REMOVAL OF SELECTED PHARMACEUTICALS SPIKED IN THE SECONDARY EFFLUENT OF A WASTEWATER TREATMENT PLANT (WWTP) BY POTASSIUM FERRATE(VI)

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ABSTRACT

This study investigated the ferrate(VI) performance in the removal of 10 target pharmaceuticals spiked in the secondary effluent of a wastewater treatment plant (WWTP). In the raw secondary effluent samples, seven pharmaceuticals of 10 were detected with a maximum concentration of 500.0 ± 28.3 ng/L for ibuprofen (IBU). In the modified effluent samples spiked with 10 target pharmaceuticals, removal efficiencies for most of target compounds were less than 50% at pH 6–9 and 1–5 mg Fe (VI) /L, whereas above 50% of reduction was observed for ciprofloxacin (CIP). Raising the ferrate(VI) dose improved the removal of pharmaceuticals to some extent, while the influence of solution pH on the treatment varied among different target compounds. Ferrate(VI) can efficiently remove pharmaceutical compounds containing electron-rich moieties (ERMs) and then is promising in the removal of pharmaceutical residues in secondary effluents.

Keywords: Potassium ferrate(VI); pharmaceuticals; secondary effluent; treatment

1. Introduction

The recent detections of trace pharmaceutical residues in the aquatic environment are of great concern because of their potential harm to human beings and the eco-system [1-3]. Wastewater treatment plants (WWTPs) play a very important role during the transportation of pharmaceuticals from the pharmaceutical manufactories to surface waters [4,5]. However, in conventional WWTPs, many pharmaceuticals were discharged without reduction, while some pharmaceuticals were only partly removed by the adsorption on sludge [6,7]. Therefore, one important step in tackling the issue of pharmaceutical micro-pollutants is to upgrade or build WWTPs with advanced treatment units. Ozone and advanced oxidation processes (AOPs) have been studied intensively in bench- and pilot-scales recently [8,9]. Besides, a few full-scale WWTPs upgraded with tertiary treatment units demonstrated good results in the removal of pharmaceuticals [10-13].

Potassium ferrate(VI) (K_2FeO_4) is a promising dual-functional chemical which has been applied to various water and wastewater treatment units [14,15]. A number of studies have been conducted to apply ferrate(VI) into the treatment of pharmaceuticals. However, most of the studies were focused on kinetic studies [16-18]. Besides, only a few studies gave information of treatment performance in wastewater samples [19-21]. Until now, little is known regarding the influence of solution pH and ferrate(VI) dosage on the removal of pharmaceuticals in secondary effluent samples. Thus, this study aimed to investigate the influence of solution pH and ferrate(VI) dose on the removal of selected pharmaceuticals spiked in the secondary effluent. Selected 10 target pharmaceuticals belonging to various therapeutic classes were chosen as target compounds and spiked in the effluent samples: 1) antibiotics: ciprofloxacin (CIP), N-acetyl sulphamethoxazole (N-SMX); 2) non-steroidal anti-inflammatory drugs (NSAID): naproxen (NPX), ibuprofen (IBU); 3) antineoplastic: cyclophosphamide (CPM), ifosfamide (IFM); 4) β-blockers: atenolol (ATN); 5) antiepileptics: carbamazepine (CBZ); 6) lipid regulator: bezafibrate (BZF); and 7) local anesthetic: lidocaine (LDC).

2. Materials and methods

2.1. Chemicals and reagents

The chemicals and reagents with analytical grade or above were purchased from Fisher Scientific (UK) and Sigma-Aldrich (USA). All chemicals and reagents were used without further purification. The stock solutions of target compounds were prepared separately in methanol at 100 mg/L. Experimental water was prepared by an Elga PureLab Option-S/R 7/15 water system (France).

2.2 Effluent samples from a WWTP

Shieldhall WWTP is located in the south of Glasgow, UK, which is the largest WWTP in Glasgow area. The facility consists of screens, preliminary settlement tanks, flotation units, oxidation ditch and secondary settlement tanks. Two batches of grab samples were collected after the secondary sedimentation tanks in different days. The secondary effluent had the following general qualities: pH 7.2–7.5; COD 26–43 mg/L as O_2; TN 3–5 mg/L as N; TP 1.0–1.3 mg/L as P; TSS 1.5–2.0 mg/L; and turbidity 1–3 NTU. After shipped to the laboratory, two litres of the raw effluent were filtered by 1.2 µm glass fibre filters (Fisher Scientific, UK) and subsequently 0.45 µm cellulose nitrate membrane filters (Milipore, USA). The two-litre sample was split into two aliquots with one litre each. The samples were adjusted to pH 2.5 by 2 M H_2SO_4 and then extracted by solid phase extraction (SPE) and further analysed by liquid chromatography and mass spectrometry (LC-MS) to determine the concentrations of target compounds in the raw secondary effluent. In addition, the remaining secondary effluent was spiked with all 12 target compounds at 10 µg/L and then treated by ferrate(VI).

2.3. Jar test

A series of jar testing experiments was employed to examine the treatment performance of secondary effluent samples by ferrate(VI). Briefly, the protocol for jar test was: (1) fast mixing at 400 rpm for 1 min; (2) slowing mixing at 40 rpm for 20–60 min; and (3) sedimentation for 60 min. Ferrate(VI) dose applied was 0–5 mg/L as Fe. And solution pH was carefully adjusted to desired values immediately after dosing ferrate(VI) by 0.05–0.1 M HCl and NaOH solutions. After sedimentation, the treated samples were filtered by 1.2 µm glass fibre filters (Fisher Scientific, UK) and 0.45 µm membrane filters (Milipore, USA) and further extracted by SPE and analysed by LC-MS.

2.4. Instrumental analysis

Prior to the SPE extraction, effluent samples were spiked with 1 mL deuterated internal standards (atenolol d7, lidocaine d10, erythromycin C13 d3, carbamazepine d8, naproxen d3, and diclofenac d4). Tandem SPE cartridges, Strata-X 1 g/20 mL cartridge (Phenomenex, UK) and Isolute ENV+ 500 mg/6 mL cartridge (Biotage, Sweden), were used for the extraction, following a pre-determined procedure.: (1) condition: 10 mL methanol and 10 mL water; (2) loading samples: flow rate 5–10 mL/min; (3) wash: 10 mL water; (4) dry: under a gentle nitrogen flow; and (5) elution: two cartridges were eluted separately by the 2/49/49 (v/v/v) formic acid/methanol/acetonitrile mixed solvent. For Strata-X cartridges, 4 × 4 mL mixed solvent was used for the elution; for ENV+ cartridges, 4 × 2 mL mixed solvent was employed. The elution was conducted on a SPE 24-position vacuum manifold (Phenomenex, UK). Two fractions of the elutes from both cartridges were combined and heated to dryness at 50 °C by the use of a Techne DB-2A Dri-Block (Bibby Scientific, UK). The dried samples were re-constituted to 1 mL by 50:50 (v/v) water/methanol for further LC-MS analysis.

The LC-MS used for the analysis of target compounds was an Agilent 1100 series LC coupled to a Bruker Daltonics Esquire 3000plus ion trap MS (USA). The separation of analytes was achieved by an Atlantis C18 column (3 µm, 150 mm × 2.1 mm, Waters, USA) using a gradient of acetonitrile (Solvent A)/ 10 mM ammonium formate in water with formic acid to pH 3.5 (Solvent B) at 0.2 mL/min. Solvent A was initially 1% and maintained at this percentage for 2 min, then the percentage was increased to 30% in the next 1 min and stayed at 30% till 20 min. Solvent A gradually increased from 20% to 99% in 13 min and maintained at the same level for 9 min, and finally back to 1% in 1 min. The analysis of target compounds was conducted in electrospray ionisation (ESI) positive mode, except for IBU which was conducted in ESI negative mode.

3. Results and discussion

3.1. Occurrence of target compounds in the raw effluent samples

Of the 10 target pharmaceuticals analysed, seven compounds were found in the secondary effluent samples with concentrations up to 500 ng/L. Specifically, CBZ and NPX were found in both batches. The remaining five compounds were only found in one batch. The highest occurrence was observed for IBU, with the concentration of 500.0 ± 28.3 ng/L, while the lowest was observed for BZF, with the concentration of 101.0 ± 5.7 ng/L. In any case, the concentrations of target compounds in the secondary effluent were much lower than their spiked concentrations.

Table 1: Occurrence of target compounds in the effluent samples.

Compound	Batch of detection	Concentration (ng/L)
CBZ	1, 2	(284.5 ± 3.5)–(293.0 ± 7.1)
NPX	1, 2	(189.5 ± 14.8)–(317.0 ± 2.8)
ATN	1	246.5 ± 9.2
LDC	1	110.5 ± 0.7
BZF	1	101.0 ± 5.7
IBU	2	500.0 ± 28.3
CIP	2	274.0 ± 8.5

3.2. Removal of selected pharmaceuticals spiked in secondary effluent samples

Antibiotics

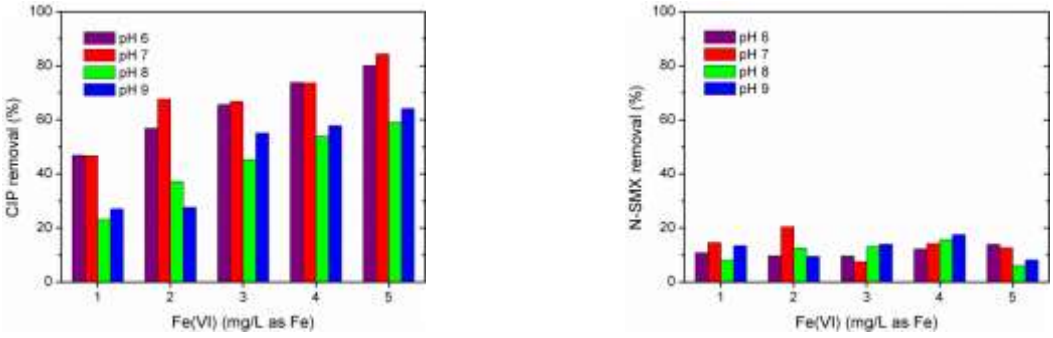
Two antibiotics, CIP, N-SMX, were spiked in the effluent samples. CIP is one of the first generation fluoroquinolones (FQs), while N-SMX belongs to sulphonamides. The results in Fig. 1 show the different removal efficiencies of two antibiotics by ferrate(VI). The treatment of CIP by ferrate(VI) was the better than that of N-SMX (Fig. 1a). Specifically, above 50% of CIP could be removed from the effluent samples at pH 6–9 when the ferrate(VI) dose reached 4 mg/L. Increasing the ferrate(VI) dose improved CIP removal. As for the influence of solution pH, CIP removal at pH 6–7 was better than that at pH 8–9 by about 20% for each ferrate(VI) dose. Besides, CIP removal at pH 6 and 7 were similar and both exceeded 80% when the applied ferrate(VI) dose was 5 mg/L.

The reduction rates of N-SMX by ferrate(VI) were less than 25% under all conditions (Fig. 1b). And in most of the cases, the removal efficiencies were 10 ± 5%. Both the ferrate(VI) dose and solution pH did not make much difference for N-SMX removal.

CIP has a secondary amine moiety in its piperazine group, and the relative high removal rates for CIP could be attributed to the high reactivity of ferrate(VI) with such electron-rich moieties (ERMs) [19,22]. On the other hand, though its precursor SMX containing an aniline functional group, the low removal rates of N-SMX with ferrate(VI) might suggest that the acetyl moiety in the aniline group of N-SMX could depress the ferrate's attack.

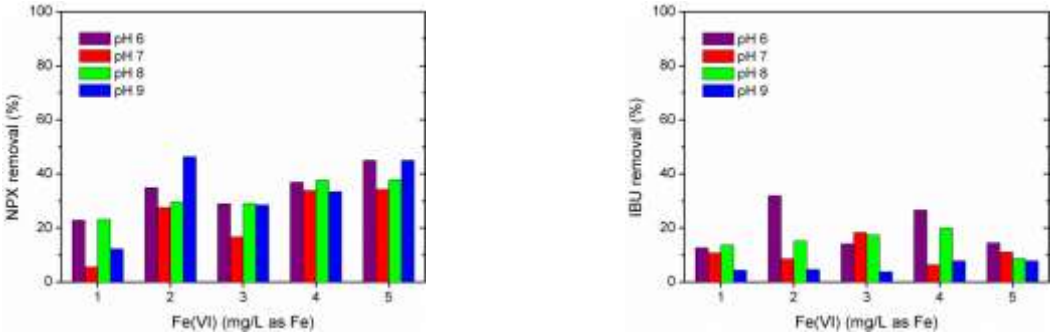
NASIDs

NPX and IBU, as two common NASIDs, were spiked in the secondary effluent samples with their treatment results presented in Fig. 2. For both compounds, the removal by ferrate was less than 50% under all conditions. For NPX removal (Fig. 2a), the increase in ferrate(VI) dose from 1 mg/L to 5 mg/L improved the NPX removal. The worst performance of NPX removal was observed at pH 7 (<35%), whereas the greatest NPX removal of 46.3% was achieved at pH 9 with ferrate dose of 2 mg/L. The electron donation by the methoxy group to the naphthalene moiety may improve the reactivity of NPX with ferrate(VI) [20,23]. On the other hand, the treatment of IBU by ferrate(VI) was worse than that of NPX (Fig. 2b). Most of the removal efficiencies for IBU were less than 20% except for two doses at pH 6. In addition, when the solution pH was 9, the IBU removal was less than 10%. A maximum IBU removal of 31.9% was observed at pH 6 with ferrate(VI) dose of 2 mg/L. The electron-withdrawing carboxylic group of IBU depressed its reactivity with ferrate(VI) [20].



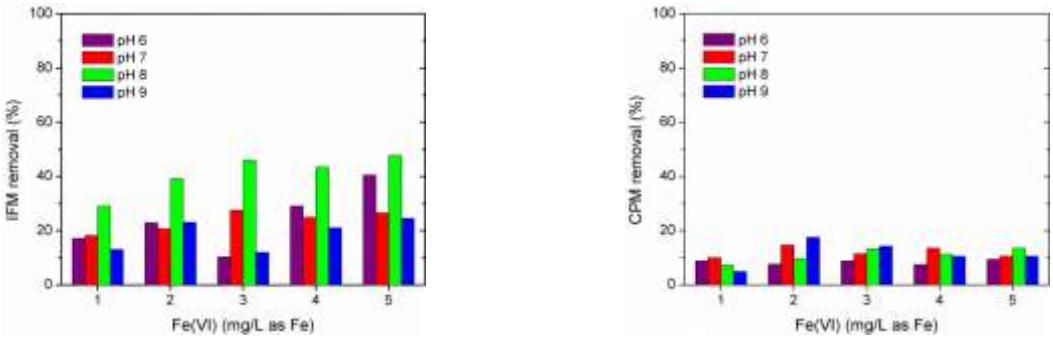
(a) (b)

Figure 1: Removal of spiked antibiotics in effluent samples: (a) CIP; (b) N-SMX



(a) (b)

Figure 2: Removal of spiked NSAIDs in effluent samples: (a) NPX; and (b) IBU



(a) (b)

Figure 3: Removal of spiked antineoplastics in effluent samples: (a) IFM; and (b) CPM

Antineoplastics

IFM and CPM are two cytostatic drugs employed in the chemotherapy of cancer, and have been found in the influent and effluent of WWTPs with concentrations up to dozens of ng/L [24]. There is little information on the treatment of such antineoplastic drugs by other technologies. Generally, the removal of IFM by ferrate(VI) was better than that of CPM from the results shown in Fig. 3. The IFM removal efficiencies were below 50% within 1–5 mg/L of ferrate(VI) (Fig. 3a). The best performance of IFM removal was observed at solution pH 8. When the ferrate(VI) exceeded 2 mg/L at pH 8, the IFM removal stayed around 45 ± 2%. On the other hand, the IFM removal at pH 9 was the worst, with less than 25% of IFM removal at 1–5 mg/L ferrate(VI). For CPM removal by ferrate(VI), the removal efficiencies were less than 20% under all operating conditions (Fig. 3b). The solution pH and ferrate(VI) dose did not influence the CPM removal significantly. The highest removal rate of CPM was observed at pH 9 with the dose 2 mg/L, where 17.5% of CPM was reduced.

Antiepileptics

The overall removal efficiencies of CBZ, an antiepileptic drug, were less than 30% with the applied ferrate(VI) dose range at pH 6–9 (Fig. 4a). At low ferrate(VI) doses (1–2 mg/L), CBZ removal was similar for all pH conditions. While at relatively high doses (3–5 mg/L), the CBZ removals at pH 8 and pH 9 were better than those at pH 6 and pH 7. Besides, the biggest improvement of CBZ removal with rising ferrate(VI) dose was observed at solution pH 8, where an approximate 20% increase happened when the dose was raised from 1 mg/L to 5 mg/L. CBZ has an electron-rich olefinic moiety in the heterocyclic ring, thus the reactivity of CBZ with ferrate(VI) was usually high [16]. The low reactivity of CBZ in the effluent samples might be attributed to the competition of co-existing pharmaceuticals and other natural organic compounds.

Lipid regulator

A blood lipid lowering drug, BZF, was also spiked in the secondary effluent samples. As shown in Fig. 4b, the removal efficiencies of BZF were less than 15% under all conditions. The greatest removal of BZF was observed at pH 9 with the dose of 4 mg/L, where 12.6% of BZF removal was achieved. Most of the removal rates were below 10%.

Beta-blockers

ATN is one of the most frequently used beta-blockers to cure cardiovascular diseases [25]. Fig. 4c gives the results of ATN removal from the secondary effluent samples. The rates of reduction were less than 30% under all conditions. The ATN removal at pH 7 was the lowest except for the dose of 3 mg/L, where ATN removal was slightly higher than that at pH 6 by 2%. Besides, the removal efficiencies at pH 6, 8 and 9 did not differ with each other considerably. Moreover, the highest removal rate of ATN was observed at pH 6 with the dose of 5 mg/L, with a 28.4% reduction of ATN.

Local anesthetic

LDC is a local anesthetic which is also an antiarrhythmic agent. The removal of LDC by ferrate(VI) was influenced by the solution pH significantly, as shown in Fig. 4d.

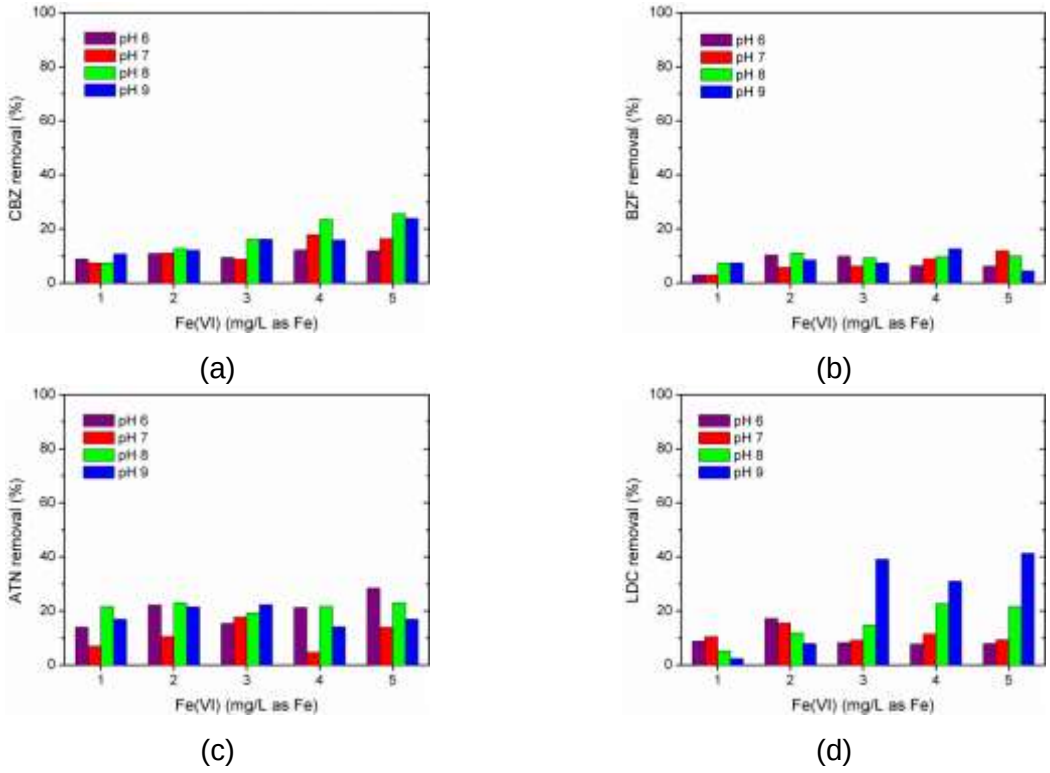


Figure 4: Removal of spiked drugs in effluent samples: (a) CBZ; (b) BZF; (c) ATN; (d) LDC

At pH 9, relatively high rates of LDC removal (> 30%) were observed when the ferrate dose reached 3 mg/L. However, the removal rates at pH 6–8 were less than 30%. More specifically,

the removal efficiencies of LDC at pH 6 and 7 were less than 20% and fluctuated with the ferrate dose. Besides, the LDC removal peaked at 2 mg/L at both pH 6 and 7, with LDC removal rates of 17.2% and 15.5%, respectively.

Comparison of removal at 5 mg/L

Figure 5 gives the comparison of the removal of target compounds by 5 mg/L ferrate(VI) at pH 6–9. All target compounds were partially removed from the wastewater by 5 mg/L ferrate(VI). Besides, for most of the target compounds, the removal efficiencies were below 50%. In contrast, CIP removal was higher than 50% when the ferrate dose 5 mg/L was applied. In addition, the removal of CIP by ferrate(VI) was the best among all target compounds at pH 6–9. On the other hand, for CPM, N-SMX, BZF and IBU, the removal efficiencies by 5 mg/L of ferrate were below 20% at pH 6–9. For all other compounds, the removal efficiencies were between 10% and 50%. The applied ferrate(VI) dose was relatively low, and it may be depleted by the co-existing organic compounds in the effluent samples.

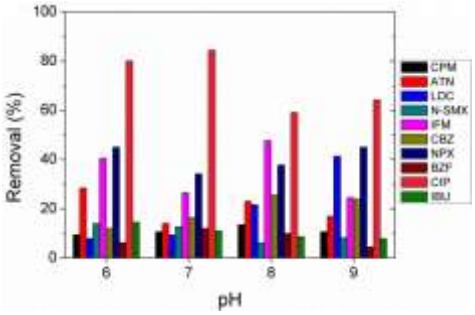


Figure 5: Comparison of the treatment of spiked pharmaceuticals by 5 mg/L ferrate(VI)

4. Conclusions

Potassium ferrate(VI) was employed to treat selected pharmaceuticals spiked in secondary effluent samples from the Shieldhall WWTP. Seven of 10 target pharmaceuticals were detected in the raw effluent samples with a maximum concentration of 500 ± 28.3 ng/L for IBU. Removal efficiencies for most of target compounds spiked in the effluent were less than 50% for pH 6–9 and ferrate(VI) dose 1–5 mg/L. Above 50% of reduction by ferrate(VI) was observed for CIP. The removal efficiencies of pharmaceuticals were improved to some extent with the rising ferrate(VI) dose, while the influence of solution pH on the treatment performance varied among different target compounds. Nonetheless, ferrate(VI) is capable to efficiently remove pharmaceutical compounds containing ERMs and can be used as an alternative technology to remove pharmaceutical residues from wastewater.

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REFERENCES

1. Schwarzenbach R. P.; Escher B. I.; Fenner K.; Hofstetter T. B.; Johnson C. A.; von Gunten U.; Wehrli B. (2006), The challenge of micropollutants in aquatic systems. Science, **313**: 1072-1077.
2. González-Pleiter M.; Gonzalo S.; Rodea-Palomares I.; Leganés F.; Rosal R.; Boltes K.; Marco E.; Fernández-Piñas F. (2013), Toxicity of five antibiotics and their mixtures towards photosynthetic aquatic organisms: Implications for environmental risk assessment. Water Res., **47**: 2050-2064.
3. Brozinski J.-M.; Lahti M.; Meierjohann A.; Oikari A.; Kronberg L. (2013), The Anti-Inflammatory Drugs Diclofenac, Naproxen and Ibuprofen are found in the Bile of Wild Fish Caught Downstream of a Wastewater Treatment Plant. Environ. Sci. Technol., **47**: 342-348.

4. Carballa M.; Omil F.; Lema J. M.; Llompart M.; Garcia-Jares C.; Rodriguez I.; Gomez M.; Ternes T. (2004), Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant. Water Res., **38**: 2918-2926.
5. Jiang J. Q.; Yin Q.; Zhou J. L.; Pearce P. (2005), Occurrence and treatment trials of endocrine disrupting chemicals (EDCs) in wastewaters. Chemosphere, **61**: 544-550.
6. Stevens-Garmon J.; Drewes J. E.; Khan S. J.; McDonald J. A.; Dickenson E. R. V. (2011), Sorption of emerging trace organic compounds onto wastewater sludge solids. Water Res., **45**: 3417-3426.
7. Zhou J. L.; Zhang Z. L.; Banks E.; Grover D.; Jiang J. Q. (2009) Pharmaceutical residues in wastewater treatment works effluents and their impact on receiving river water. J. Hazard. Mater., **166**: 655-661.
8. Huber M. M.; Gobel A.; Joss A.; Hermann N.; Loffler D.; McArdell C. S.; Ried A.; Siegrist H.; Ternes T. A.; von Gunten U. (2005), Oxidation of pharmaceuticals during ozonation of municipal wastewater effluents: A pilot study. Environ. Sci. Technol., **39**: 4290-4299.
9. Shu Z.; Bolton J. R.; Belosevic M.; Gamal El Din M. (2013), Photodegradation of emerging micropollutants using the medium-pressure UV/H2O2 Advanced Oxidation Process. Water Res., **47**: 2881-2889.
10. Hollender J.; Zimmermann S. G.; Koepke S.; Krauss M.; McArdell C. S.; Ort C.; Singer H.; von Gunten U.; Siegrist H. (2009), Elimination of Organic Micropollutants in a Municipal Wastewater Treatment Plant Upgraded with a Full-Scale Post-Ozonation Followed by Sand Filtration. Environ. Sci. Technol., **43**: 7862-7869.
11. Yang X.; Flowers R. C.; Weinberg H. S.; Singer P. C. (2011), Occurrence and removal of pharmaceuticals and personal care products (PPCPs) in an advanced wastewater reclamation plant. Water Res., **45**: 5218-5228.
12. Reungoat J.; Escher B. I.; Macova M.; Argaud F. X.; Gernjak W.; Keller J. (2012), Ozonation and biological activated carbon filtration of wastewater treatment plant effluents. Water Res., **46**: 863-872.
13. Li W.; Shi Y.; Gao L.; Liu J.; Cai Y. (2013), Occurrence and removal of antibiotics in a municipal wastewater reclamation plant in Beijing, China. Chemosphere, **92**: 435-444.
14. Jiang J. Q. (2007), Research progress in the use of ferrate(VI) for the environmental remediation. J. Hazard. Mater., **146**: 617-623.
15. Jiang J.-Q. (2014), Advances in the development and application of ferrate(VI) for water and wastewater treatment. J. Chem. Technol. Biotechnol., **89**: 165-177.
16. Hu L.; Martin H. M.; Arcs-Bulted O.; Sugihara M. N.; Keatlng K. A.; Strathmann T. J. (2009), Oxidation of carbamazepine by Mn(VII) and Fe(VI): Reaction kinetics and mechanism. Environ. Sci. Technol., **43**: 509-515.
17. Anquandah G. A. K.; Sharma V. K.; Knight D. A.; Batchu S. R.; Gardinali P. R. (2011), Oxidation of Trimethoprim by Ferrate(VI): Kinetics, Products, and Antibacterial Activity. Environ. Sci. Technol., **45**: 10575-10581.
18. Zimmermann S. G.; Schmukat A.; Schulz M.; Benner J.; von Gunten U.; Ternes T. A. (2012) Kinetic and mechanistic investigations of the oxidation of tramadol by ferrate and ozone. Environ. Sci. Technol., **46**: 876-884.
19. Lee Y.; Zimmermann S. G.; Kieu A. T.; von Gunten U. (2009), Ferrate (Fe(VI)) application for municipal wastewater treatment: A novel process for simultaneous micropollutant oxidation and phosphate removal. Environ. Sci. Technol., **43**: 3831-3838.
20. Yang B.; Ying G.-G.; Zhao J.-L.; Liu S.; Zhou L.-J.; Chen F. (2012), Removal of selected endocrine disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs) during ferrate(VI) treatment of secondary wastewater effluents. Water Res., **46**: 2194-2204.
21. Jiang J.-Q.; Stanford C.; Mollazeinal A. (2012), The application of ferrate for sewage treatment: Pilot- to full-scale trials. Global NEST J., **14**: 93-99.
22. Lee Y.; von Gunten U. (2010), Oxidative transformation of micropollutants during municipal wastewater treatment: Comparison of kinetic aspects of selective (chlorine, chlorine dioxide, ferrate(VI), and ozone) and non-selective oxidants (hydroxyl radical). Water Res., **44**: 555-566.
23. Nakada N.; Shinohara H.; Murata A.; Kiri K.; Managaki S.; Sato N.; Takada H. (2007), Removal of selected pharmaceuticals and personal care products (PPCPs) and endocrine-disrupting chemicals (EDCs) during sand filtration and ozonation at a municipal sewage treatment plant. Water Res., **41**: 4373-4382.
24. Buerge I. J.; Buser H. R.; Poiger T.; Muller M. D. (2006), Occurrence and fate of the cytostatic drugs cyclophosphamide and ifosfamide in wastewater and surface waters. Environ. Sci. Technol., **40**: 7242-7250.
25. Hapeshi E.; Achilleos A.; Vasquez M. I.; Michael C.; Xekoukoulotakis N. P.; Mantzavinos D.; Kassinos D. (2010), Drugs degrading photocatalytically: Kinetics and mechanisms of ofloxacin and atenolol removal on titania suspensions. Water Res., **44**: 1737-1746.