1.5	97 ± 6	82	0.22	0.74	96 ± 1	81	0.15	0.49
Ketoprofen	0.9996	2.9	4.9	103 ± 6	91	1.25	4.17	**123 ± 1**	107	3.19	10.64
Naproxen	0.9981	2.5	6.9	77 ± 3	71	0.06	0.20	98 ± 2	91	1.06	3.55
Fenoprofen	0.9992	2.6	3.4	99 ± 7	96	0.20	0.66	**127 ± 4**	121	2.34	7.81
Diclofenac	0.9982	1.7	4.6	93 ± 6	78	0.43	1.43	**129 ± 6**	110	0.35	1.16
Indometacin	0.9998	3.9	14.5	**68 ± 7**	65	0.65	2.17	91 ± 7	88	1.88	6.25
Ibuprofen	0.9995	3.7	9.2	82 ± 11	65	1.25	4.17	**160 ± 10**	130	1.51	5.03
Meclofenamic Acid	0.9948	6.2	11.6	108 ± 3	98	4.23	14.08	113 ± 14	102	1.36	4.52
Mefenamic Acid	0.9980	3.8	9.3	102 ± 10	85	2.70	9.01	111 ± 5	91	0.63	2.11
Gemfibrozil	0.9984	1.4	10.0	89 ± 7	89	0.16	0.53	77 ± 11	77	0.08	0.26
Tolfenamic acid	0.9963	4.0	2.7	109 ± 4	88	0.14	0.46	**177 ± 14**	142	0.26	0.87
Neutral pharmaceuticals											
Paracetamol	0.9899	1.6	9.3	**208 ± 10**	182	0.15	0.49	72 ± 6	63	2.94	9.80
Primidone	0.9992	6.7	3.8	70 ± 14	70	0.18	0.59	**69 ± 4**	69	0.33	1.11
Cyclophosphamide	0.9908	7.6	20.5	103 ± 18	86	0.06	0.21	**43 ± 4**	35	0.03	0.09
Carbamazepine	0.9999	0.9	1.2	103 ± 1	91	0.05	0.15	**123 ± 21**	108	0.02	0.06

[a] Matrix-matched calibration curve at the concentrations of 1 to 200 ng/L for each standard;
[b] Bold letters represent those recoveries outside the range of 70–120 %.
[c] BPA: bisphenol-A; E2: estradiol; EE2: ethynylestradiol; E1: estrone; DES: Diethylstilbestrol; TCC: triclocarban; TCS: triclosan; 4-*t*-OP: 4-tert-octylphenol; 4-NP: 4-nonylphenols.

to be persistent in soil and water;[58–60] therefore, it is not a surprise to find their presence in the irrigated soils. As found in the irrigation water samples, 4-NP was found to have the highest concentrations in the soils from the four irrigated plots. The compound 4-NP has been reported in various environmental media;[61] thus the 4-NP detected in the irrigated soils might also originate from other sources in addition to effluent-contaminated waters.

Table 6. Concentrations (ng/L) of the analytes detected in irrigation waters during September 2008 (mean ± RSD, $n = 2$).

Site	*4-t-OP*	*4-NP*	*BPA*	*TCS*	*Salicylic acid*	*Ibuprofen*	*Ketoprofen*
WA	4.4 ± 1.7	206 ± 69.7	22.4 ± 0.38	2.4 ± 0.08	ND	ND	ND
WB	3.1 ± 0.24	162 ± 9.9	24.3 ± 1.1	2.2 ± 0.14	2.8 ± 0.24	11.5 ± 0.09	71.2 ± 0.14
WC	3.9 ± 0.33	196 ± 11.6	58.7 ± 6.5	2.9 ± 0.37	ND	ND	ND
WD	7.8 ± 2.2	323 ± 27.2	72.9 ± 5.4	2.1 ± 0.18	101 ± 17.0	ND	103 ± 2.9

ND: not detected. 4-*t*-OP: 4-tert-octylphenol; 4-NP: 4-nonylphenols; BPA: bisphenol-A; TCS: triclosan.

Table 7. Concentrations (ng/g) of the analytes detected in irrigated soil from three different depths during September 2008 (mean ± RSD, n =5).

Site	*Depth (cm)*	*BPA*	*TCC*	*TCS*	*4-NP*	*Salicylic acid*	*Clofibric acid*
SA	0–10	3.4 ± 3.6a	<LOQ	<LOQ	11.2 ± 5.5a	10.7 ± 3.3b	<LOQ
	10–20	<LOQ	<LOQ	<LOQ	11.9 ± 3.0a	10.8 ± 3.6c	<LOQ
	20–30	<LOQ	<LOQ	<LOQ	19.9 ± 7.2a	8.9 ± 8.2ab	<LOQ
SB	0–10	<LOQ	26.1 ± 53.2a	<LOQ	27.6 ± 23.8ab	8.2 ± 3.0b	<LOQ
	10–20	<LOQ	26.4 ± 55.6a	<LOQ	47.4 ± 51.4a	8.7 ± 2.2bc	<LOQ
	20–30	<LOQ	6.2 ± 12.2a	<LOQ	13.0 ± 6.8a	6.5 ± 0.8ab	<LOQ
SC	0–10	5.3 ± 0.9a	5.2 ± 5.3a	<LOQ	24.5 ± 12.2ab	9.5 ± 4.3b	<LOQ
	10–20	3.6 ± 2.2a	4.0 ± 4.1a	3.2 ± 7.1	165 ± 242a	5.9 ± 4.5ab	<LOQ
	20–30	<LOQ	3.8 ± 5.0a	<LOQ	15.9 ± 13.2a	12.5 ± 3.8b	0.49 ± 0.3
SD	0–10	<LOQ	0.70 ± 1.6a	<LOQ	37.3 ± 10.1b	2.5 ± 1.0a	<LOQ
	10–20	<LOQ	1.3 ± 1.6a	<LOQ	93.0 ± 88.9a	3.6 ± 1.2a	0.49 ± 0.3
	20–30	<LOQ	0.82 ± 1.8a	<LOQ	47.4 ± 21.2b	3.3 ± 1.4a	<LOQ

*data were statistically analyzed using SPSS software at a significant level of $P < 0.05$.
<LOQ: below limit of quantitation.
BPA: bisphenol-A; TCC: triclocarban TCS: triclosan; 4-NP: 4-nonylphenol.

Conclusion

Robust and sensitive multiresidue analytical methods were developed and validated for 9 EDCs and 19 PPCPs in environment samples (soil and water) using RRLC-ESI-MS/MS. The target compounds were separated into three groups, which were run under different instrumental conditions. The phenolic EDCs and acidic pharmaceuticals were analyzed under the negative ionization mode, while the neutral pharmaceuticals were analyzed under the positive ionization mode. Matrix effects were observed in the RRLC-MS/MS analysis, but reduced by the use of internal standard addition and matrix-matched calibration. The developed methods were successfully applied to analyze the target compounds in irrigation waters and irrigated soils. Some compounds among the 28 target compounds were detected in these samples, and 4-NP was found to have the highest concentrations both in waters and soils.

Acknowledgments

The authors would like to acknowledge the financial support from the National Natural Science Foundation of China (NSFC 40771180, 40688001 and 40821003) and Guangdong Provincial Natural Science Foundation (8251064004000001). We would also like to thank HC Su, LH Yang and LX Kong for their assistance in sample collection. This is Contribution No. 1233 from GIG CAS.

References

[1] Kavlock, R.J.; Daston, G.P.; DeRosa, C.; Fenner-Crisp, P.; Gray, L.E.; Kaattari, S.; Lucier, G.; Luster, M.; Mac, M.J.; Maczka, C.; Miller, R.; Moore, J.; Rolland, R.; Scott, G.; Sheehan, D.M.; Sinks, T.; Tilson, H.A. Research needs for the risk assessment of health and environmental effects of endocrine disruptors: a report of the U.S. EPA-sponsored workshop. Environ. Health Persp. **1996**, *104* (supplement 4), 715–740.

[2] Kolpin, D.W.; Furlong, E.T.; Meyer, M.T.; Thurman, E.M.; Zaugg, S.D.; Barber, L.B.; Buxton, H.T. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999−2000: a national reconnaissance. Environ. Sci. Technol.**2002**, *36*, 1202–1211.

[3] Fang, H.; Tong, W.; Shi, L.M.; Blair, R.; Perkins, R.; Branham, W.; Hass, B.S.; Xie, Q.; Dial, S.L.; Moland, C. L.; Sheehan, D.M. Structure−Activity Relationships for a Large Diverse Set of Natural, Synthetic, and Environmental Estrogens. Chem. Res. Toxicol. **2001**, *14* (3), 280–294.

[4] Carlsen, E.; Giwercman, A.; Keiding, N.; Skakkebæk, N.E. Evidence for decreasing quality of semen during past 50 years. Brit. Med. J. **1992,** *305*, 609–613.

[5] Colborn, T.; Saal, F.S.V.; Soto, A.M. Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Humans. Environ. Health Persp. **1993**, *101* (5), 378–384.

[6] Sharpe, R.M.; Skakkebaek, N.E. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? The Lancet **1993**, *341*, 1392–1395.

[7] Yager, J.D.; Davidson, N.E. Estrogen Carcinogenesis in Breast Cancer. N. Engl. J. Med. **2006**, *354* (3), 270–282.

[8] Aerni, H.R.; Kobler, B.; Rutishauser, B.V.; Wettstein, F.E.; Fischer, R.; Giger, W.; Hungerbühler, A.; Marazuela, M.D.; Peter, A.; Schönenberger, R.; Vögeli, A.C.; Suter, M.J.F.; Eggen, R.I.L. Combined biological and chemical assessment of estrogenic activities in wastewater treatment plant effluents. Anal. Bioanal. Chem. **2004**, *378*, 688–696.

[9] Esperanza, M.; Suidan, M.T.; Nishimura, F.; Wang, Z.M.; Sorial, G.A. Determination of Sex Hormones and Nonylphenol Ethoxylates in the Aqueous Matrixes of Two Pilot-Scale Municipal Wastewater Treatment Plants. Environ. Sci. Technol. **2004**, *38* (11), 3028–3035.

[10] Kuster, M.; López de Alda, M. J.; Hernando, M.D.; Petrovic, M.; Martín-Alonso, J.; Barceló, D. Analysis and occurrence of pharmaceuticals, estrogens, progestogens and polar pesticides in sewage treatment plant effluents, river water and drinking water in the Llobregat river basin (Barcelona, Spain). J. Hydrol. **2008**, *358* (1–2), 112–123.

[11] Salste, L.; Leskinen, P.; Virta, M.; Kronberg, L. Determination of estrogens and estrogenic activity in wastewater effluent by chemical

analysis and the bioluminescent yeast assay. Sci. Total Environ. **2007**, *378* (3), 343–351.

[12] Snyder, S.A.; Keith, T.L.; Verbrugge, D.A.; Snyder, E.M.; Gross, T.S.; Kannan, K.; Giesy, J.P. Analytical methods for detection of selected estrogenic compounds in aqueous mixtures. Environ. Sci. Technol. **1999**, *33* (16), 2814–2820.

[13] Vieno, N.M.; Tuhkanen, T.; Kronberg, L. Analysis of neutral and basic pharmaceuticals in sewage treatment plants and in recipient rivers using solid phase extraction and liquid chromatography-tandem mass spectrometry detection. J. Chromatogr. A **2006**, *1134* (1–2), 101–111.

[14] Ying, G.G.; Kookana, R.S.; Kumar, A. Fate of estrogens and xenoestrogens in four sewage treatment plants with different technologies. Environ. Toxicol. Chem. **2008**, *27* (1), 87–94.

[15] Ying, G.G.; Kookana, R.S.; Kumar, A.; Mortimer, M. Occurrence and implications of estrogens and xenoestrogens in sewage effluents and receiving waters from South East Queensland. Sci. Total Environ. **2009**, *407* (18), 5147–5155.

[16] Ying, G.G.; Kookana, R.S. Triclosan in wastewaters and biosolids from Australian wastewater treatment plants. Environ. Int. **2007**, *33* (2), 199–205.

[17] Zhang, Y.; Geißen, S.U.; Gal, C. Carbamazepine and diclofenac: Removal in wastewater treatment plants and occurrence in water bodies. Chemosphere **2008**, *73* (8), 1151–1161.

[18] Daughton, C.G.; Ternes, T.A. Pharmaceuticals and personal care products in the environment: agents of subtle change? Environ. Health Persp. **1999**, *107* (Supplement 6), 907–938.

[19] Gómez, M.J.; Agüera, A.; Mezcua, M.; Hurtado, J.; Mocholí, F.; Fernández-Alba, A.R. Simultaneous analysis of neutral and acidic pharmaceuticals as well as related compounds by gas chromatography-tandem mass spectrometry in wastewater. Talanta **2007**, *73* (2), 314–320.

[20] Hibberd, A.; Maskaoui, K.; Zhang, Z.; Zhou, J.L. An improved method for the simultaneous analysis of phenolic and steroidal estrogens in water and sediment. Talanta **2009**, *77* (4), 1315–1321.

[21] Moeder, M.; Martin, C.; Harynuk, J.; Górecki, T.; Vinken, R.; Corvini, P.F.X. Identification of isomeric 4-nonylphenol structures by gas chromatography-tandem mass spectrometry combined with cluster analysis. J. Chromatogr. A **2006**, *1102* (1–2), 245–255.

[22] Zhao, J.L.; Ying, G.G.; Wang, L.; Yang, J.F.; Yang, X.B.; Yang, L.H.; Li, X. Determination of phenolic endocrine disrupting chemicals and acidic pharmaceuticals in surface water of the Pearl Rivers in South China by gas chromatography–negative chemical ionization–mass spectrometry. Sci. Total Environ. **2009**, *407* (2), 962–974.

[23] Beck, I.C.; Bruhn, R.; Gandrass, J.; Ruck, W. Liquid chromatography-tandem mass spectrometry analysis of estrogenic compounds in coastal surface water of the Baltic Sea. J. Chromatogr. A **2005**, *1090* (1–2), 98–106.

[24] Chang, H.; Wan, Y.; Naile, J.; Zhang, X.; Wiseman, S.; Hecker, M.; Lam, M.H.W.; Giesy, J.P.; Jones, P.D. Simultaneous quantification of multiple classes of phenolic compounds in blood plasma by liquid chromatography-electrospray tandem mass spectrometry. J. Chromatogr. A **2010**, *1217* (4), 506–513.

[25] Gabet-Giraud, V.; Miege, C.; Herbreteau, B.; Hernandez-Raquet, G.; Coquery, M. Development and validation of an analytical method by LC-MS/MS for the quantification of estrogens in sewage sludge. Anal. Bioanal. Chem. **2010**, *396* (5), 1841–1851.

[26] Hosogi, J.; Tanaka, H.; Fujita, K.; Kuwabara, T.; Ikegawa, S.; Kobayashi, N.; Mano, N.; Goto, J. LC-MS/MS coupled with immunoaffinity extraction for determination of estrone, 17β-estradiol and estrone 3-sulfate in human plasma. J. Chromatogr. B **2010**, *878* (2), 222–227.

[27] Pedrouzo, M.; Borrull, F.; Pocurull, E.; Marcé, R.M. Estrogens and their conjugates: Determination in water samples by solid-phase extraction and liquid chromatography-tandem mass spectrometry. Talanta **2009**, *78* (4–5), 1327–1331.

[28] Wang, J.; Pan, H.F.; Liu, Z.Z.; Ge, F. Ultra-high-pressure liquid chromatography-tandem mass spectrometry method for the determination of alkylphenols in soil. J. Chromatogr. A **2009**, *1216* (12), 2499–2503.

[29] Zhao, X.; Metcalfe, C. D. Characterizing and Compensating for Matrix Effects Using Atmospheric Pressure Chemical Ionization Liquid Chromatography-Tandem Mass Spectrometry: Analysis of Neutral Pharmaceuticals in Municipal Wastewater. Anal. Chem. **2008**, *80* (6), 2010–2017.

[30] Conley, J.M.; Symes, S.J.; Kindelberger, S.A.; Richards, S.M. Rapid liquid chromatography-tandem mass spectrometry method for the determination of a broad mixture of pharmaceuticals in surface water. J. Chromatogr. A **2008**, *1185* (2), 206–215.

[31] Gros, M.; Petroviğ, M.; Barcelć, D. Development of a multi-residue analytical methodology based on liquid chromatography-tandem mass spectrometry (LC-MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. Talanta **2006**, *70* (4), 678–690.

[32] Sun, L.; Yong, W.; Chu, X.G.; Lin, J.M. Simultaneous determination of 15 steroidal oral contraceptives in water using solid-phase disk extraction followed by high performance liquid chromatography-tandem mass spectrometry. J. Chromatogr. A**2009**, *1216* (28), 5416–5423.

[33] Xu, L.; Spink, D. C. Analysis of steroidal estrogens as pyridine-3-sulfonyl derivatives by liquid chromatography electrospray tandem mass spectrometry. Anal. Biochem. **2008**, *375* (1) 105–114.

[34] Chambers, E.; Wagrowski-Diehl, D.M.; Lu, Z.; Mazzeo, J.R. Systematic and comprehensive strategy for reducing matrix effects in LC/MS/MS analyses. J. Chromatogr. B **2007**, *852* (1–2), 22–34.

[35] Gómez, M. J.; Petrovič, M.; Fernández-Alba, A.R.; Barcelć, D. Determination of pharmaceuticals of various therapeutic classes by solid-phase extraction and liquid chromatography-tandem mass spectrometry analysis in hospital effluent wastewaters. J. Chromatogr. A **2006**, *1114* (2), 224–233.

[36] Kasprzyk-Hordern, B.; Dinsdale, R.M.; Guwy, A.J. Multi-residue method for the determination of basic/neutral pharmaceuticals and illicit drugs in surface water by solid-phase extraction and ultra performance liquid chromatography-positive electrospray ionisation tandem mass spectrometry. J. Chromatogr. A **2007**, *1161* (1–2), 132–145.

[37] Van De Steene, J.C.; Mortier, K.A.; Lambert, W.E. Tackling matrix effects during development of a liquid chromatographic-electrospray ionisation tandem mass spectrometric analysis of nine basic pharmaceuticals in aqueous environment samples. J. Chromatogr. A **2006**, *1123* (1), 71–81.

[38] Viglino, L.; Aboulfadl, K.; Prévost, M.; Sauvé, S. Analysis of natural and synthetic estrogenic endocrine disruptors in environmental waters using online preconcentration coupled with LC-APPI-MS/MS. Talanta **2008**, *76* (5), 1088–1096.

[39] Wu, J.; Qian, X.; Yang, Z.; Zhang, L. Study on the matrix effect in the determination of selected pharmaceutical residues in seawater by solid-phase extraction and ultra-high-performance liquid chromatography-electrospray ionization low-energy collision-induced dissociation tandem mass spectrometry. J. Chromatogr. A **2010**, *1217* (9), 1471–1475.

[40] Asano, T.; Levine, A.D. Wastewater reclamation, recycling and reuse: past, present, and future. Water Sci. Technol. **1996**, *33* (10–11), 1–14.

[41] Bixio, D.; Thoeye, C.; De Koning, J.; Joksimovic, D.; Savic, D.; Wintgens, T.; Melin, T. Wastewater reuse in Europe. Desalination **2006**, *187* (1–3), 89–101.

[42] Lopez, A.; Pollice, A.; Lonigro, A.; Masi, S.; Palese, A.M.; Cirelli, G.L.; Toscano, A.; Passino, R. Agricultural wastewater reuse in southern Italy. Desalination **2006**, *187* (1–3), 323–334.

[43] Toze, S. Water reuse and health risks—real vs. perceived. Desalination **2006**, *187* (1–3), 41–51.

[44] Weber, S.; Khan, S.; Hollender, J. Human risk assessment of organic contaminants in reclaimed wastewater used for irrigation. Desalination **2006**, *187* (1–3), 53–64.
[45] Kinney, C.A.; Furlong, E.T.; Werner, S.L.; Cahill, J.D. Presence and distribution of wastewater-derived pharmaceuticals in soil irrigated with reclaimed water. Environ. Toxicol. Chem. **2006**, *25*, 317–326.
[46] Tao, S.; Cui, Y.H.; Xu, F.L.; Li, B.G.; Cao, J.; Liu, W.X.; Schmitt, G.; Wang, X.J.; Shen, W.R.; Qing, B.P.; Sun, R. Polycyclic aromatic hydrocarbons (PAHs) in agricultural soil and vegetables from Tianjin. Sci. Total Environ. **2004**, *320*, 11–24.
[47] Hao, C.; Zhao, X.; Tabe, S.; Yang, P. Optimization of a Multiresidual Method for the Determination of Waterborne Emerging Organic Pollutants Using Solid-Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry and Isotope Dilution Mass Spectrometry. Environ. Sci. Technol. **2008**, *42* (11), 4068–4075.
[48] Ingrand, V.; Herry, G.; Beausse, J.; de Roubin, M.R. Analysis of steroid hormones in effluents of wastewater treatment plants by liquid chromatoraphy-tandem mass spectrometry. J. Chromatogr. A **2003**, *1020* (1), 99–104.
[49] Kasprzyk-Hordern, B.; Dinsdale, R.M.; Guwy, A.J. The effect of signal suppression and mobile phase composition on the simultaneous analysis of multiple classes of acidic/neutral pharmaceuticals and personal care products in surface water by solid-phase extraction and ultra performance liquid chromatography-negative electrospray tandem mass spectrometry. Talanta **2008**, *74* (5), 1299–1312.
[50] Vanderford, B.J.; Pearson, R.A.; Rexing, D.J.; Snyder, S.A. Analysis of Endocrine Disruptors, Pharmaceuticals, and Personal Care Products in Water Using Liquid Chromatography/Tandem Mass Spectrometry. Anal. Chem. **2003**, *75* (22), 6265–6274.
[51] Benijts, T.; Dams, R.; Günther, W.; Lambert, W.; Leenheer, A.D. Analysis of estrogenic contaminants in river water using liquid chromatography coupled to ion trap based mass spectrometry. Rapid Comm. Mass Spectrom. **2002**, *16*, 1358–1364.
[52] Benijts, T.; Dams, R.; Lambert, W.; Leenheer, A.D. Countering matrix effects in environmental liquid chromatography-electrospray ionization tandem mass spectrometry water analysis for endocrine disrupting chemicals. J. Chromatogr. A **2004**, *1029* (1–2), 153–159.
[53] Grujič, S.; Vasiljevič, T.; Lauševič, M. Determination of multiple pharmaceutical classes in surface and ground waters by liquid chromatography-ion trap-tandem mass spectrometry. J. Chromatogr. A **2009**, *1216* (25), 4989–5000.
[54] Chen, H.C.; Wang, P.L.; Ding, W.H. Using liquid chromatography-ion trap mass spectrometry to determine pharmaceutical residues in Taiwanese rivers and wastewaters. Chemosphere **2008**, *72* (6), 863–869.
[55] Miao, X.S.; Koenig, B.G.; Metcalfe, C.D. Analysis of acidic drugs in the effluents of sewage treatment plants using liquid chromatography-electrospray ionization tandem mass spectrometry. J. Chromatogr. A **2002**, *952* (1–2), 139–147.
[56] Halden, R.U.; Paull, D.H. Co-occurrence of triclocarban and triclosan in U.S. water resources. Environ. Sci. Technol. **2005**, *39* (6), 1420–1426.
[57] Tauxe-Wuersch, A.; De Alencastro, L.F.; Grandjean, D.; Tarradellas, J. Occurrence of several acidic drugs in sewage treatment plants in Switzerland and risk assessment. Water Res. **2005**, *39* (9), 1761–1772.
[58] Ying, G.G.; Yu, X.Y.; Kookana, R.S. Biological degradation of triclocarban and triclosan in a soil under aerobic and anaerobic conditions and comparison with environmental fate modelling. Environ. Pollut. **2007**, *150* (3), 300–305.
[59] Zwiener, C.; Glauner, T.; Frimmel, F.H. Biodegradation of pharmaceutical residues investigated by SPE-GC/ITD-MS and on-line derivatization. J. High Resolut. Chrom. **2000**, *23* (7/8), 474–478.
[60] Zwiener, C.; Frimmel, F.H. Short-term tests with a pilot sewage plant and biofilm reactors for the biological degradation of the pharmaceutical compounds clofibric acid, ibuprofen, and diclofenac. Sci.Total Environ. **2003**, *309* (1–3), 201–211.
[61] Ying, G.G.; Williams, B.; Kookana, R. Environmental fate of alkylphenols and alkylphenol ethoxylates ? a review. Environ. Int. **2002b**, *28* (3), 215–226.