Chemosphere 91 (2013) 888–894

Contents lists available at SciVerse ScienceDirect

Chemosphere

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

Sulfonamides and tetracyclines in livestock wastewater

Hyunook Kim [a,*], Youngmin Hong [a], Jae-eun Park [a], Virender K. Sharma [b], Sung-il Cho [c]

[a] Department of Energy & Environmental System Engineering, The University of Seoul, Seoul 130-743, South Korea
[b] Department of Chemistry, Florida Institute of Technology, Melbourne, FL 32901, USA
[c] Department of Biological & Chemical Engineering, Yanbian University of Science and Technology, Yanji City, 3458, China

HIGHLIGHTS

- IT–ToF MS for quantitation of tetracyclines and sulfonamides in swine wastewater.
- QA and QC information of applied analytical method provided.
- Removal efficiency of tetracyclines and sulfonamides by livestock WWTP investigated.

ARTICLE INFO

Article history:
Received 9 October 2012
Received in revised form 28 January 2013
Accepted 11 February 2013
Available online 15 March 2013

Keywords:
Pharmaceutical
Tandem MS
Sulfonamide
Tetracycline
Livestock wastewater

ABSTRACT

Antibiotics (sulfonamides and tetracyclines) have attractive increasing attention due to their persistence for a long time, which lead to concern of widespread antibiotic resistant bacteria and resistance genes in the aquatic environment. Investigation of the occurrence and elimination of antibiotics in the wastewater treatment plant (WWTP) effluent is thus imperative. This paper presents the method development of the liquid chromatography–ion-trap mass spectrometer (IT-MS)–time-of-flight mass spectrometer in series (LC-IT–ToF/MS) hybrid technique to determine concentrations of sulfonamides and tetracyclines in the effluent of animal WWTP. Detection limits of the developed method were 22.8, 23.0, 25.8, 23.6, and 9.8 ng L^{-1} for sulfathiazole, sulfamethazine, sulfamethoxazole, oxytetracycline, and chlortetracycline, respectively. Average recovery efficiencies of the method for sulfonamides fortified in effluent samples of ananimal WWTP at 1.0, and 4.0 μg L^{-1} were 73–95%, and 89–104%, respectively, while that of the method for tetracyclines fortified at 0.4 and 4.0 μg L^{-1} was 76–104%, and 101–107%, respectively. The analysis of effluent of the WWTP showed that more than 90% of analyzed antibiotics were removed by the treatment consisted of biological, a UF membrane, and a coagulation process. The maximum concentrations of sulfonamide and tetracycline in the WWTP were 49.5 and 4.1 μg L^{-1}, respectively.

1. Introduction

There has been increasing administer of antibiotics worldwide in order to prevent diseases to animals (Zhang and Li, 2011). Veterinary antibiotics are commonly applied to prevent livestock diseases, to treat infections and to promote animal growth in animal farms (Huber, 1971). Sulfonamides, which are structurally similar to *p*-aminobenzoic acid, oppress a production of dihydrofolic acid and impede proliferation of germs (Marzo and Bo, 1998). In Korea, antibiotics containing these two chemical groups accounts for more than 60% of total pharmaceuticals used for animals (Lim et al., 2009). These antibiotics can be released to the environment via various routes; the most common route is via wastewater from animal housings (Kümmerer, 2009; Oberlé et al., 2012). Wastewater from animal farms can then be directly released to surface water, e.g., rivers and lakes. Because antibiotics cannot be usually removed completely in a conventional wastewater treatment plant (WWTP), residues of antibiotics have been found in surface water (Hirsch et al., 1999). This has caused concern of widespread antibiotic resistant bacteria and antibiotic resistance genes in the aquatic environment (Liu et al., 2012; Luo et al., 2011). Therefore, in the last decade, several studies have been carried out to determine concentrations of antibiotics in rivers and wastewater effluents (Kolpin et al., 2002; Wei et al., 2011; Du and Liu, 2012; Li et al., 2012; Gao et al., 2012).

Chromatographic techniques are commonly applied to determine low levels of antibiotics in water samples. Gas chromatography (GC)–mass spectrometry (MS) (GC–MS) or GC–MS/MS techniques are widely used due to their high selectivity and low detection limits (Ternes et al., 2002; Boyd et al., 2003). Because most pharmaceutical chemicals are polar and non-volatile, labor-demanding derivatization of hydroxyl or carboxyl groups is required prior to the quantitation step using GC–MS or GC–MS/MS

* Corresponding author. Tel.: +82 2 2210 5408; fax: +82 2 2210 2917.
E-mail address: h_kim@uos.ac.kr (H. Kim).

0045-6535/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.chemosphere.2013.02.027

(Hao et al., 2007). This tedious derivatization step in the GC analysis has recently made liquid chromatography (LC)–MS or LC–MS/MS (especially, triple quadrupole MS) prevalent (Meyer et al., 2000; Ternes, 2001; Ternes et al., 2001; Cahill et al., 2004; USEPA, 2007). However, application of these techniques is challenging when the sample matrix under study is complex, for examples, wastewater, swine slurry, and sludge. In these matrices, peaks from other molecules generally super impose each other and interfere with the identification of target molecules (Cole, 1997).

The identification of drug candidates or metabolites usually involves the application of MS or MS/MS systems. The triple quadrupole (QqQ) MS gives excellent quantitative ability, but has poor mass accuracy and resolution compared to other configurations. The ion trap (IT) MS provides the utility of MS^n analysis. However, its usability is limited because of poor mass accuracy and resolution. Comparatively, the time of flight (ToF) MS offers the high mass accuracy and resolution power. This high resolution power (e.g., >10000) can accurately measure masses of target analytes with a wide range of molecular weight at a very high rate without deterioration of sensitivity, and can thus differentiate isobaric species (Ferrer and Thurman, 2009). LC–ToF/MS can also show the same resolving power both in the full scan and in the selected ion modes. The unique feature of QqQ/MS is to identify parent compounds or metabolites by using neutral-loss and precursor ion scans. However, the sensitivity of its full-scan mode may not be adequate in certain situations. Therefore, IT MS and ToF MS are required for some applications. Moreover, a hybrid IT–ToF/MS has the potential to provide high resolution and high accuracy mass spectra in the MS and the MS^n modes.

This paper thus demonstrates the development of the analytical method for the first time to analyze sulfonamides and tetracyclines in the animal WWTP using a hybrid tandem MS system consisting of an IT/MS and a ToF/MS in series (i.e., IT–ToF/MS). The objectives of the papers are two folds: (i) develop and validate the method for complex matrix of effluent of the WWTP to quantify sulfonamides (sulfathiazole, sulfamethazine, and sulfamethoxazole) and tetracyclines (oxytetracycline, and chlortetracycline), and (ii) apply the method to determine concentration levels of target antibiotics in order to assess the removal efficiency of the treatment processes applied in a WWTP.

2. Materials and methods

2.1. Standards and reagents

High-purity reference materials for tetracyclines and sulfonamides were purchased from Sigma–Aldrich (MO, USA). Terbuthylazine (Fluka, Germany) and $^{13}C_3$-sulfamethazine (Cambridge Isotope Laboratories, MA, USA) were used as an internal standard, and as a surrogate, respectively. $Na_2EDTA{\cdot}2H_2O$, NH_4OH, and CH_3COONH_3 of high purity used in the sample pre-treatment were also purchased from Sigma–Aldrich (MO, USA). Solvents, such as methanol and acetonitrile used in this study, were all of HPLC grade (Baker, NJ, USA). The purchased reference materials and internal reference materials were diluted with methanol to produce stock solutions of 1000 μg mL^{-1}.

Hydrophilic-lipophilic balance (HLB; 200 mg, 6 mL) and mixed-mode cation exchange (MCX; 150 mg, 6 mL) SPE cartridges were purchased from Supelco (PA, USA) and Waters (MA, USA), respectively. GF/C filters (Whatman, UK) were used for sample pre-filtration.

2.2. Instrumental analysis

Quantitation of target pharmaceuticals were performed using an LC (LC-20A, Shimadzu, Kyoto, Japan) and a high resolution tandem IT–ToF/MS system (Shimadzu, Kyoto, Japan) with an electrospray ionization (ESI) probe. The separation of target analytes in samples was done using a Shim-pack FC-ODS (length: 75 × 3.0 mm; particle size: 3 μm; Shimadzu, Kyoto, Japan) column at 40 °C. Two mobile phases were used to separate target analytes. One (A) consisted of a mixture of 0.3% (v/v) formic acid and 0.1% (w/v) ammonium acetate in water, and the other (B) contained a mixture of methanol and acetonitrile (50:50, v/v). The linear gradient elution was as followed: initial composition of the mobile phases A and B was set at 90:10. Mobile phase B was then increased to 100% in 4.5 min. The injection volume of a sample was 5 μL. ESI probe capillary's voltage was set at +4.5 kV, and the temperature of MS interface was set at 250 °C. The accumulation time of the IT for quantitative analysis was adjusted to 30 ms, and mass ions within the range of *m/z* 100–1000 were scanned by the ToF/MS.

Suspended solids (SS) concentration was measured according to the Standard Methods 2540 D (APHA, 2005). Total organic carbon was measured using a TOC analyzer (TOC-V, Shimadzu, Kyoto, Japan).

2.3. Sample pre-treatment procedure

The tandem SPE method with an HLB cartridge and an MCX to selectively extract sulfonamides and tetracyclines is briefly described below. The schematic of the extraction procedure is presented in Fig. SI-1.

Particles in wastewater samples were centrifuged at 10000 rpm and filtered through a GF/C filter. 20 μL $^{13}C_3$-sulfamethazine of 10 mg L^{-1} was added to a 0.5 L filtered sample, along with 5 mL Na_2-EDTA of 0.1 mg mL^{-1} as a chelating agent. Sample pH was then adjusted to pH 3.0 by adding 3.5 M sulfuric acid. The addition of Na_2-EDTA and the acid was performed to prevent the chelation of metals by tetracyclines in samples. Prior to extracting target chemicals, the SPE cartridge was conditioned with 2 mL pure water, 2 mL methanol, and 2 mL distilled water of pH 3.0. Then, a sample underwent the loading process under approximately 3 kPa to allow target analytes to be adsorbed onto an HLB cartridge. The HLB cartridge was then mounted on a vacuum manifold, washed with 2 mL water, and eluted with 2 mL methanol for the subsequent extraction of the adsorbed target analytes. The washed HLB cartridge was reconnected to an MCX, and re-eluted with 6 mL methanol to extract residual target compounds. Afterwards, the HLB cartridge was destroyed and the remaining MCX was eluted with 4 mL ammonium hydroxide of 5% (w/w). The eluted sample was enriched to below 0.5 mL using a nitrogen concentrator (MGS-2200, Eyela, Japan). Then, 20 μL terbuthylazine of 10 mg L^{-1} was added to the remaining solution, the final volume of which was subsequently adjusted to 2.0 mL by adding 20 mM ammonium acetate. Lastly, the sample was filtered with a 0.2 μm polytetrafluoroethylene filter (Advantec, Tokyo, Japan), and injected into the LC-IT–ToF/MS for quantification of target compounds.

2.4. Validation of analytical method

In order to evaluate the effectiveness of the developed analytical method, method detection limit (MDL) and recovery efficiency of the method for each compound were determined. In order to determine the MDLs of the method for sulfonamides and tetracyclines, each analyte was spiked to effluent samples collected from a local domestic WWTP to make final concentration of 0.20 μg L^{-1}. SSs and total organic carbons (TOCs) concentrations of the treated wastewater samples were 5 ± 1 mg L^{-1}, 19.7 ± 0.2 mg L^{-1}, respectively (n = 7). The spiked sample was then analyzed 7 times in a row to determine MDLs.

The recovery efficiency of the developed method was evaluated with the same wastewater samples. Reference materials for sulfonamides were added to the effluent samples at two concentration levels of 1.0, and 4.0 μg L^{-1}, while those for tetracyclines were added to the levels of 0.4, and 4.0 μg L^{-1}. For real sample analysis, the average of the surrogate recovery efficiency was 95%. The prepared samples were then analyzed 10 times in a row with the proposed method, and the standard deviations of the repeated analyses were calculated to determine the method recovery efficiency.

2.5. Application of method to water samples from animal WWTP

The analytical method developed in this study was applied to quantitation of sulfonamides and tetracyclines in water samples collected from each unit processes of a local WWTP for livestock wastewater. This plant used biological process, a UF membrane, and a coagulation process (Fig. SI-2). The WWTP consists of a series of the first denitrification/nitrification process (① and ② in Fig. SI-2) and their sedimentation (③ in Fig. SI-2), the second denitrification/nitrification process (④ and ⑤ in Fig. SI-2), ultra-filtration (UF, ⑥ in Fig. SI-2), and a coagulation/sedimentation (⑦ in Fig. SI-2). Especially, the WWTP is operating the UF process to remove small particulate organic materials. For removing dissolved organic substances in the effluent of the UF process, activated carbons are added to the coagulation/sedimentation process (i.e., ⑦ in Fig. SI-2).

3. Results and discussion

3.1. Physico-chemical characteristics of antibiotics

Physico-chemical characteristics of sulfonamides and tetracyclines are presented in Table 1. Since the pK_{OW}, water solubility, and half-life in water for the target compounds are not readily available, they were estimated with the EPI Suite (USEPA, 2012). There was a large difference in the predicted water solubility of the analytes under study; from 0.6 to 20 mg mL^{-1}. However, the solubility of chemicals is much higher than the levels detected in the aquatic environment (Halling-Sørensen et al., 1998; Ternes, 1998). Values of pK_{OW} of the pharmaceuticals range from −2.87 to 0.76, characterizing relatively high hydrophilicity. A hydrophilic organic chemical was thus easily extracted with the SPE pretreatment in our study.

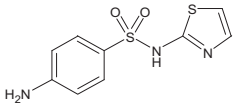
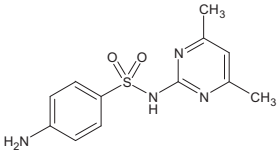
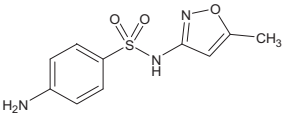
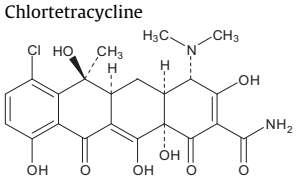
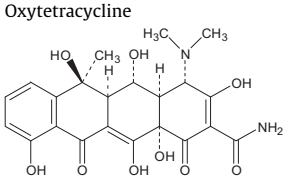
Tetracyclines consist of a total of 4 rings in a hydronaphtacene form. Both tetracyclines under study have 3 different pK_as depending on deprotonation of hydroxyl and of dimethylammonium functional groups, and easily can get affected by the solution pH. Solution pH can result in different forms of tetracycline epimers (Halling-Sørensen et al., 2002; Søeberg et al., 2004); the presence of epimers often makes the peaks of tetracycline chromatograms split in an LC analysis, which was also observed in our study.

3.2. Chromatogram from analysis of sulfonamides and tetracyclines

A chromatogram and a mass spectrum for a mixture of sulfonamides and tetracyclines are presented in Figs. 1 and 2, respectively. Peaks of sulfathiazole, sulfamethazine, and sulfamethoxazole were observed at the RTs of 1.72, 2.04, and 2.35 min, respectively (Fig. 1). Peaks of oxytetracycline and chlortetracycline subsequently occurred at the RTs of 3.53 and 4.05 min. On the other hand, the peak of the internal standard, terbuthylazine was detected at the RT of 2.10 min (Fig. 1). As shown in the figures, all the peaks for the compounds are very clear except for chlortetracycline; which was split into two. A split of chlortetracycline chromatogram is not uncommon, since chlortetracycline reference materials often contain epimers (Lindsey et al., 2001). Therefore, chlortetracycline concentration was determined with the total area of the two split peaks.

Nonetheless, each of target compounds could be easily ionized to a $[M + H]^+$ form using the ESI probe (Fig. 2).

Table 1
Physico-chemical properties of sulfonamides and tetracyclines under study.

Sulfonamides	Sulfathiazole	Sulfamethazine	Sulfamethoxazole
Structure			
Molecular formula	$C_9H_9N_3O_2S_2$	$C_{12}H_{14}N_4O_2S$	$C_{10}H_{11}N_3O_3S$
Molecular weight	255.3	278.3	253.3
Accurate mass	255.014	278.084	253.052
pK_a	7.2	7.4	6.9
pK_{OW}[a]	0.72	0.76	0.48
Water solubility[a] (mg mL^{-1})	20.0	11.3	3.9
Half-life in water[a] (h)	900	900	900
Tetracyclines	Chlortetracycline	Oxytetracycline	
Structure			
Molecular formula	$C_{22}H_{23}ClN_2O_8$	$C_{22}H_{24}N_2O_9$	
Molecular weight	478.9	460.4	
Accurate mass	478.114	460.148	
pK_a[b]	3.33/7.55/9.33	3.22/7.46/8.94	
pK_{OW}[a]	−0.68	−2.87	
Water solubility[a] (mg mL^{-1})	0.6	1.4	
Half-life in water[a] (h)	4320	1440	

[a] pK_{OW}, water solubility, and half-life values were estimated in water by EPI Suite™ program.
[b] pK_a values were measured in water by potentiometric method [29].

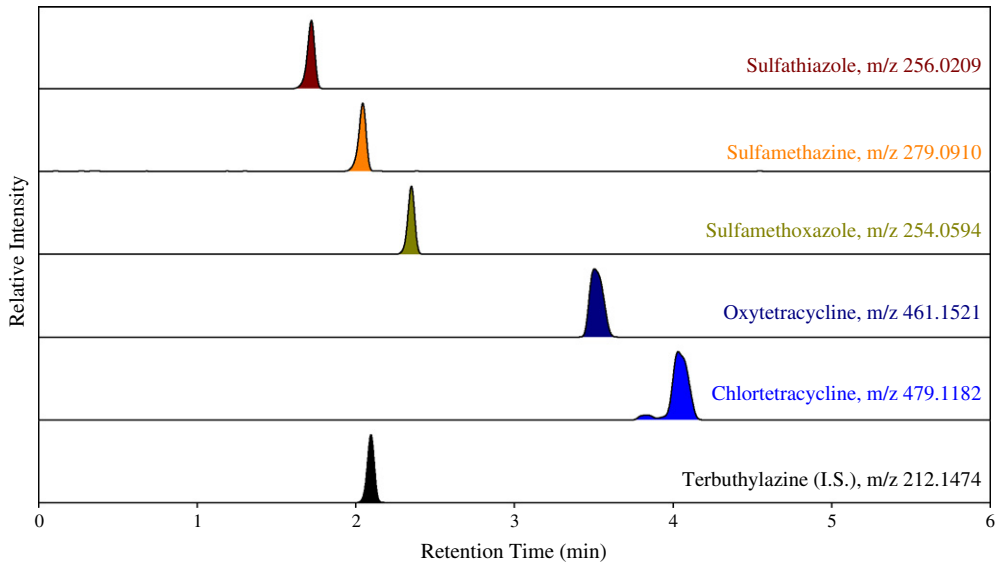


Fig. 1. Chromatograms of quantitation ions for standard sulfonamides and tetracyclines.

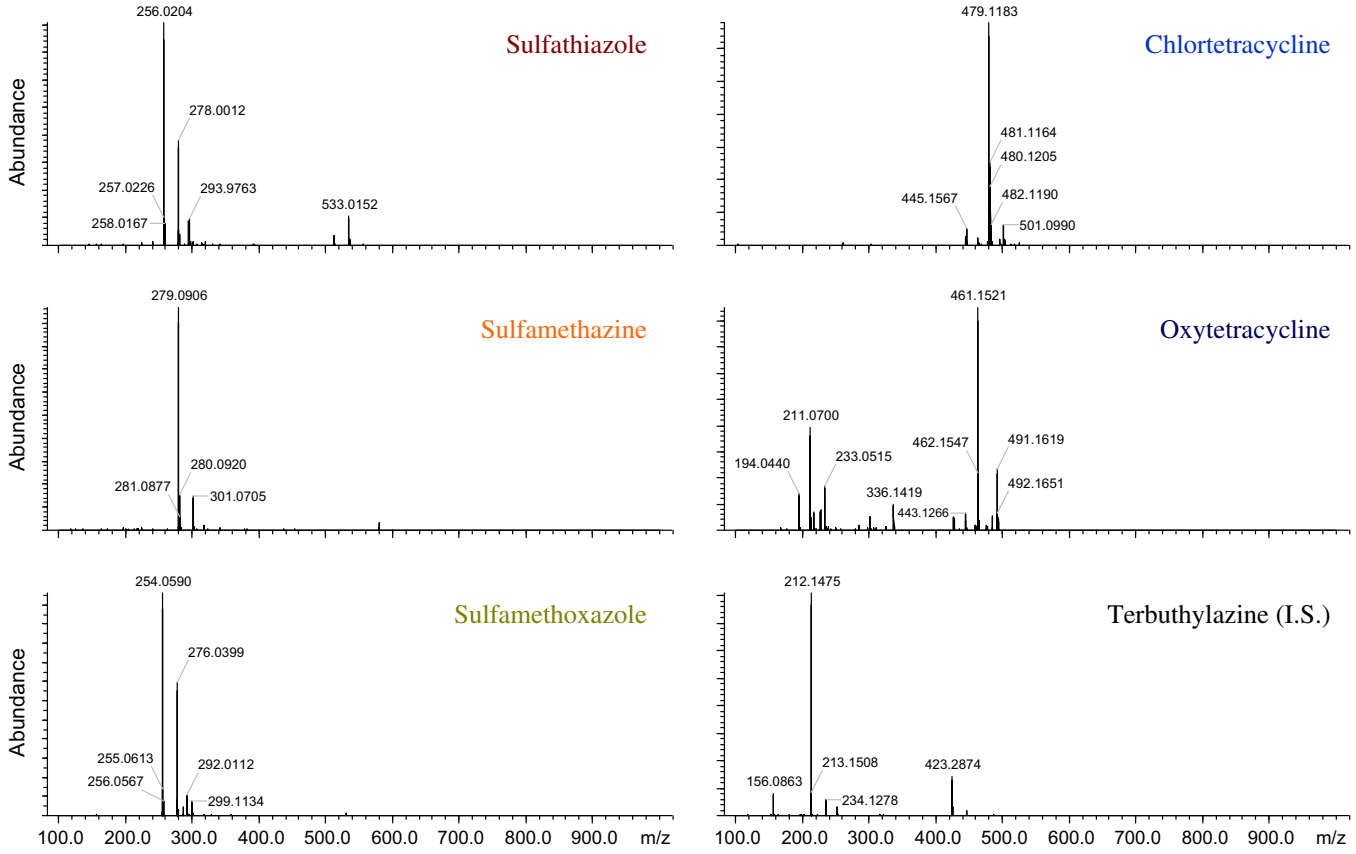


Fig. 2. Full scan spectrum for 5 target compounds and internal standard.

3.3. Development of calibration curves for antibiotics

Prior to the determination of sulfonamides and tetracyclines in real animal wastewater samples, the calibration curves of the chemicals were prepared. The calibration curve for each analyte was performed within the concentration range of 10–1000 μg L^{-1}, and is presented in Fig. 3. All the curves show good linearity within the calibration ranges ($R^2 > 0.99$), which indicate that the newly developed method can be reliably applied to the quantitation of sulfonamides and tetracyclines in wastewater samples.

3.4. Determination of method detection limits

For the determination of MDLs of the proposed method for sulfonamides and tetracyclines, a total of 7 samples were prepared with WWTP effluent samples, each of which was added with standard sulfonamides and tetracyclines to the final concentration of 0.2 μg L^{-1}. The samples were then analyzed with the proposed method to calculate MDLs. The obtained MDLs for the compounds were within the range of 9–25 ng L^{-1}. For comparison, the more conventional quantitation method using an LC–MS/MS consisting of an LC (LC-20A, Shimadzu, Kyoto, Japan) and a triple quadruple mass spectrometer (API-3200, AB-Sciex, MA, USA) was applied, and similar or slightly higher MDL values (i.e., 10–34 ng L^{-1}) were obtained. The MDLs obtained with the LC-IT–ToF/MS were also compared with those reported by others. Karthikeyan and Meyer (2006) utilized an LC–MS to quantitate sulfonamides and tetracyclines in the effluent of a WWTP. The MDLs of their method for the compounds were all within the range of 50–100 ng L^{-1}, which are about four times higher than those determined using our methods. Those of USEPA's method using an LC–MS/MS system for stream water samples were 0.4–2.1 ng L^{-1} (USEPA, 2007). However, the method proposed by Yang et al. (2005) showed slightly higher MDLs; i.e., 30–70 ng L^{-1}. They used an LC–IT-MS system to analyze 5 sulfonamides and 6 tetracyclines in river samples. Considering that the MDLs of the developed method in our study were estimated with WWTP effluent samples and the concentration levels of the analytes frequently detected from surface waters are within the range from 10 to 500 ng L^{-1} (Ternes, 2006), the analytical method will be readily applicable to the quantitation of the target analytes in surface water samples.

3.5. Determining recovery efficiency of proposed method

For evaluating the recovery efficiency of the proposed method, standard sulfonamide and tetracycline materials were mixed with WWTP effluent samples. In summary, average recovery efficiency of the method for sulfonamides fortified in the effluent samples at 1.0, and 4.0 μg L^{-1} was 73–95%, and 89–104%, respectively, while that of the method for tetracyclines fortified at 0.4, and 4.0 μg L^{-1} was 76–104%, and 101–107%, respectively (Table 2). The reproducibility of the proposed method for each compound was within 10% except for chlortetracycline at the low level (Table 2). For comparison, the average recovery efficiency and reproducibility for the effluent samples at 4.0 μg L^{-1} obtained using an LC–MS/MS in our laboratory were 105%, and 4%, respectively.

3.6. Analysis of sulfonamides and tetracycline in samples collected from livestock WWTP

Concentrations of sulfonamides and tetracyclines in water samples collected from each unit process of a WWTP for livestock wastewater were determined using the developed method. The results from the analysis of the effluent from each unit process of the plant using the proposed method are summarized in Table 3. All five target chemicals were detected from each unit process. Sulfathiazole and sulfamethazine were detected at concentrations more than 30 μg L^{-1} in the 1st denitrification process (① in Fig. SI-2), while sulfamethoxazole was less than 1 μg L^{-1}. In the case of tetracyclines, the concentration of chlortetracycline (i.e., 4.0 μg L^{-1}) was higher than that of oxytetracycline (i.e., 0.8 μg L^{-1}). Interestingly, the levels of sulfonamides and tetracyclines in the first and the second biological processes (i.e., ① through ⑤ in Fig. SI-2) did not change much except sulfathiazole and sulfamethazine; indicating they are quite resistant to biological processes. In the

Table 2
Result from recovery test of proposed method (n = 10).

Compounds	Fortified level (μg L^{-1})	Recovery efficiency (%)	Average recovery efficiency (%)	Standard deviation (μg L^{-1})	RSD (%)
Sulfathiazole	4.0	94–102	98	2	3
	1.0	81–102	89	6	7
Sulfamethazine	4.0	110–117	113	2	2
	1.0	89–98	94	3	3
Sulfamethoxazole	4.0	92–108	104	5	5
	1.0	63–81	73	6	9
Oxytetracycline	4.0	96–114	107	8	7
	0.4	68–82	76	7	9
Chlortetracycline	4.0	98–105	101	4	4
	0.4	85–118	104	13	13

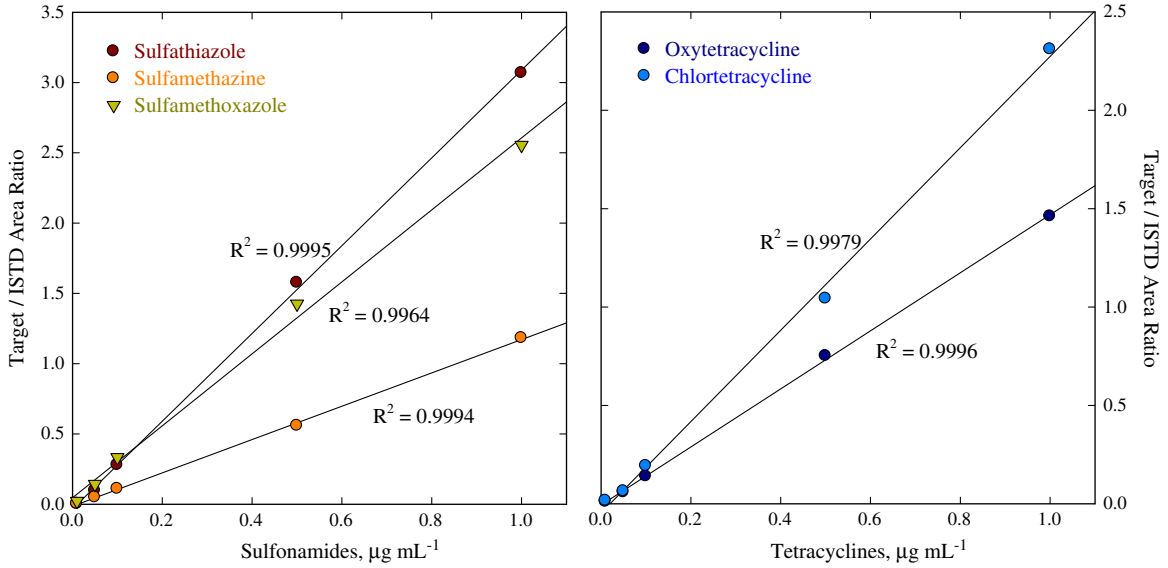


Fig. 3. Calibration curves for sulfonamides and tetracyclines under study.

Table 3
Concentrations of sulfonamides and tetracyclines in samples collected from livestock WWTP (unit: μg L^{-1}, $n = 3$).

	Sulfathiazole	Sulfamethoxazole	Sulfamethazine	Oxytetracycline	Chlortetracycline
1st Denitrification	34.3 (±1.7)	0.2 (±0.0)	41.8 (±2.2)	0.8 (±0.0)	4.0 (±0.7)
1st Nitrification	31.9 (±1.3)	0.4 (±0.0)	49.5 (±2.7)	0.2 (±0.0)	4.1 (±0.5)
Sedimentation	22.9 (±0.8)	0.3 (±0.0)	38.9 (±1.3)	1.1 (±0.0)	4.0 (±0.6)
2nd Denitrification	8.7 (±0.2)	0.1 (±0.0)	24.1 (±1.9)	0.2 (±0.0)	3.4 (±0.4)
2nd Nitrification	7.8 (±0.3)	0.1 (±0.0)	20.5 (±1.4)	0.9 (±0.0)	4.0 (±0.5)
UF treatment	5.1 (±0.2)	0.1 (±0.0)	12.4 (±1.1)	0.1 (±0.0)	0.2 (±0.0)
Effluent	0.4 (±0.1)	0.0 (±0.0)	0.8 (±0.2)	n.d.[a] (±0.0)	0.1 (±0.0)

[a] n.d.: not detected.

second biological processes, the levels of sulfathiazole and sulfamethazine were lowered to about half of those observed in the first denitrification process.

Significantly, more than 97% of sulfonamides and tetracyclines detected in the very first process could be removed while they underwent through the whole treatment processes of the WWTP. Each unit process contributed to the removal of sulfonamides; their concentration was gradually decreasing at each unit process. Noticeably, sulfonamides were effectively removed in the coagulation/sedimentation process, indicating dissolved sulfa-chemicals were well adsorbed onto activated carbons. Adams et al. (2002) also reported effective removal of sulfonamides from water using activated carbon. Most tetracyclines were, however, removed by the UF process. It has been reported that tetracyclines could be removed together with total suspended solids (Kim et al., 2005). Several hydroxyl functional groups of tetracyclines (Table 1) might facilitate these compounds to adhere to the surface of suspended solids. Importantly, it was confirmed that the proposed analytical method could be applied to a study on fates of the target analytes in an animal WWTP.

4. Conclusions

The developed method using a high resolution LC-IT–ToF/MS system could be applied successfully to quantitate residual sulfonamides and tetracyclines in samples from an animal WWTP. The calibration curves developed with this method showed a good linearity ($R^2 > 0.99$) for all the target antibiotics. The MDLs and recovery efficiencies of the method, determined for the selected analytes in effluent samples, collected from a domestic WWTP, were 9–25 ng L^{-1}, and 73–113%, respectively, which were equal to or better than those obtainable with a conventional LC–MS/MS system. The MDLs and recovery efficiencies of the proposed method were comparable to those obtained with conventional methods using an LC–MS/MS for stream water samples. The developed method showed the removal of more than 97% of sulfonamides and tetracyclines in the treatment processes for livestock wastewater. The potential benefit of the developed analytical method using LC-IT–ToF/MS system includes qualitative analysis of intermediates from any degradation reaction involving antibiotics. Therefore, the method can contribute to the design of a process to monitor residual sulfonamides and tetracyclines from wastewater by potentially evaluate fates of the target compounds.

Acknowledgments

The financial support for the current research was from the R&D Program Program of MKE/KEIT [10037331, Development of Core Water Treatment Technologies based on the Intelligent BT-NT-IT Fusion Platform], which is greatly appreciated. We thank anonymous reviewers for their comments which improved the paper.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.chemosphere.2013.02.027.

References

Adams, C., Wang, Y., Meyer, M., 2002. Removal of antibiotics from surface and distilled water in conventional water treatment processes. J. Environ. Eng. 128 (3), 253–260.
APHA, 2005. Standard Methods for the Examination of Water and Wastewater, 21st ed. American Public Health Association, Washington, DC.
Boyd, G.R., Reemtsma, H., Grimm, D.A., Mitra, S., 2003. Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario. Can. Sci. Total Environ. 311 (1–3), 135–149.
Cahill, J.D., Furlong, E.T., Burkhardt, M.R., Kolpin, D., Anderson, L.G., 2004. Determination of pharmaceutical compound in surface- and ground-water samples by solid phase extraction and high-performance liquid chromatography-electrospray ionization mass spectrometry. J. Chromatogr. A 1041 (1–2), 171–180.
Cole, R.B., 1997. Electrospary Ionization Mass Spectrometry, first ed. John Wiley, New York, USA.
Du, L., Liu, W., 2012. Occurrence, fate, and ecotoxicity of antibiotics in agro-ecosystems. A review. Agron. Sust. Dev. 32 (2), 309–327.
Ferrer, I., Thurman, E.M., 2009. Liquid Chromatography–Time of Flight Mass Spectrometry: Principles, Tools and Applications for Accurate Mass Analysis. John Wiley, New York, USA.
Gao, L., Shi, Y., Li, W., Niu, H., Liu, J., Cai, Y., 2012. Occurrence of antibiotics in eight sewage treatment plants in Beijing. China. Chemosphere 86 (6), 665–671.
Halling-Sørensen, B., Nielsen, S.N., Lanzky, P.F., Ingerslev, F., Lützhøft, H.C.H., Jørgensen, S.E., 1998. Occurrence, fateand effects of pharmaceutical substances in the environment – a review. Chemosphere 36 (2), 357–393.
Halling-Sørensen, B., Sengeløv, G., Tjørnelund, J., 2002. Toxicity of tetracyclines and tetracycline degradation products to environmentally relevant bacteria, including selected tetracycline-resistant bacteria. Arch. Environ. Contam. Toxicol. 42 (3), 263–271.
Hao, C., Zhao, X., Yang, P., 2007. GC–MS and HPLC–MS analysis of bioactive pharmaceuticals and personal-care products in environmental matrices. Trend. Anal. Chem. 26 (6), 569–580.
Hirsch, R., Ternes, T., Haberera, K., Kratzb, K.L., 1999. Occurrence of antibiotics in the aquatic environment. Sci. Total Environ. 225 (1–2), 109–118.
Huber, W.G., 1971. Antibaterial drugs as environmental contaminants. Advances in Environmental Science and Technology, vol. 2. John Wiley, New York (USA).
Karthikeyan, K.G., Meyer, M.T., 2006. Occurrence of antibiotics in wastewater treatment facilities in WI, USA. Environ. Sci. Technol. 361 (1–3), 196–207.
Kim, S., Eichhorn, P., Jensen, J.N., Weber, A.S., Aga, D.S., 2005. Removal of antibiotics in wastewater: effect of hydraulic and solid retention times on the fate of tetracycline in the activated sludge process. Environ. Sci. Technol. 39 (15), 5816–5823.
Kolpin, D.W., Furlong, E.T., Meyer, M.T., Thurman, E.M., Zaugg, S.D., Barber, L.B., Buxton, H.T., 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: a national reconnaissance. Environ. Sci. Technol. 36 (6), 1202–1211.
Kümmerer, K., 2009. The presence of pharmaceuticals in the environment due to human use – present knowledge and future challenges. J. Environ. Manage. 90 (8), 2354–2366.
Li, W., Shi, Y., Gao, L., Liu, J., Cai, Y., 2012. Occurrence of antibiotics in water, sediments, aquatic plants, and animals from Baiyangdian Lake in North China. Chemsphere 89 (11), 1307–1315.
Lim, J.E., Kim, S.C., Lee, H.Y., Kwon, O.K., Yang, J.E., Ok, O.S., 2009. Occurrence and distribution of selected veterinary antibiotics in soils, sediments and water adjacent to a cattle manure composting facility in Korea. J. Korean Soc. Environ. Eng. 31 (10), 845–854.

Lindsey, M.E., Meyer, M.T., Thurman, E.M., 2001. Analysis of trace levels of sulfonamide and tetracycline antimicrobials in groundwater and surface water using solid-phase extraction and liquid chromatography/mass spectrometry. Anal. Chem. 73 (19), 4640–4646.

Liu, M., Zhang, Y., Yang, M., Tian, Z., Ren, L., Zhang, S., 2012. Abundance and distribution of tetracycline resistance genes and mobile elements in an oxytetracycline production wastewater treatment system. Environ. Sci. Tech. 46 (14), 7551–7557.

Luo, Y., Xu, L., Rysz, M., Wang, Y., Zhang, H., Alvarez, P.J.J., 2011. Occurrence and transport of tetracycline, sulfonamide, quinolone, and macrolide antibiotics in the Haihe River basin, China. Environ. Sci. Tech. 45 (5), 1827–1833.

Marzo, A., Bo, L.D., 1998. Chromatography as an analytical tool for selected antibiotic classes: a reappraisal addressed to pharmacokinetic applications. J. Chromatogr. A 812 (1–2), 17–34.

Meyer, M.T., Bumgarner, J.E., Varns, J.L., Daughtridge, J.V., Thurman, E.M., Hostetler, K.A., 2000. Use of radioimmunoassay as a screen for antibiotics in confined animal feeding operations and confirmation by liquid chromatography/mass spectrometry. Environ. Sci. Technol. 248 (2–3), 181–188.

Oberlé, K., Capdeville, M.-J., Berthe, T., Budzinski, H., Petit, F., 2012. Evidence for a complex relationship between antibiotics and antibiotic-resistant *Escherichia coli*: From medical center patients to a receiving environment. Environ. Sci. Tech. 46 (3), 1859–1868.

Søeberg, T., Ingerslev, F., Halling-Sørensen, B., 2004. Chemical stability of chlortetracycline and chlortetracycline degradation products and epimers in soil interstitial water. Chemosphere 57 (10), 1515–1524.

Ternes, T.A., 2001. Analytical methods for the determination of pharmaceuticals in aqueous environmental samples. Trend. Anal. Chem. 20 (8), 419–434.

Ternes, T.A., 2006. Assessment of technologies for the removal of pharmaceuticals and personal care products in sewage and drinking water facilities to improve the indirect potable water reuse. POSIEDON project final report, E.U. <http://poseidon.bafg.de>.

Ternes, T.A., 1998. Occurrence of drugs in German sewage treatment plants and rivers. Water Res. 32 (11), 3245–3260.

Ternes, T.A., Andersen, H., Gilberg, D., Bonerz, M., 2002. Determination of estrogens in sludge and sediments by liquid extraction and GC/MS/MS. Anal. Chem. 74 (14), 3498–3504.

Ternes, T.A., Bonerz, M., Schmidt, T., 2001. Determination of neutral pharmaceuticals in wastewater and rivers by liquid chromatography-electrospray tandem mass spectrometry. J. Chromatogr. A 938 (1–2), 175–185.

USEPA, 2012. EPI Suite™. <http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm>.

USEPA, 2007. Method 1694: Pharmaceuticals and Personal Care Products in Water, Soil, Sediment, and Biosolids by HPLC/MS/MS. EPA-821-R-08-002, U.S. Environmental Protection Agency, Washington, NW, USA.

Wei, R., Ge, F., Huang, S., Chen, M., Wang, R., 2011. Occurrence of veterinary antibiotics in animal wastewater and surface water around farms in Jiangsu Province, China. Chemosphere 82 (10), 1408–1414.

Yang, S., Cha, J., Carlson, K., 2005. Simultaneous extraction and analysis of 11 tetracycline and sulfonamide antibiotics in influent and effluent domestic wastewater by solid-phase extraction and liquid chromatography-electrospray ionization tandem mass spectrometry. J. Chromatogr. A 1097 (1–2), 40–53.

Zhang, T., Li, B., 2011. Occurrence, transformation, and fate of antibiotics in municipal wastewater treatment plants. Crit. Rev. Environ. Sci. Tech. 41 (11), 951–998.