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Simultaneous determination of 20 trace organic chemicals in waters by solid-phase extraction (SPE) with triple-quadrupole mass spectrometer (QqQ-MS) and hybrid quadrupole Orbitrap high resolution MS (Q-Orbitrap-HRMS)

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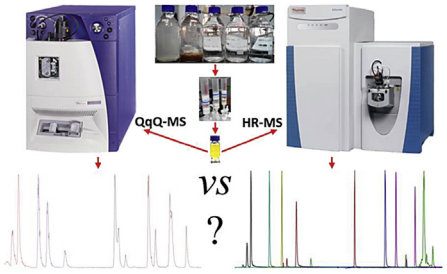
HIGHLIGHTS

- Twenty trace organic chemicals in waters were simultaneously determined by two different LC-MS systems.
- Triple-quadrupole MS (QqQ-MS) and hybrid quadrupole Orbitrap high resolution MS (Q-Orbitrap-HRMS) instruments were compared.
- Fewer matrix effects and lower detection limits were provided by Q-Orbitrap-HRMS, with more stable performance for the QqQ-MS.

GRAPHICAL ABSTRACT



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ABSTRACT

A sensitive method for simultaneous determination of 20 trace organic chemicals (TOrCs, including preservatives, antioxidants, disinfectants, oestrogens, alkyl-phenols and bisphenol-A) in surface water and wastewater has been developed and validated based on the optimisation of solid-phase extraction (SPE) followed by liquid chromatography-mass spectrometry (LC-MS) analysis. 500 mL acidified (pH = 2.5) water samples were pre-concentrated by Supel-Select HLB cartridge (200 mg, 6 mL) and eluted with 12 mL mixture of acetonitrile and ethyl acetate (50:50, v/v). This optimised SPE procedure could provide >75% recoveries for the majority of TOrCs. The instrumental methods were developed using two different LC-MS systems: a triple-quadrupole MS (QqQ-MS) and a hybrid quadrupole Orbitrap high resolution MS (Q-Orbitrap-HRMS). Both showed good performance data, but the former system provided better linearity and method precision, with the latter system providing 2–33 times lower detection limits. Different matrix effects were observed for both systems: No remarkable matrix effects were observed for Q-Orbitrap-HRMS but significant matrix effects were found in influent and river water samples for the QqQ-MS. This analytical method was subsequently employed to analyse the TOrCs in river waters and wastewaters from China successfully, which confirmed its applicability to environmental samples.

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1. Introduction

Preservatives, antioxidants, disinfectants, oestrogens, alkyl-phenols and bisphenol-A are among the trace organic chemicals (TOrCs) (Anumol and Snyder, 2015) that are often present in house and personal care products and pharmaceuticals (Gorga et al., 2013; Guo and Kannan, 2013; Liu et al., 2015b; Tanoue et al., 2015) and discharged to the aquatic environment across the world (Kolpin et al., 2002; Brausch and Rand, 2011; Boxall et al., 2012; Bu et al., 2013; Ortiz de García et al., 2013; Haman et al., 2015; Petrie et al., 2015). As a result, attention has been paid to their potential long-term effects on human health (Guo and Kannan, 2013; Błędzka et al., 2014; Wang et al., 2015) and wildlife (Tanoue et al., 2015; Xue et al., 2015). Monitoring the concentrations of these chemicals and studying their fate and behaviour in aquatic environment enables an assessment of their potential transport through food chains and an evaluation of potential risks on ecosystems and human health.

Many of the analytical methods for these chemicals in water samples have been developed based on pre-treatment, normally solid-phase extraction (SPE) (Zhao et al., 2009; Yu et al., 2011; Richardson, 2012; Gorga et al., 2013; Anumol and Snyder, 2015), followed by instrumental determination by gas chromatography-mass spectrometry (GC-MS) (Zhang et al., 2006; Peng et al., 2008; Zhao et al., 2009) or liquid chromatography-tandem mass spectrometry (LC-MS/MS) (Kasprzyk-Hordern et al., 2008; Gonzalez-Marino et al., 2009; Anumol and Snyder, 2015; Liu et al., 2015a). With the rapid development of the technology, LC-MS/MS techniques have become the preferred analytical method for polar and/or non-volatile TOrCs (Richardson, 2012), which have advantages such as high selectivity, sensitivity and throughput, reduced analytical time and do not require derivatisation as some GC-MS procedures do (Zhao et al., 2009). This has led to their widespread application for water/wastewater sample analysis (Gonzalez-Marino et al., 2009; Gorga et al., 2013). More recently, LC systems equipped with high resolution MS (LC-HRMS), such as time-of-flight (TOF) and Orbitrip MS, are increasingly popular as it is beneficial for both quantifying target analytes and identifying non-target analytes (Richardson, 2012; Hernández et al., 2014; Schymanski et al., 2015).

A considerable amount of research has been conducted to determine certain TOrCs, such as preservatives (Gonzalez-Marino et al., 2009; Li et al., 2009; Yu et al., 2011; Gorga et al., 2013; Guo and Kannan, 2013; Asimakopoulos et al., 2014), antioxidants (Li et al., 2009; Liu et al., 2015a), disinfectants (Yu et al., 2011; Gorga et al., 2013; Asimakopoulos et al., 2014; Anumol and Snyder, 2015), oestrogens (Yu et al., 2011; Gorga et al., 2013) or alkyl-phenols (Gorga et al., 2013), in different matrixes (water/wastewater (Gonzalez-Marino et al., 2009; Gorga et al., 2013; Anumol and Snyder, 2015; Liu et al., 2015a), sludge (Yu et al., 2011; Liu et al., 2015a), cosmetics (Guo and Kannan, 2013), foodstuffs (Li et al., 2009), biota (Asimakopoulos et al., 2014)) using LC-MS/MS, but few studies have provided their simultaneous determination. Furthermore, few studies have conducted a comparative evaluation for conventional LC-MS/MS (triple-quadrupole MS) and LC-HRMS (Kaufmann et al., 2010; Zacs et al., 2014), such an assessment would be of great interest for laboratories that have access to one or the other instrument setup.

Therefore, the aims of this study were to 1) develop and optimise a rapid and sensitive method for the simultaneous extraction and determination of 20 TOrCs (preservatives, antioxidants, disinfectants, oestrogens, alkyl-phenols and bisphenol-A) by SPE and LC-MS/MS, 2) compare the performance of two different LC-MS systems: a triple-quadrupole MS (QqQ-MS) system and a hybrid quadrupole Orbitrap high resolution MS (Q-Orbitrap-HRMS) system for these chemicals, and 3) apply this analytical method to determine the occurrence of these substances in river water and municipal wastewater collected from a city in Central China.

2. Materials and methods

2.1. Chemicals and materials

Twenty typical chemicals from 6 groups of TOrCs (preservatives, antioxidants, disinfectants, oestrogens, alkyl-phenols and bisphenol-A) were selected for analysis in this study. High purity standards of these compounds, including six preservatives and one of their metabolites (methylparaben (MEP), ethylparaben (ETP), propylparaben (PRP), butylparaben (BUP), benzylparaben (BEP), heptyl paraben (HEP) and 4-hydroxybenzoic acid (PHBA)), two antioxidants (butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT)), three disinfectants (ortho-phenylphenol (OPP), triclosan (TCS) and triclocarban (TCC)), five oestrogens (diethylstilbestrol (DES), estrone (E1), β-estradiol (E2), estriol (E3) and 17α-ethinylestradiol (EE2)), two alkyl-phenols (4-*tert*-octylphenol (4-*t*-OP) and nonylphenol (NP)) and bisphenol-A (BPA), were purchased from Sigma-Aldrich (UK). Detailed information of these TOrCs is provided in the Supplementary data Table S1. Internal standards (ISs, purity information was listed in Table S2) including methyl 4-hydroxybenzoate-ring-^{13}C6 (^{13}C MEP), ethyl 4-hydroxybenzoate-ring-^{13}C6 (^{13}C ETP), propyl 4-hydroxybenzoate-ring-^{13}C6 (^{13}C PRP), butyl 4-hydroxybenzoate-ring-^{13}C6 (^{13}C BUP), butylated hydroxyanisole (methoxyl-d_3) (BHA-d_3), 2-phenyl-^{13}C6-phenol (^{13}C OPP) and BPA-d_{16} were purchased from Sigma-Aldrich (UK), other ISs including 4-hydroxybenzoic-2,3,5,6-d_4 acid (PHBA-d_4), BHT-d_{24}, TCS-d_3, estrone-2,4,16,16-d_4 (E1-d_4), 17β-Estradiol-2,4,16,16,17-d_5 (E2-d_5), estriol-2,4-d_2 (E3-d_2), 17α-ethinylestradiol-2,4,16,16-d_4 (EE2-d_4), 4-n-octyl-d_{17}-phenol (4-n-OP-d_{17}) and 4-n-nonylphenol-2,3,5,6-d_4 (4-n-NP-d_4) were purchased from QMX Laboratories (UK).

All reagents are analytical grade or better and $\geq$99% purity, organic solvents are HPLC grade. Formic acid (FA), acetic acid (HAc) and ammonia solution (NH_4OH, 5 M) were purchased from Sigma-Aldrich (UK). Hydrochloric acid (HCl, 35.5–37.5%), ammonium formate (AF), ammonium acetate (NH_4Ac), methanol (MeOH), acetonitrile (ACN) and ethyl acetate (EA) were obtained from Fisher Scientific (UK). Water used in the experiments was supplied by a Milli-Q water (MQ water) purification system (>18.2 MΩ cm^{-1}, Millipore, UK).

Stock solutions of each chemical standard (1000 mg L^{-1}) were prepared in MeOH and stored in sealed amber bottles in the dark at −20 °C for later use. Working standard solutions (10 mg L^{-1}) were prepared weekly by diluting the stock solutions with MeOH and stored at 4 °C before use. The calibration standards with increasing concentrations of analytes and 100 μg L^{-1} ISs were prepared in MeOH/MQ water (1:1, v/v) with/without additives.

2.2. Water samples

Freshwater samples from the River Conder (Lancaster, UK) and wastewater samples (both influent and effluent) from Lancaster WWTP were collected in clean amber bottles for the optimisation experiments. River water and wastewater samples from a city in Central China (Wuhan) were collected for environmental analysis. The bottles were fully immersed and soaked in Decon 90 solution (4%) overnight and then rinsed thoroughly with tap water and MQ water, followed by baking at 450 °C for 4 hours (h) before use. The bottles were rinsed by water samples from sampling locations for 3 times before taking final samples. The water samples were transported to the laboratory after collected and stored in the dark at

4 °C and processed within 24 h.

2.3. Solid-phase extraction and reconstitution

Solid-phase extraction (SPE) was used for extracting the TOrCs from the water samples. Reversed-phase SPE cartridges are commonly-used for extraction of TOrCs in wastewaters (Gonzalez-Marino et al., 2009; Yu et al., 2011). Three types of widely-used reversed-phase SPE cartridges were used in this study: Oasis-HLB SPE cartridges, Supel-Select HLB tubes and Strata-X tubes, purchased from Waters (UK), Sigma-Aldrich (UK) and Phenomenex (UK), respectively.

To optimise the SPE method, several procedures were carried out including 1) adjustment of pH (2.5 or 7) for water samples before filtration, 2) selection of SPE cartridges (Oasis-HLB, Supel-Select HLB and Strata-X) and 3) selection of elution solvents (MeOH, ACN, EA). 100 ng L^{-1} of individual TOrCs were spiked into the river water samples for SPE optimisation, followed by determination using System A, the LC-QqQ-MS.

After pH adjustment, the water samples were filtered (Whatman GF/F filter, 0.7 μm) to remove suspended particles. 500 mL of samples was extracted separately by SPE using the three cartridges mentioned above. 100 ng of individual IS was added into filtered samples before extraction. The SPE cartridges were preconditioned with 10 mL of ACN, EA (or combination), followed by 10 mL MeOH and 10 mL MQ water, and the water samples were then introduced into the cartridges at a flow rate of about 3 mL min^{-1}. The sample bottle was then rinsed twice with two aliquots of 50 mL of 5% (v/v) MeOH in MQ water, which were also passed through the cartridge. After loading, the cartridges were rinsed with 10 mL MQ water and vacuum dried for 20 min. The TOrCs retained by the cartridges were finally eluted with 12 mL of elution solvent (MeOH, ACN, EA or combination). For the SPE optimisation on pH adjustment and SPE cartridge selection, MeOH was used as the elution solvent, as it is the most commonly used SPE solvent for the chemicals studied here.

Sample extracts were reduced to 1 mL under a gentle flow of N_2, followed by syringe filtration (Whatman, PTFE, 0.22 μm) and transferred to amber vials, stored at −20 °C before instrumental analysis. Just prior to the instrumental analysis, 300 μL aliquot of each sample extract (200 μL for influent) was dried under a gentle N_2 flow and reconstituted in 100 μL of MQ water and MeOH mixture (50:50, v/v) with the same additives in the optimised mobile phase.

2.4. Instrumental analysis

For comparative purposes, the same samples were analysed by two different LC-MS systems. These two systems were selected in terms of equipment and running cost, and expected performance. System A, LC-QqQ-MS: The system consisted of an Agilent 1100 series HPLC system and a Quattro Micro triple-quadrupole mass spectrometer (QqQ MS, Micromass, Manchester, UK) with an electrospray ionisation (ESI) source. System B, LC-Q-Orbitrap-HRMS: An ultrahigh performance liquid chromatography-high resolution mass spectrometer system (UHPLC-HRMS) with an Ultimate 3000 UHPLC (Dionex) coupled to a hybrid quadrupole-Orbitrap mass spectrometer (Q-Orbitrap-HRMS, Q-Exactive, Thermo Fisher Scientific, Germany) equiped with a heated electrospray ionization probe (HESI-II). Details for the instruments can be found in the Supplementary data.

The selection of MS parameters was based on the most intense signal of fragmentation products for each chemical in negative ion mode. These MS parameters for both systems were optimised by a continuous-flow mode of direct infusion. The procedures for the optimisation of the individual parameters were described in the Supplementary data. To improve separation by the LC and the MS performance, especially the ESI sensitivity performance, several mobile phases (MeOH, ACN and MQ water) and their additives were considered and studied by the same procedure of direct infusion as described above.

After initial analyses, the composition of mobile phase and additives, and the gradient procedure was optimised for LC separation and maximisation of the MS responses for both systems. The detailed setting of the LC and MS parameters was given in the Supplementary data.

2.5. Recoveries and matrix effect

Based on the published literature (Matuszewski et al., 2003; Quintana and Reemtsma, 2004; Trufelli et al., 2011), distinction between SPE recoveries for the sample pre-treatment, matrix effects during the LC-MS/MS analysis and overall method recoveries for the whole method were conducted by spiking samples before/after the optimised SPE procedures with the same amount of analytes. Samples (river water, wastewater influent and effluent) were spiked with the TOrCs and ISs before or after SPE. Additionally, non-spiked samples (no additional TOrCs added in whole process) were also measured to allow for subtraction of the signal from the spiked samples. The TOrCs response factors (RFs, after non-spiked sample signal subtraction) of all the spiked samples were then compared with RFs of the standards. Thus, three types of RFs were acquired: one from the pure standard ($R1$), another from the pre-spiked samples ($R2$), and the last one from the post-spiked samples ($R3$). The matrix effect (ME, %), SPE recovery (RE_{SPE}, %) and the overall method recovery ($RE_{OVERALL}$, %) can be expressed by Equations (1), (2) and (3), respectively:

$$\text{Matrix effect}: \ ME(\%) = \frac{R3}{R1} \times 100 \tag{1}$$

$$\text{SPE recovery}: \ RE_{SPE}(\%) = \frac{R2}{R3} \times 100 \tag{2}$$

$$\text{Overall recovery}: \ RE_{OVERALL}(\%) = \frac{R2}{R1} \times 100 \tag{3}$$

ME (%) > 100% indicates a signal enhancement, whereas the value < 100% indicates signal suppression. It should be pointed out that the RE_{SPE} represents a true recovery for the SPE extraction procedures only, which is not affected by matrix (Trufelli et al., 2011).

2.6. Quantification and method validation

The quantification of the target TOrCs was based on the precursor ion/product ion transitions or target ions. For System A, the target TOrCs were quantified by simultaneously recording at least two highest characteristic transitions from the $[M-H]^-$ precursor ion to the selected product ions in the multiple reaction monitoring (MRM) mode. For each chemical, the most intense transition was selected for quantification and the second one used for confirmation (Table 1 for the target TOrCs, Tables S2 for ISs and Fig. S1 for the chromatograms). The optimisation of precursor ion/product ion transitions was based on the QuanOptimize function in Masslynx 4.1. For System B, the quantification of the target compounds was carried out at both target-selected ion monitoring (t-SIM) and target-MS2 (t-MS2) scanning modes (TCS and BHT for t-SIM mode only, due to the instability of product ions). The t-SIM mode of HRMS working at 70 000 full width at half-maximum (FWHM)

Table 1
Optimised LC-MS/MS scan parameters for target TOrCs by both instruments.

TOrCs	Accurate MW[a]	LC-QqQ-MS				LC-Q-Orbitrap-HRMS		
		Parent ion	Daughter ions	CV	CE	Parent ion	Daughter ions	NCE
MEP	152.0473	151	92/136[b]	25	25/15	151.0388	92.0248/136.0145	50
ETP	166.0630	165	92/136	30	20/15	165.0546	92.0248/136.0145	55
PRP	180.0786	179	92/136	30	25/15	179.0704	92.0248/136.0145	55
BUP	194.0943	193	92/136	30	25/15	193.0862	92.0248/136.0145	55
BEP	228.0786	227	92/136	30	25/15	227.0708	92.0248/136.0145	50
HEP	236.1412	235	92/136	35	20/15	235.1335	92.0248/136.0145	50
PHBA	138.0317	137	93	20	15	137.0231	93.0326	20
BHA	180.1150	179	164/149	20	15/25	179.1067	164.0824/149.0588	55
BHT	220.1827	219	204/163	30	25/30	219.1748	-[c]	–
OPP	170.0732	169	141/115	35	25/30	169.0648	141.0690/115.0533	90
TCS	287.9512	287/289	35	15	5	286.9443/288.9412	–	–
TCC	313.9780	313/315	160/162	20	15/15	312.9713/314.9682	159.9707/161.9676	10
BPA	228.1150	227	212/133	35	15/25	227.1072	212.0822/133.0638	60
DES	268.1463	267	237/251	40	30/25	267.1388	237.0905/215.1063	60
E1	270.1620	269	145/143	50	35/55	269.1545	145.0639/159.0806	70
E2	272.1776	271	183/145	55	40/40	271.1702	145.0639/183.0797	85
E3	288.1725	287	145/183	55	40/45	287.1649	145.0638/171.0795	90
EE2	296.1776	295	145/159	55	40/45	295.1700	145.0639/159.0796	75
4-*t*-OP	206.1671	205	134/133	35	25/20	205.1590	133.0638	60
NP	220.1827	219	133/147	35	35/30	219.1748	133.0638	60

[a] MW: molecular weight.
[b] A/B: quantification ion/confirmation ion.
[c] Not applicable.

resolution power is capable enough for determination of TOrCs in complex matrices using the accurate parent ions. For the t-MS2 mode of System B, the parent ions specified in the inclusion list were selected by the quadrupole, fragmented in the higher energy collision dissociation (HCD) cell with the specific fragmentation energy and then collected in the C-trap, with the daughter ions accurately recorded by the Orbitrap detector. To simplify the quantification procedures for HRMS, the highest response of the accurate ion for each chemical at the t-SIM scan mode was used for quantification (Table 1 and S2, Fig. S2).

Some instrumental and method validation parameters, such as linearity, range and calibration curves, accuracy and precision, and detection limits were also discussed for quantification purposes.

2.6.1. Linearity, range and calibration curves

Linearity and range of the analytical procedure was tested by dilution of stock solutions. Concentration levels from 0 to 1000 $\mu g\ L^{-1}$ were used for each TOrC. A multi-component internal standard calibration curve (0.1, 0.25, 0.5, 1, 2.5, 5, 10, 25, 50, 100, 250, 500 and 1000 $\mu g\ L^{-1}$ for each TOrC, and 100 $\mu g\ L^{-1}$ for each internal standard) was established for quantification.

2.6.2. Accuracy and precision

Method accuracy was evaluated with the percentage of deviation of results for samples with known (added) amounts of analytes. Precision was estimated by the intra-day and inter-day reproducibility using the relative standard deviation (RSD) of replicate measurements for both instrument and analytical method. 12 injections for spiked river water samples with 2 concentrations (10 and 200 $\mu g\ L^{-1}$ of TOrCs were added before extraction, three replicates of each concentration) and standard samples with 2 concentrations (10 and 200 $\mu g\ L^{-1}$, three replicates of each concentration), were analysed over a short time interval on the same day under the same operating conditions to assess the intra-day precision. Similarly, 12 injections undertaken on three different days with the same concentrations were conducted to verify the inter-day precision.

2.6.3. Detection limits (DL)

DLs for TOrCs were determined based on the signal-to-noise (S/N) methodology. DL is defined as the concentration that represents 3 times of the S/N. The IDLs (instrument DLs) of each TOrC were calculated using standards with low concentrations, and MDLs (method DLs) for river water, wastewater influent and effluent were estimated by IDLs, SPE absolute recoveries (RE_{SPE}, %) and the concentration factors (*CF*, 1000 for the influent and 1500 for effluent and river water) for TOrCs, using Equation (4) (Kasprzyk-Hordern et al., 2008):

$$MDL = \frac{IDL}{RE_{SPE} \times CF} \times 100 \quad (4)$$

2.7. Data analysis and statistics

All the laboratory experiments and field sample collection were carried out in triplicate unless stated specifically, and the results were expressed as the average ± standard deviation (SD). The statistical analysis was conducted by IBM *SPSS* Statistics software (Version 22), the significant differences were statistically tested by analysis of variance (ANOVA) at 5% significant level.

3. Results and discussion

3.1. Effect of mobile phases and additives

To optimise the LC separation and ESI ionisation, different organic mobile phases and the effect of mobile phase additives were studied. ACN was selected as the major organic mobile phase, because it could provide better separation and lower column pressure than MeOH. A small proportion (2.5%) of MeOH and MQ water was added into organic mobile phase to enhance the solubility of additives.

Acid additives such as FA in the mobile phases are known to strongly suppress the signal in ESI negative mode (Gonzalez-Marino et al., 2009) when comparing with pure mobile phases,

which was confirmed in this study (Table S3). The suppression for all the compounds increased with higher concentrations of acids which is due to the presence of these organic acids converting the target chemicals into their neutral form, which decreased their MS response in negative ESI mode. The results using AF and NH_4Ac indicated that the presence of AF in the mobile phase could also suppress the signals for all the compounds in negative ESI mode, but showed less suppression than FA. The addition of NH_4Ac at about 5 mM concentration caused enhancement of signals for antioxidants, disinfectants, oestrogens and alkyl-phenols, but resulted in a slight suppression of signals for parabens.

Basic additives such as ammonia and amines can also be used for LC-ESI-MS analysis. In this study, only ammonia was tested with amines not considered because of their strong retention in the LC-MS system, which may lead to signal suppression. The results showed strong enhancement of the ESI negative response for most TOrCs and slight suppression for the others when adding NH_4OH at 5–10 mM into the mobile phase. The majority of the tests were conducted with System A but also confirmed using System B.

Based on the results of the effect of mobile phase additives on signal response, a 5 mM ammonia solution was added into both organic and aqueous mobile phases for the optimised instrumental analysis procedures. The same concentration of ammonia solution was also added into the final samples prior to the LC-MS analysis.

3.2. Optimisation of SPE conditions

The SPE conditions were optimised using 500 mL river water samples spiked with 100 ng L^{-1} (50 ng) of individual TOrCs, followed by further pre-treatment and processing. The effects of water sample pH, elution solvents and different SPE cartridges were tested to achieve the best recoveries for target TOrCs.

3.2.1. pH effect

Water sample pH was normally adjusted for better retention on reversed-phase SPE cartridges. It has been suggested that the pH for the samples should be adjusted to 2 pH units below the most acidic analytes' pK_a (Waters Corporation, 2008). Thus, river water samples were adjusted to pH 2.5 (the smallest pK_a value for all target compounds is about 4.38 for PHBA) or pH 7, followed by extraction using Supel-Select HLB tubes to test the effect of sample pH on recoveries. The results (Fig. S3A) showed that recoveries at pH 2.5 (51.0 ± 9.5 to 91.9 ± 2.5%) were better than at pH 7 (21.3 ± 11.4 to 90.6 ± 1.8%) for most TOrCs, especially for HEP, PHBA and BHT. There were no significant differences (ANOVA, $p > 0.05$) in recoveries for oestrogens and alkyl-phenols between pH 2.5 and 7, which was similar to results from Liu et al. and Gonzalez-Marino et al. (Liu et al., 2004; Gonzalez-Marino et al., 2009). As a result of the improved performance under pH 2.5, all water samples were acidified to pH 2.5 for further SPE optimisation.

3.2.2. SPE cartridge selection and eluting solvent effect

The results in Fig. S3B indicated that, for the majority of TOrCs, no significant differences (ANOVA, $p > 0.05$) of SPE recoveries were found among three kinds of SPE cartridges. All these three SPE cartridges could provide good and stable recoveries (>75%) for the majority of TOrCs, with the exception of BHA, BHT, TCC and DES. Considering other factors such as the availability and price, Supel-Select HLB tubes were selected for further test with the elution solvents.

Three organic solvents (MeOH, ACN and EA) were tested to assess which achieved the best SPE recoveries, especially for PHBA, BHA, BHT, TCC and DES. The results (Fig. S3C) showed that each individual solvent still had some drawbacks for eluting all the target chemicals: ACN could achieve better recoveries for PHBA (96.3 ± 3.1%) but not for BHT, TCC and DES, EA could elute more BHT, TCC and DES but less PHBA, and MeOH had medium eluting potential for these chemicals. Thus, the mixture of ACN and EA (50:50, v/v) was selected for further assessment and good recoveries (>75%) were obtained for all TOrCs except BHA and BHT (61.7 ± 6.8% and 58.8 ± 11.3%), which ranged from 75.7 ± 3.2% to 91.8 ± 1.9%.

3.2.3. SPE recoveries for optimised procedures

Based on the tests above, the extraction procedures were fully optimised and applied to SPE recoveries, overall recoveries and matrix effect tests, and the field application for the environmental samples. The SPE recoveries were evaluated using the optimised SPE procedures, spiked at 100 ng L^{-1} of TOrCs in the influent, effluent and river water, and then analysed by both instruments. The results are shown in Fig. 1, providing good SPE recoveries for the majority of the TOrCs when both systems were applied for the analysis.

3.3. LC-MS/MS and LC-HRMS quantification, performance and method validation

The MS parameters for both LC-MS systems were optimised based on the most intense signal of fragmentation products for each TOrC. The results from the optimisation of the MS parameters and quantification for both LC-MS systems are contained in parts of **2.4 Instrumental analysis** and the Supplementary data, and Table 1 and S2. Following this the instruments were operated for sample analysis. Due to the scan range limitation (50 Da minimum) of the HRMS, no daughter ion of TCS could be detected. As the resolution of 70 000 FWHM is capable enough for determination of the selected TOrCs, only results from t-SIM mode of LC-HRMS were used for the comparative evaluation with LC-QqQ-MS.

The equations, linear ranges and linearity correlation coefficients (R^2) of the calibration curves, the IDLs and MDLs for both systems are contained in Table S4 and Table 2. The linear ranges of LC-QqQ-MS and LC-Q-Orbitrap-HRMS systems were 1 or 2.5–1000 $\mu g\ L^{-1}$ and 0.25 or 0.5 –500 $\mu g\ L^{-1}$ for the majority of TOrCs, respectively, showing good linear ranges for both instruments. Both instruments could achieve excellent linearity ($R^2 > 0.99$ for all TOrCs, and $R^2 > 0.999$ for some of them). Precision of both the instruments and method were evaluated for intra-day and inter-day variability using the two LC-MS systems by injection of 3 replicates of standard solutions and spiked river water samples at both 10 and 200 $\mu g\ L^{-1}$. Good method precision for both systems was obtained showing the intra-day and inter-day RSDs ranged from 0.5 to 4.5% and 2.1 to 8.1% for LC-QqQ-MS and 0.5 to 8.4% and 0.8 to 9.5% for LC-Q-Orbitrap-HRMS taking the results of 200 $\mu g\ L^{-1}$ as an example. Better linearity (closer to 1 of R^2) and smaller RSDs for the majority of TOrCs were observed for LC-QqQ-MS compared to the LC-Q-Orbitrap-HRMS, which was similar to a previous study on hexabromocyclohexane (HBCD) using QqQ-MS and Orbitrap-HRMS (Zacs et al., 2014). These results demonstrated that the LC-QqQ-MS system was relatively more suitable for batch analysis of large number of environmental samples.

The instrument detection limits (IDLs) and method detection limits (MDLs) in wastewater and river water for individual TOrCs are listed in Table 2. Remarkable differences were observed between the two systems with the LC-Q-Orbitrap-HRMS system being more sensitive than the LC-QqQ-MS system which provided 2–33 times lower IDLs for individual TOrCs. This may have resulted from the loss of response when daughter ions were produced in the collision cell. The MDLs for the LC-QqQ-MS system were calculated based on the IDLs, and ranged from 0.48 to 23.3 ng L^{-1}, 0.33 to 16.4 ng L^{-1} and 0.32 to 15.6 ng L^{-1} for the influent, effluent and

river water, respectively, showing comparable data with recent publications (Gorga et al., 2013; Anumol and Snyder, 2015; Liu et al., 2015a). These values were low enough for analysis of the environmental samples. The MDLs provided by the LC-Q-Orbitrap-HRMS system were lower than these publications, which were 0.06–1.41 ng L^{-1}, 0.04–1.04 ng L^{-1} and 0.04–0.91 ng L^{-1} for the influent, effluent and river water, respectively.

3.4. Matrix effect and overall recoveries

Matrix effects are one of the main drawbacks of LC-MS with ESI mode, which can lead to signal suppression or enhancement due to the presence of matrix in the sample (Matuszewski et al., 2003; Trufelli et al., 2011). This phenomenon is difficult to eliminate through sample pre-treatment procedures, but can be compensated/corrected by the use of stable isotope-labelled internal standards (SIL-ISs) (Trufelli et al., 2011). Matrix effects were studied and evaluated by processing samples of river water, wastewater effluent and influent with the optimised SPE method and pre-/post-spiking with 100 ng of the individual analytes. The matrix effects (*ME*, %) for the influent, effluent and river water were calculated using Equation (1) and presented in Fig. 2 for both systems.

No remarkable signal suppression or enhancement was observed for the majority of TOrCs when LC-Q-Orbitrap-HRMS was employed to analyse the samples. Similar results were observed for effluent samples when the LC-QqQ-MS system was used, but significant ME of influent and river water samples were found for the majority of TOrCs, especially for those chemicals that did not have the SIL-ISs such as BEP, HEP, TCC and DES. Similar phenomena of SIL-ISs influence on *MEs* were also observed in previous studies on preservatives, antioxidants (Gonzalez-Marino et al., 2009) and oestrogens (Liu et al., 2011), confirming the advantage of SIL-ISs on the compensation for *ME*. Relatively large differences of *ME* were observed between the two LC-MS systems in this study, which is consistent with previous studies (Gonzalez-Marino et al., 2009), showing that the matrix effects may vary greatly between different LC-MS systems due to the different design of ESI sources among manufacturers (Gonzalez-Marino et al., 2009; Trufelli et al., 2011). These results indicated that *ME* should be considered and re-evaluated when translating a LC-MS method among different instruments.

Table 2
Performance (R^2, IDLs and MDLs) of both instruments for standard & environmental samples (A: LC-QqQ-MS system and B: LC-Q-Orbitrap-HRMS system).

TOrCs	R^2		IDL, $\mu g\ L^{-1}$		MDL, ng L^{-1}					
					Influent water		Effluent water		River water	
	A	B	A	B	A	B	A	B	A	B
MEP	0.9992	0.9990	0.88	0.38	1.07	0.40	0.68	0.32	0.66	0.30
ETP	0.9996	0.9973	2.47	0.37	2.73	0.41	1.93	0.31	2.14	0.29
PRP	0.9998	0.9981	1.22	0.15	1.38	0.17	0.92	0.12	0.98	0.12
BUP	0.9994	0.9991	1.47	0.13	1.67	0.15	1.12	0.10	1.07	0.10
BEP	0.9998	0.9995	2.24	0.11	2.27	0.13	1.61	0.08	1.74	0.09
HEP	0.9986	0.9951	3.00	0.09	3.76	0.11	2.54	0.08	2.35	0.07
PHBA	0.9997	0.9996	3.95	0.62	5.24	0.73	3.31	0.47	2.95	0.53
BHA	0.9987	0.9982	3.42	0.13	4.17	0.15	3.29	0.11	3.69	0.14
BHT	0.9964	0.9979	13.7	0.78	23.3	1.41	16.4	1.04	15.6	0.91
OPP	0.9992	0.9992	0.63	0.05	0.67	0.06	0.47	0.04	0.56	0.04
TCS	0.9904	0.9986	2.16	0.07	2.87	0.08	1.91	0.06	1.68	0.06
TCC	0.9950	0.9958	0.44	0.05	0.53	0.06	0.47	0.04	0.33	0.04
BPA	0.9973	0.9959	1.10	0.19	1.28	0.23	0.80	0.14	0.87	0.15
DES	0.9994	0.9985	1.78	0.16	2.10	0.19	1.47	0.14	1.36	0.10
E1	0.9994	0.9995	2.80	0.14	3.31	0.16	2.22	0.10	2.12	0.11
E2	0.9984	0.9983	0.89	0.33	0.91	0.35	0.76	0.25	0.68	0.27
E3	0.9997	0.9987	0.42	0.26	0.48	0.30	0.33	0.20	0.32	0.21
EE2	0.9986	0.9949	0.89	0.13	1.08	0.16	0.72	0.11	0.70	0.10
4-*t*-OP	0.9994	0.9993	1.80	0.47	2.34	0.62	1.38	0.35	1.39	0.36
NP	0.9989	0.9988	0.75	0.36	1.02	0.65	0.71	0.34	0.65	0.30

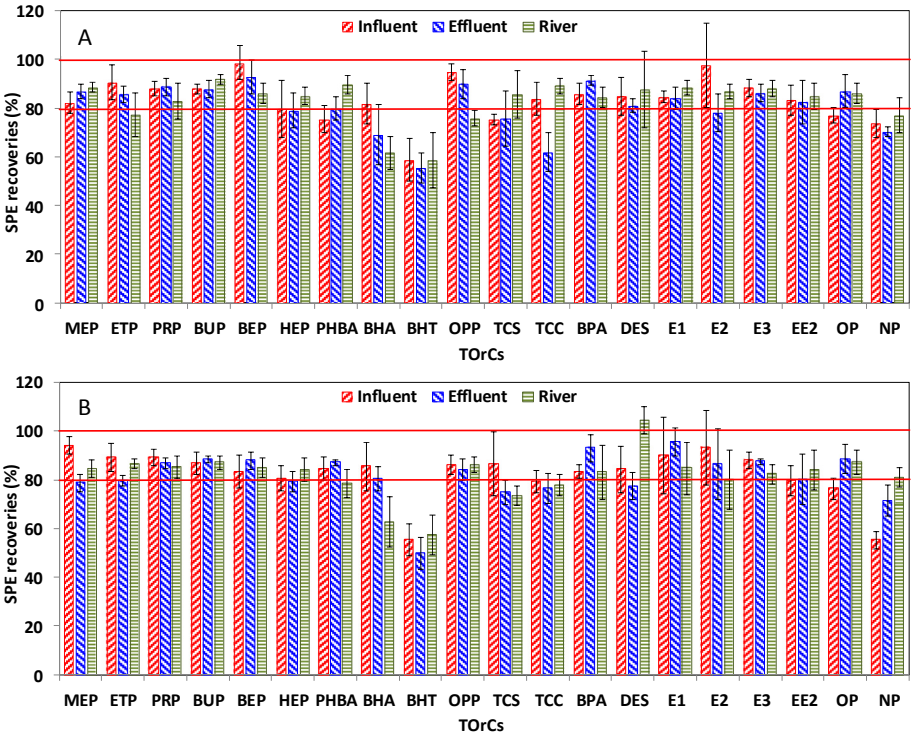

Fig. 1. SPE recoveries of trace organic chemicals in influent, effluent and river water samples (n = 3) with both instruments (A: LC-QqQ-MS system and B: LC-Q-Orbitrap-HRMS system), Error bar: 1SD.

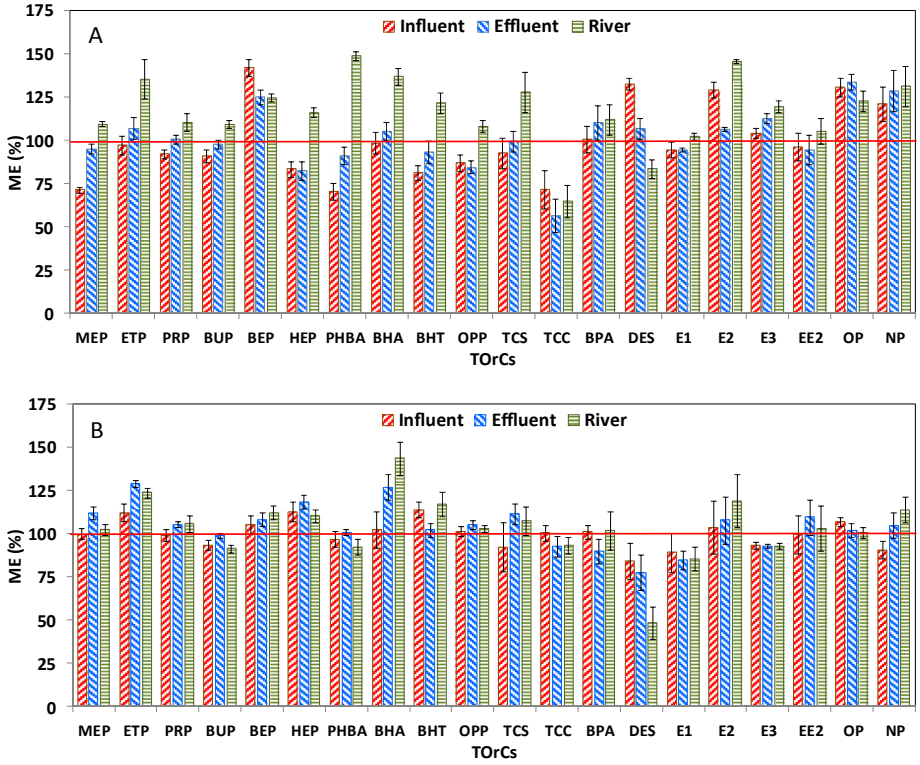

Fig. 2. Matrix effects of TOrCs in influent, effluent and river water samples (n = 3) with both instrumental setups (A: LC-QqQ-MS system and B: LC-Q-Orbitrap-MS system), Error bar: 1SD Error bar: 1SD.

Optimised SPE procedures were conducted to measure the overall recoveries analysed by both instruments for river water and wastewater spiked with different concentrations of selected TOrCs (10 and 100 ng L^{-1} for river water, 20 and 200 ng L^{-1} for effluent, and 50 and 400 ng L^{-1} for influent). Table 3 (the full data including average and SD were listed in Table S5) shows the average of overall recoveries for spiked wastewater and river water samples analysed by both instruments. All recoveries were acceptable for both freshwater and wastewater samples. Due to the smaller matrix effect for the LC-Q-Orbitrap-HRMS system, better overall recoveries were observed for this system, and the overall recoveries fell into the range of 80–120% for the majority of TOrCs.

3.5. Environmental application

This new multi-residue method for analysing TOrCs was utilized

Table 3
Overall recoveries (average, %) for both instruments (A: LC-QqQ-MS system and B: LC-Q-Orbitrap-HRMS system).

TOrCs	Influent				Effluent				River water			
	50 ng L^{-1}		400 ng L^{-1}		20 ng L^{-1}		200 ng L^{-1}		10 ng L^{-1}		100 ng L^{-1}	
	A	B	A	B	A	B	A	B	A	B	A	B
MEP	71.8	91.8	72.1	93.6	76.6	110	96.1	87.7	69.7	83.9	98.0	86.2
ETP	83.9	119	97.4	110	92.1	85.5	107	113	96.4	97.8	105	118
PRP	101	94.5	103	96.9	95.9	93.5	113	99.7	94.4	94.8	103	98.3
BUP	82.8	96.5	87.8	95.3	82.5	91.7	94.4	103	81.9	85.6	97.1	93.6
BEP	113	111	148	101	113	98.8	130	109	95.5	97.6	112	109
HEP	59.4	114	71.6	117	60.6	104	70.8	121	72.7	96.2	84.9	119
PHBA	64.9	127	59.4	94.2	69.4	118	76.7	101	87.9	118	113	83.4
BHA	83.4	94.3	93.3	103	88.3	100	99.8	110	80.3	103	105	106
BHT	77.9	80.5	90.2	86.8	79.0	86.9	103	92.8	71.6	74.0	79.2	91.7
OPP	88.1	101	101	110	86.2	87.9	97.6	111	86.2	88.8	94.8	111
TCS	110	105	85.0	106	109	108	91.5	110	105	91.4	101	104
TCC	105	107	103	114	49.6	91.7	80.9	101	65.7	83.4	82.5	103
BPA	120	118	121	109	108	96.4	133	108	88.4	88.1	114	109
DES	125	118	118	100	71.5	84.6	94.7	84.8	46.1	56.7	64.8	71.1
E1	111	91.7	100	107	96.8	86.3	100	108	94.9	87.2	95.5	96.5
E2	97.0	98.6	102	99.4	101	90.5	83.9	96.0	98.6	91.2	99.8	98.3
E3	106	87.7	101	95.9	97.5	81.8	110	95.1	99.6	79.9	102	89.6
EE2	86.2	90.0	99.4	88.7	85.7	79.3	97.6	98.2	84.9	80.8	92.4	97.1
4-*t*-OP	142	108	121	97.2	136	103	124	108	125	92.3	130	105
NP	115	67.8	125	70.4	108	88.8	133	100	98.9	105	112	123

to determine concentrations in surface waters and wastewaters. Grab water samples were collected from a river and a WWTP (influent and effluent) in a city of Central China. Both instruments were used to analyse river water and wastewater samples after the SPE, with similar results (Table S6) being found by these two instruments. Fewer chemicals were detected by LC-QqQ-MS due to the higher MDLs. Very low concentrations, or below the MDLs could be observed in the river water samples, but higher concentrations were present in the wastewater, especially in the influent. These results are shown in Table S6 indicating that the WWTP did not efficiently remove all the TOrCs, resulting in their discharge into the receiving water. This demonstrated that the analytical method was capable of determining the TOrCs in the environmental samples.

4. Conclusion

A sensitive and reliable analytical method has been developed for the simultaneous determination of preservatives, antioxidants, disinfectants, oestrogens, alkyl-phenols and BPA in surface water and wastewater samples by SPE followed by LC-MS analysis. SPE optimisation showed that extraction of 500 mL acidified (pH 2.5) water samples with Supel-Select HLB tubes (200 mg, 6 mL) followed by elution with 12 mL acetonitrile and ethyl acetate (50:50, v/v) mixture could provide good SPE recoveries (>75%) for most TOrCs selected for this study. The instrumental method was validated and evaluated for matrix effects using a QqQ-MS and a Q-Orbitrap-HRMS. Good performance with linearity and precision could be achieved by both systems, although the LC-QqQ-MS system performed relatively better (closer to 1 of R^2) with a higher method precision (smaller RSDs), while the HRMS was more sensitive and less affected by matrix. Both instruments could achieve acceptable overall recoveries although better recoveries were observed for the LC-Q-Orbitrap-HRMS system.

The results from a field sampling campaign of collecting river water and WWTP influent and effluent from a city in Central China confirmed the applicability of this proposed method to environmental samples.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.chemosphere.2016.07.080.

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