Reaction kinetics and oxidation products formation in the degradation of ciprofloxacin and ibuprofen by ferrate(VI)

Zhou, Zhengwei; Jiang, Jia-Qian

Published in:
Chemosphere

DOI:
10.1016/j.chemosphere.2014.04.006

Publication date:
2015

Document Version
Peer reviewed version

Reaction kinetics and oxidation products formation in the degradation of ciprofloxacin and ibuprofen by ferrate(VI)

Zhengwei Zhou, Jia-Qian Jiang*

School of Engineering and Built Environment, Glasgow Caledonian University, Glasgow G4 0BA, Scotland, United Kingdom

* Corresponding author: J-Q Jiang, Tel: +44 141 331 8850; E-mail: jiaqian.jiang@gcu.ac.uk

Abstract

The treatment of ciprofloxacin (CIP) and ibuprofen (IBU) in test solutions by ferrate(VI) was investigated in this study. A series of jar test was performed in bench-scale at pH 6–9 and ferrate(VI) dose of 1–5 mg/L. Results demonstrated that ferrate(VI) removed CIP from test solutions efficiently, with above 70% of reduction under study conditions. In contrary, the removal rates of IBU were very low, less than 25% in all conditions. Raising ferrate(VI) dose could improve the treatment performance, while the influence of solution pH was not significant at pH 6–9. In addition, kinetic studies of ferrate(VI) with both compounds were carried out at pH 8 and pH 9 (20 ℃). Ferrate(VI) had a much higher reactivity with CIP than IBU at pH 8 and pH 9, with CIP's apparent second-order rate constants of 113.7 ± 6.3 M^{-1} s^{-1} and 64.1 ± 1.0 M^{-1} s^{-1}, respectively. The rate constants of ferrate(VI) with IBU were less than 0.2 M^{-1} s^{-1} at pH 8 and pH 9. Furthermore, seven oxidation products (OPs) were formed during CIP oxidised by ferrate(VI). The attack on the piperazinyl ring of the CIP by ferrate(VI) appeared to lead to the cleavage or hydroxylation of the rings, and

the attack on the quinolone moiety by ferrate(VI) might lead to the cleavage of the double bond at the six-member heterocyclic ring. No OP of IBU was detected during ferrate(VI) oxidation due to very small part of IBU was degraded by ferrate(VI).

Key words: Ciprofloxacin; Ferrate(VI); Ibuprofen; · Kinetics; Oxidation products; Waste water treatment

1 Introduction

In recent years, the fate and environmental impact of pharmaceuticals present in the nature has gained increasing attention, among which antibiotics and non-steroidal anti-inflammatory drugs (NSAID) represent two most frequently detected therapeutic group in the environment (Comeau et al. 2008;, Lindqvist et al. 2005; Ternes 1998). Ciprofloxacin (CIP), as one of the first generation fluoroquinolones (FQs), shows broad activity against both gram-positive and gram-negative bacteria (Lee et al. 2007). Ibuprofen (IBU) is one of the most widely used groups of over-the-counter (OTC) NSAID. Both chemicals (Table 1) were in the 10 high priority list of pharmaceuticals relevant for water cycle (de Voogt et al. 2009), and commonly present in raw sewage, effluents of sewage treatment plants (STP) and surface waters with the concentration up to dozens of μg/L (Hartmann et al. 1998; Jiang et al. 2013).

Table 1 Information about CIP and IBU

Exposure of pharmaceuticals present in the aquatic environment will pose negative impact to human beings and the eco-system although the chronic effects still

require further research (Crane et al. 2006; Santos et al. 2010). Therefore, a number of studies on eliminating pharmaceuticals from the aquatic environment have been carried out recently including ozonation, chemical oxidation and several advanced oxidation processes (AOPs) (De la Cruz et al. 2012; De Witte et al. 2008, 2009; Lee et al 2012; Wols et al 2012).

As an alternative, ferrate(VI) (FeO_4^{2-}) is a promising dual-functional chemical as an oxidant and a subsequent coagulant (Fe^{3+} or $Fe(OH)_3$), which has been successfully applied into many water remediation processes (Jiang 2013). Hence, several researches on the elimination of pharmaceuticals by ferrate(VI) have been conducted recently. Kinetic profiles of ferrate (VI) with some pharmaceuticals along with transforming by-products have been identified (Lee and von Gunten 2010; Sharma 2006, 2008). In addition, results on treating effluents from wastewater treatment plants (WWTPs) by ferrate(VI) demonstrate good performance on the elimination of pharmaceuticals containing electron-rich moieties (ERMs) (Lee et al. 2009; Yang et al. 2012; Jiang et al., 2012). Solution pH has been proved to affect the treatment of many organic matters by ferrate (VI) (Graham et al. 2004; Lee et al. 2005a), e.g. phenolic compounds. However, these studies gave little information on the treatment of CIP and IBU by ferrate(VI) in terms of optimum conditions such as solution pH and ferrate(VI) dose, and the oxidation products (OPs) formation. Hence, the objectives of this study were: 1) to assess the influence of solution pH and ferrate(VI) dose on the removal of CIP and IBU; 2) to compare the rate constants of ferrate(VI) with CIP and IBU; and (3) to identify the OPs of CIP and IBU during ferrate(VI) oxidation. To our best knowledge, this is the first paper to study the OPs of CIP and IBU during ferrate(VI) treatment.

2. Experimental section

2.1. Chemical and reagents

Ciprofloxacin (CIP), ibuprofen (IBU), ibuprofen sodium and potassium ferrate(VI) (>90%) were purchased from Sigma-Aldrich (UK); ciprofloxacin hydrochloride was bought from VWR (UK); other chemicals and reagents used were obtained from Fisher Scientific (UK). The solubility of CIP and IBU was very low in water, thus ciprofloxacin hydrochloride and ibuprofen sodium of high solubility in water were used for kinetic studies. For the writing purpose, ciprofloxacin hydrochloride and ibuprofen sodium are still marked as CIP and IBU in this paper, respectively. All chemicals and reagents were used without further purification. Experimental water was generated by an Elga PureLab Option–R 7/15 pure water system (Veolia Water, France). The ferrate(VI) working solution (1 g/L) was freshly prepared by the addition of solid K_2FeO_4 to 0.0125 M $Na_2B_4O_7{\cdot}10H_2O$/0.005 M HCl buffer solution at pH 9.0. Stock solutions of CIP and IBU were prepared separately in methanol at 100 mg/L, which were used for jar testing experiments and identification of OPs. Besides, for kinetic studies, stock solution of CIP and IBU were separately prepared in pure water at 1 g/L.

2.2. Jar testing experiments

Test solutions of 1 L with two levels of initial concentrations for each compound, 100 and 10 μg/L, were prepared in buffer solutions at pH 6–9, the pH range which is usually applied in the practical water and wastewater treatment. Buffer solutions used were 0.05 M KH_2PO_4/0.005–0.05 M NaOH for pH 6–8 and 0.0125 M $Na_2B_4O_7{\cdot}10H_2O$/0.005 M HCl for pH 9.

92 A series of jar testing experiments was performed with a six-unit stirrer (Kemira
93 flocculator 2000, Kemwater) under the following protocol: fast mixing for 1 min at
94 400 rpm; slow mixing for 60–180 min at 40 rpm; and then sedimentation for 60 min.
95 The ferrate(VI) dose applied was 0–5 mg/L as Fe. All experiments were conducted in
96 duplicate.

97 Certain amount of the supernatant was filtered sequentially by 1.2 μm glass fibre
98 filters (Fisher Scientific, UK) and 0.45 μm membrane filters (Milipore, USA) after
99 sedimentation. Solution pH of the filtrate was adjusted to 2.5 by 1 M H_2SO_4 and then
100 subject to solid phase extraction (SPE) and further analysis by high performance
101 liquid chromatography (HPLC)-UV.

102 *2.3. Kinetic studies*

103 Kinetic studies of ferrate(VI) with CIP and IBU were performed at pH 8 and pH 9
104 at room temperature under pseudo first-order conditions with the pharmaceuticals in
105 excess. The room temperature was 20±2 ℃ throughout the kinetic studies. A low
106 ferrate(VI) dosage (2.5–10 μM) was applied to lower the self-decomposition rate of
107 ferrate(VI), which were also determined at pH 8 and pH 9. The 500-mL buffered test
108 solutions were stirred at 200 rpm and added with ferrate(VI) solution. At certain time
109 intervals, aliquots of the reacting solution were quenched with ABTS solution. The
110 remaining ferrate(VI) was then measured by the ABTS method at 415 nm (Lee et al.
111 2005b) at a DR3900 Vis spectrophotometer (Hach-Lange, USA). Briefly, the stock
112 solutions of ABTS reagent were prepared by dissolving 0.01 g 2,2'-azino-bis(3-
113 ethylbenzothiazoline-6-sulfonic acid) diammonium salt (Sigma-Aldrich) in 0.01 L
114 pure water (1.82 mM) and stored at 4 ^{0}C. Besides, 50 mM KHP/0.1 mM HCl was
115 used as the buffer solution for pH 4. For the determination of ferrate (VI), 0.5 mL of

the reacting solution was added into a mixed solution in a glass vial containing 1.42 mL pH 4.0 buffer solutions and 0.08 mL 1 g/L ABTS reagent. After the complete reaction between ABTS and ferrate (VI) (within 1 second), which generates green radical cations ($ABTS^{\cdot+}$), the absorbance of the $ABTS^{\cdot+}$ solutions was measured at 415 nm using 1 cm path-length cuvettes. The corresponding ferrate (VI) concentration was calculated based on the molar absorptivity of 3.4×10^4 M^{-1} cm^{-1}. The kinetic runs were performed in triplication under each condition.

2.4. Identification of Oxidation Products

Test solutions of 10 mg/L target compounds were prepared separately in pure water. Two levels of ferrate(VI) doses (5 mg/L and 10 mg/L as Fe) were applied into the stirred test solutions at 200 rpm to investigate whether the higher dose (10 mg/L) would improve the formation of OPs. Besides, the solution pH was carefully adjusted by 0.01 M H_2SO_4 or 0.02 M NaOH to make the final pH at 6.5–7.5. Certain amount of the solution was filtered by 0.45 μm Puradisc syringe filters (Whatman, USA) after the reaction was completed. Then the solution pH was adjusted to 2.5 using 1 M H_2SO_4 for further liquid chromatography (LC)-mass spectrometry (MS) analysis. The experiments were operated in parallel under identical conditions.

2.5. Analytical Methods

The remaining pharmaceutical compounds present in the treated test solutions were enriched by solid phase extraction (SPE). The SPE cartridges employed were Strata-X 1 g/12 mL giga tubes (Phenomenex, UK). Generally, the extraction method was: (1) condition: 6 mL methanol; (2) equilibrate: 6 mL water; (3) loading samples: desired amount of water samples under vaccum at a flow rate of 5–10 mL/min; (4) wash: 2 × 6 mL water; (5) dry: 15 min under gentle nitrogen flow; and (6) elute: 2 × 6 mL 2:49:49 (v/v/v) formic acid/methanol/acetonitrile. The elutes were evaporated to

dryness at 50 °C using a DB-2A Dri-Block (Techne, UK), and then re-constituted to 1 mL by 50:50 (v/v) methanol/water. The final enriched samples were filtered by 0.45 μm Puradisc syringe filters (Whatman, USA) and then subject to HPLC analysis.

An Agilent 1100 system (Agilent Technologies, USA) with a diode array detector (DAD) was employed for the measurement of target compounds. The column utilised for the separation of compounds was a 2.6 μm, 100 mm × 2.10 mm reversed phase Kinetex XB-C_{18} column (Phenomenex, UK). The column was kept at 25 °C and eluted by acetonitrile (Solvent A) and 0.1% formic acid in pure water (Solvent B) at a flow rate of 0.2 mL/min. The elution was initiated with 20% solvent A. Then the percentage of solvent A was increased to 45% over the next 6 min, held at this percentage for 15 min and finally lowered to 20% in 1 min. The DAD wavelengths for CIP and IBU detection were pre-determined and set at 280 nm and 220 nm, respectively.

An Agilent 1100 HPLC plus a Bruker Daltonics Esquire 3000 ion trap MS were employed to identify OPs of target compounds treated by ferrate (VI). The separation was achieved by an Atlantis C_{18} column (3 μm, 150 mm × 2.1 mm, Waters, USA) using a gradient of acetonitrile (Solvent A)/ ammonium formate and formic acid in water (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. After, the percentage of solvent A was gradually increased from 20% to 99% in 13 min, maintained at the same level for 9 min, and finally back to 1% in 1 min. CIP was analysed in electrospray ionisation (ESI) positive mode, while IBU was analysed in ESI negative mode.

3. Results and discussion

3.1. Effect of solution pH on the removal of mixed CIP & IBU

To investigate the effect of solution pH on the ferrate(VI) performance to treat mixed CIP and IBU solutions, a series of jar-test experiments under buffered conditions at pH 6–9 was performed at two initial concentration levels: 100 μg/L and 10 μg/L for each compound.

Initial concentration of 100 μg/L

Generally, CIP removal in the mixed solution samples by ferrate(VI) was not significantly affected by the solution pH (Fig. 1a). Though there was a slight fluctuation in CIP removal versus solution pH at 1 mg/L ferrate(VI), the average reduction rates of CIP by 1–5 mg/L ferrate(VI) under four pH conditions were above 80%. More specifically, when the ferrate(VI) dose reached or exceeded 2 mg/L, the removal efficiencies of CIP by ferrate(VI) levelled off at 90 ± 2% between pH 6 and pH 9. On the other hand, when the dose of ferrate(VI) was 1 mg/L, CIP reduction peaked at pH 9 and bottomed at pH 8, with the removal efficiency of 91.5% and 83.8%, respectively. Nevertheless, solution pH in the range of 6–9 played a minor role in the removal of CIP by ferrate(VI).

The influence of solution pH on IBU removal was slightly stronger under relatively high ferrate(VI) doses (4–5 mg/L) than that under low doses (1–3 mg/L). More specifically, in the low dose range (1–3 mg/L), IBU removal rates were below 13% and the influence of solution pH could be neglected. On the other hand, when the ferrate(VI) dose exceeded 3 mg/L, IBU removal at pH 6 was slightly higher than those under other pH conditions, with the biggest gap of 7% observed at 4 mg/L

ferrate(VI). However, comparing with CIP, the reduction efficiency of IBU in the mixed solution with pH range of 6–9 was much lower than that of CIP by at least 60%.

Fig. 1 The removal of compounds at 100 μg/L versus solution pH: (a) CIP; and (b) IBU

Initial concentration of 10 μg/L

The influence of solution pH on the removal of CIP became slightly stronger when the initial concentration was lowered from 100 μg/L to 10 μg/L (Fig. 2a). Specifically, when the ferrate(VI) dose exceeded 1 mg/L, the reduction rates of CIP at pH 6 and pH 8 were slightly higher than those at pH 7 and pH 9. The CIP removal by ferrate(VI) bottomed at 1 mg/L ferrate(VI) when the solution pH was 6, with the removal rate of about 70%. Nevertheless, the difference in the CIP removal at different pH was within 15% in the applied dose range, with all the removal efficiencies above 70%.

For IBU removal, the removal efficiencies at pH 6 were slightly greater than those at pH 7–9 by about 5% when relatively low ferrate(VI) doses were applied (1–3 mg/L), as shown in Fig. 2b . In the relatively high dose range (4–5 mg/L), IBU removal rates at pH 6–7 were similar, a little higher than those at pH 8–9. Nonetheless, the removal of IBU by ferrate(VI) was still much lower than that of CIP at this concentration level, with all the reduction rates less than 20%.

Fig. 2 The removal of compounds at 10 μg/L versus solution pH: (a) CIP; and (b) IBU

Generally, the solution pH at pH 6–9 did not exert significant influence on the ferrate(VI) oxidation of both CIP and IBU at two concentration levels. The pK_a value of $HFeO_4^-$ is 7.3. In the applied pH range 6–9, ferrate(VI) undergoes the equilibrium of protonation/de-protonation ($HFeO_4^- \leftrightarrow FeO_4^{2-} + H^+$). The mono-protonated ferrate(VI) species, $HFeO_4^-$, has been considered the most reactive species of ferrate(VI) [16]. When the solution pH was increased from 6 to 9, the fraction of $HFeO_4^-$ in the solution decreased accordingly, which very likely meant the oxidation ability of ferrate(VI) solution decreased as well. On the other hand, CIP has a secondary amine moiety in its piperazinyl group, which is an electron-rich moiety (ERM). Ferrate(VI) usually has great reactivity with ERMs-containing compounds [18, 19]. Thus, the high reactivity of ferrate(VI) with CIP appeared to make the influence of solution pH (pH 6–9) on CIP removal be negligible. IBU, on the other hand, has no ERMs in its structure, and such compounds without ERMs are usually hard to be degraded by ferrate(VI) [18, 19]. Thus the removal of IBU was less than 25% under all conditions. Such low removal rate also made the influence of solution pH (pH 6–9) on IBU removal negligible. The partial IBU removal could be attributed to the subsequent coagulation process initiated by the degradation of ferrate(VI) to ferric(III).

3.2. Kinetics

Kinetics of ferrate(VI) with CIP and IBU were studied under pseudo first-order conditions at pH 8 and pH 9. The concentrations of target compounds were at

least ten times higher than that of ferrate (VI). Thus, the reaction could be regarded as first-order with respect to [Fe(VI)]. The experimental results also confirmed this first-order relationship. As shown in Fig. 3, the plot of ferrate(VI) degradation versus reaction time fitted nicely to single exponential decay with good coefficient of correlation (0.997), which suggests that the reaction is first-order with respect to [Fe(VI)] (Sharma et al. 2012). The pseudo first-order rate constants (*k'*) were determined at different concentrations of target compounds. In addition, the *k'* values were corrected with the ferrate(VI) self-decay rate at pH 8 and pH 9 (Table 2). The *k'* values obtained at different concentrations showed a linear relationship to [CIP] (Fig. 4), which indicates the reactions are also first-order with respect to [CIP]. Therefore, the apparent second-order rate constant (k_{app}) for the reaction was then determined as the slope of the plot *k'* versus [CIP]. The kinetic runs of ferrate (VI) with IBU were performed following the same procedure. The k_{app} values for both compounds are stated in Table 3.

Fig. 3 Degradation of ferrate (VI) versus reaction time in the CIP solution at pH 9

Table 2 Self-decomposition rates of ferrate (VI) at pH 8 and pH 9

Fig. 4 *k*' values versus [CIP] at pH 9

Table 3 Apparent second-order rate constants of CIP and IBU at pH 8 and pH 9

255

256 The k_{app} values of CIP were four orders of magnitude higher than the k_{app} values
257 of IBU at pH 8 and pH 9. IBU contains a carboxylic group, which is an electron-
258 withdrawing functional group and can depress the reactivity of aromatic ring with
259 ferrate(VI) (Yang et al. 2012). Thus, the low reactivity of ferrate(VI) with IBU may
260 be attributed to the carboxylic functional group in its structure. The decreasing
261 solution pH increased the rate constants for both CIP and IBU, which is in agreement
262 with many other studies (Sharma et al. 2006a, 2006b) and has been explained in the
263 early section.

264

265 *3.3. Oxidation products*

266 The IBU removal by 5 mg/L and 10 mg/L ferrate(VI) were very low as shown
267 in Table 4. Besides, no OP of IBU was detected in its treated solutions. In treating test
268 solution samples with initial concentrations of 100 μg/L and 10 μg/L, up to 20% of
269 IBU could be removed by 5 mg/L ferrate(VI). The extremely low remove rates of
270 IBU obtained in this section might be explained by: 1) the slight removal of IBU by
271 ferrate(VI) was very likely attributed to the coagulation effect of ferric ions reduced
272 from ferrate(VI); and 2) the test solutions in this section were stirred at 200 rpm
273 constantly, which was not ideal for the formation and aggregation of flocs and then
274 reduced the coagulation effect substantially. Since there were no degradation of IBU
275 occurred, it can be expected that there should be no OPs to be detected.

276 **Table 4** Removal of CIP and IBU by 5 mg/L and 10 mg/L ferrate (VI)

277

278 A number of OPs resulting from the CIP degradation were detected by LC-MS
279 in ESI positive mode. Besides, most of the OPs for each compound were detected
280 under both ferrate(VI) dose conditions. Moreover, for most of the detectable products,
281 their instrumental response in the MS at 10 mg/L ferrate(VI) was stronger than that at
282 5 mg/L (Table 5), which indicated again the formation of OPs during ferrate(VI)
283 oxidation. Based on the measured *m/z* values, the best-fit chemical structures of such
284 OPs were tentatively proposed by referring to prior knowledge with considerations of
285 the molecule pattern of target compounds and the mechanism of ferrate(VI) oxidation
286 (An et al. 2010; De Witte et al. 2008, 2009; Liu et al. 2012; Vasconcelos et al. 2009).
287 Ferrate(VI) oxidation of organic compounds is via one/two electron transfer,
288 hydrogen abstraction or oxygen transfer (Huang et al. 2001; Sharma 2010).

289 **Table 5** Response of selected OPs of CIP in the MS

290

291 Seven OPs of CIP are presented in Table 6 with their probable formulas and
292 chemical structures. Most of the proposed OPs were produced by the transformation
293 of the piperazinyl moiety of CIP. Besides, the transformation could also happen at the
294 quinolone rings of CIP which were attacked by ferrate(VI) and this could lead to the
295 cleavage or hydroxylation of the rings and form OPs, e.g. CIP-1 and CIP-2a. On the
296 other hand, the attack on the quinolone moiety by ferrate(VI) might lead to the
297 cleavage of the double bond at the six-member heterocyclic rings and form CIP-2b.

298 **Table 6** OPs formation from the CIP degradation and detected by LC-MS in ESI
299 positive mode

300

Figure 5 gives the probable pathway of CIP degradation during the treatment by ferrate(VI). The oxidation product, CIP-1, was formed with loss of an ethylene group from the piperazine group. Further loss of a C_2H_5N group led to the formation of CIP-4, while an addition of C=O group on CIP-1 produced CIP-5. Besides, the ethylamine group in CIP-5 could also be eliminated which yielded CIP-7. Moreover, the dihydroxylation of the piperazinyl group with the addition of two oxygen atoms on CIP formed CIP-2a. Further oxidation of one hydroxyl group could lead to the loss of two hydrogen atoms and then the formation of a keto-derivative of CIP, CIP-3. In addition, the attack on the quinolone ring of CIP by ferrate(VI) formed CIP-2b. Finally, CIP-6 was generated by replacing the fluorine atom with a hydroxyl group.

Fig. 5 Pathways of CIP degradation by ferrate(VI)

4. Conclusions

The treatment of CIP and IBU in test solution samples by ferrate(VI) was investigated. Results demonstrated that ferrate(VI) could remove CIP from test solutions effectively, with at least 70% of removal under the applied experimental conditions. Besides, ferrate(VI) also had considerable rate constants with CIP at pH 8 and pH 9, with the apparent second-order rate constants of 113.7 ± 6.3 M^{-1} s^{-1} and 64.1 ± 1.0 M^{-1} s^{-1} at 20℃, respectively. Moreover, a number of oxidation products (OPs) of CIP during ferrate(VI) oxidation were detected and its degradation pathways were tentatively proposed. In contrast, the removal of IBU by ferrate(VI) was less than 25%, with its rate constants less than 0.2 M^{-1} s^{-1} at pH 8 and pH 9. Besides, no

OPs of IBU was detected during ferrate(VI) oxidation. Generally, raising ferrate(VI) dose could improve the treatment performance, while the influence of solution pH on ferrate(VI) performance was not significant at pH 6–9. The attack on the piperazinyl ring of the CIP by ferrate(VI) appeared to lead to the cleavage or hydroxylation of the rings, and the attack on the quinolone moiety by ferrate(VI) might lead to the cleavage of the double bond at the six-member heterocyclic ring. Ferrate(VI) demonstrated a sound potential to removal CIP and other ERMs-containing pharmaceuticals in the test solutions.

Acknowledgments

The authors thank Glasgow Caledonian University Research Committee for offering the PhD studentship to Zhengwei Zhou. Besides, thanks also go to Joanne Roberts who assisted the analysis of oxidation products formation by the LC-MS.

References

An TC, Yang H, Li GY, Song WH, Cooper WJ, Nie XP (2010) Kinetics and mechanism of advanced oxidation processes (AOPs) in degradation of ciprofloxacin in water. Appl Catal B-Environ 94: 288-294

Comeau F, Surette C, Brun GL, Losier R (2008) The occurrence of acidic drugs and caffeine in sewage effluents and receiving waters from three coastal watersheds in Atlantic Canada. Sci Total Environ 396: 132-146

Crane M, Watts C, Boucard T (2006) Chronic aquatic environmental risks from exposure to human pharmaceuticals. Sci Total Environ 367: 23-41

346 De la Cruz N, Giménez J, Esplugas S, Grandjean D, de Alencastro LF, Pulgarín C (2012)
347 Degradation of 32 emergent contaminants by UV and neutral photo-fenton in domestic
348 wastewater effluent previously treated by activated sludge. Water Res 46: 1947-1957

349 De Voogt P, Janex-Habibi ML, Sacher F, Puijker L, Mons M (2009) Development of a
350 common priority list of pharmaceuticals relevant for the water cycle. Water Sci Technol
351 59: 39-46

352 De Witte B, Dewulf J, Demeestere K, De Vyvere VV, De Wispelaere P and Van Langenhove
353 H (2008) Ozonation of ciprofloxacin in water: HRMS identification of reaction products
354 and pathways. Environ Sci Technol 42: 4889-4895

355 De Witte B, Dewulf J, Demeestere K, Van Langenhove H (2009) Ozonation and advanced
356 oxidation by the peroxone process of ciprofloxacin in water. J Hazard Mater 161: 701-
357 708

358 Graham N, Jiang CC, Li XZ, Jiang JQ, Ma J (2004) The influence of pH on the degradation
359 of phenol and chlorophenols by potassium ferrate. Chemosphere 56: 949-956

360 Hartmann A, Alder AC, Koller T, Widmer RM (1998) Identification of fluoroquinolone
361 antibiotics as the main source of umuC genotoxicity in native hospital wastewater.
362 Environ Toxicol Chem 17: 377-382

363 Huang H, Sommerfeld D, Dunn BC, Eyring EM, Lloyd CR (2001) Ferrate(VI) oxidation of
364 aqueous phenol: Kinetics and mechanism. J Phys Chem A 105: 3536-3541

365 Jiang J-Q, Zhou Z, Sharma VK (2013) Occurrence, transportation, monitoring and treatment
366 of emerging micro-pollutants in waste water — A review from global views. Microchem.
367 J. 110, 292-300.

368 Jiang J-Q (2013) Advances in the development and application of ferrate(VI) for water and
369 wastewater treatment. J Chem Technol Biot. 89 (2), 165-177.

370 Jiang J-Q, Zhou Z, Pahl O (2012) Preliminary study of ciprofloxacin (cip) removal by
371 potassium ferrate(VI). Sep. Purif. Technol, 88, 95-98.

372 Lee CO, Howe KJ, Thomson BM (2012) Ozone and biofiltration as an alternative to reverse
373 osmosis for removing PPCPs and micropollutants from treated wastewater. Water Res 46:
374 1005-1014.

375 Lee HB, Peart TE, Svoboda ML (2007) Determination of ofloxacin, norfloxacin, and
376 ciprofloxacin in sewage by selective solid-phase extraction, liquid chromatography with
377 fluorescence detection, and liquid chromatography-tandem mass spectrometry. J
378 Chromatogr A 1139: 45-52

379 Lee Y, von Gunten U (2010) Oxidative transformation of micropollutants during municipal
380 wastewater treatment: Comparison of kinetic aspects of selective (chlorine, chlorine
381 dioxide, ferrate(VI), and ozone) and non-selective oxidants (hydroxyl radical). Water
382 Res 44: 555-566

383 Lee Y, Yoon J, von Gunten U (2005a) Kinetics of the oxidation of phenols and phenolic
384 endocrine disruptors during water treatment with ferrate (Fe(VI)). Environ Sci Technol
385 39: 8978-8984

386 Lee Y, Yoon J, von Gunten U (2005b) Spectrophotometric determination of ferrate (Fe(Vl))
387 in water by ABTS. Water Res 39: 1946-1953

388 Lee Y, Zimmermann SG, Kieu AT, von Gunten U (2009) Ferrate (Fe(VI)) Application for
389 municipal wastewater treatment: A novel process for simultaneous micropollutant
390 oxidation and phosphate removal. Environ Sci Technol 43: 3831-3838

391 Lindqvist N, Tuhkanen T, Kronberg L (2005) Occurrence of acidic pharmaceuticals in raw
392 and treated sewages and in receiving waters. Water Res 39: 2219-2228

393 Liu C, Nanaboina V, Korshin GV, Jiang W (2012) Spectroscopic study of degradation
394 products of ciprofloxacin, norfloxacin and lomefloxacin formed in ozonated wastewater.
395 Water Res 46: 5235-5246

396 Santos L, Araujo AN, Fachini A, Pena A, Delerue-Matos C, Montenegro M (2010)
397 Ecotoxicological aspects related to the presence of pharmaceuticals in the aquatic
398 environment. J Hazard Mater 175: 45-95

399 Sharma VK (2008) Oxidative transformations of environmental pharmaceuticals by Cl_2, ClO_2,
400 O_3, and Fe(VI): Kinetics assessment. Chemosphere 73: 1379-1386

401 Sharma VK (2010) Oxidation of inorganic compounds by ferrate(VI) and ferrate(V): One-
402 electron and two-electron transfer steps. Environ Sci Technol 44: 5148-5152

403 Sharma VK, Mishra SK (2006) Ferrate(VI) oxidation of ibuprofen: A kinetic study. Environ
404 Chem Lett 3: 182-185

405 Sharma VK, Mishra SK, Ray AK (2006). Kinetic assessment of the potassium ferrate(VI)
406 oxidation of antibacterial drug sulfamethoxazole. Chemosphere 62: 128-134.

407 Sharma VK, Sohn M, Anquandah GAK, Nesnas N (2012) Kinetics of the oxidation of
408 sucralose and related carbohydrates by ferrate(VI). Chemosphere 87: 644-648

409 Ternes TA (1998) Occurrence of drugs in German sewage treatment plants and rivers. Water
410 Res 32: 3245-3260

411 Vasconcelos TG, Henriques DM, Konig A, Martins AF, Kummerer K (2009) Photo-
412 degradation of the antimicrobial ciprofloxacin at high pH: Identification and
413 biodegradability assessment of the primary by-products. Chemosphere 76: 487-493

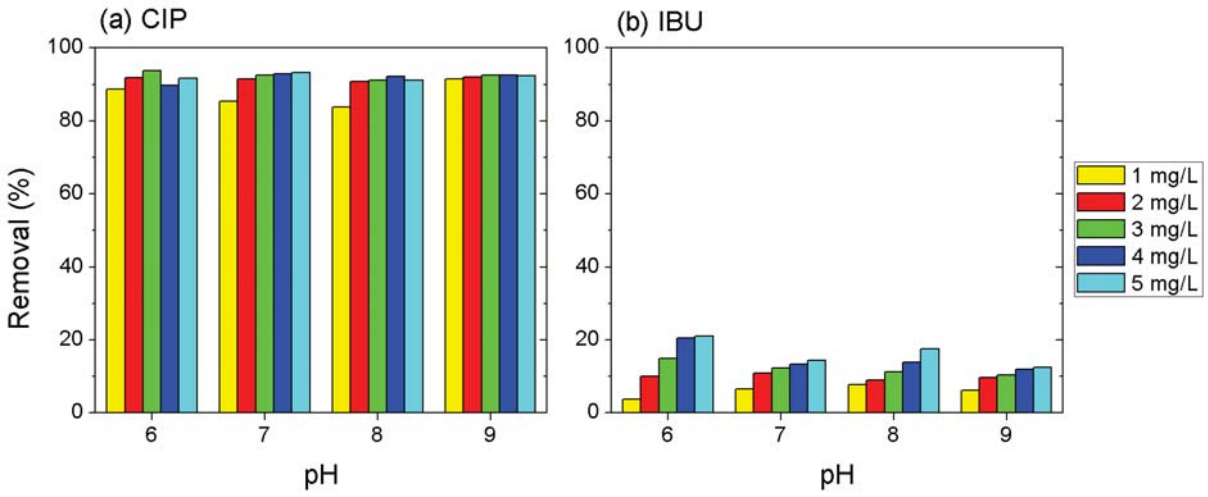
414 Wols BA, Hofman-Caris CHM (2012) Review of photochemical reaction constants of organic
415 micropollutants required for UV advanced oxidation processes in water. Water Res 46:
416 2815-2827

417 Yang B, Ying GG, Zhao JL, Liu S, Zhou LJ, Chen F (2012) Removal of selected endocrine
418 disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs)
419 during ferrate(VI) treatment of secondary wastewater effluents. Water Res 46: 2194-
420 2204

421

422

423

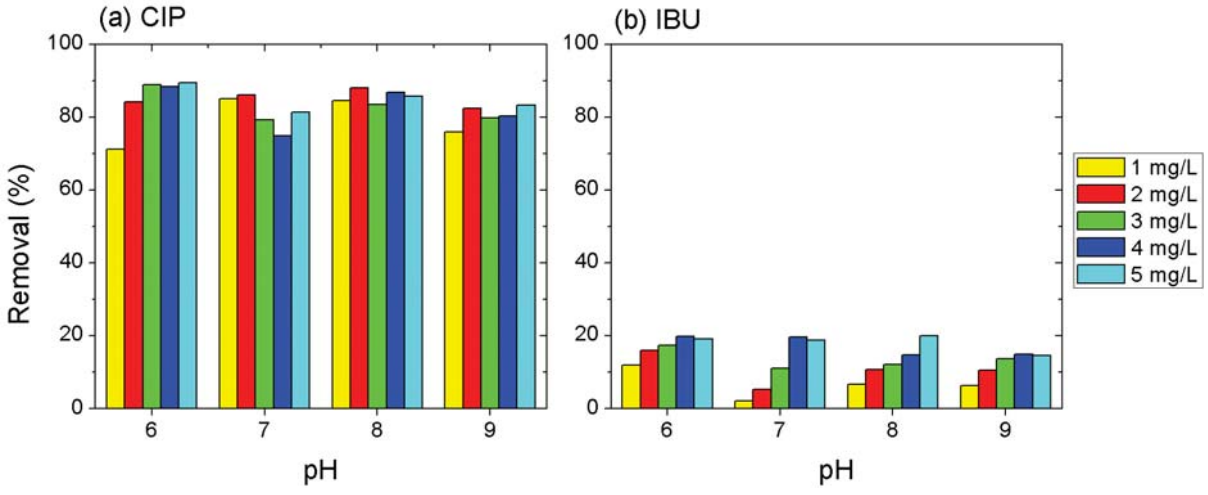


424

425 **Fig. 1** The removal of compounds at 100 μg/L versus solution pH: (a) CIP; and (b)

426 IBU

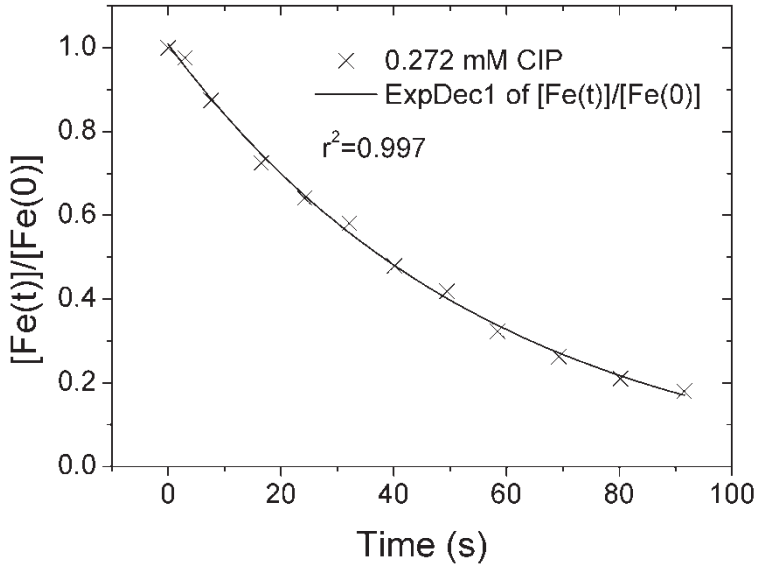
427



428

429 **Fig. 2** The removal of compounds at 10 μg/L versus solution pH: (a) CIP; and (b)

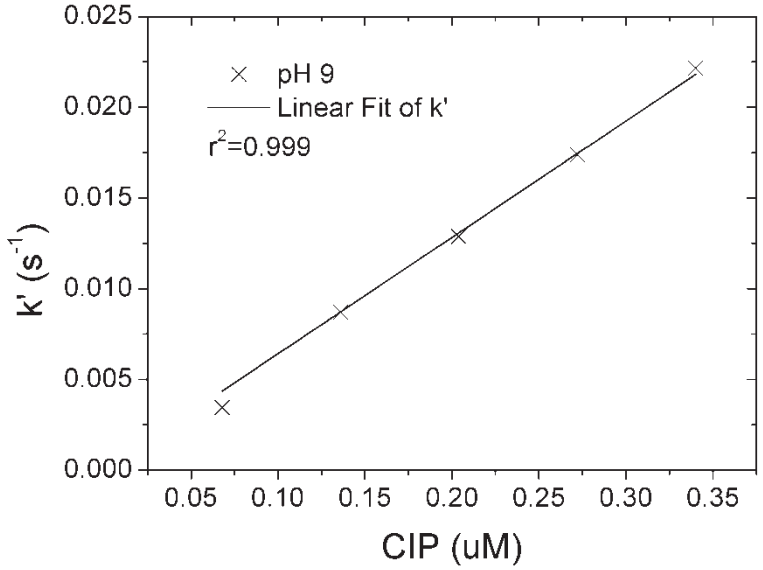
430 IBU



431

432 **Fig. 3** Degradation of ferrate (VI) versus reaction time in the CIP solution at pH 9

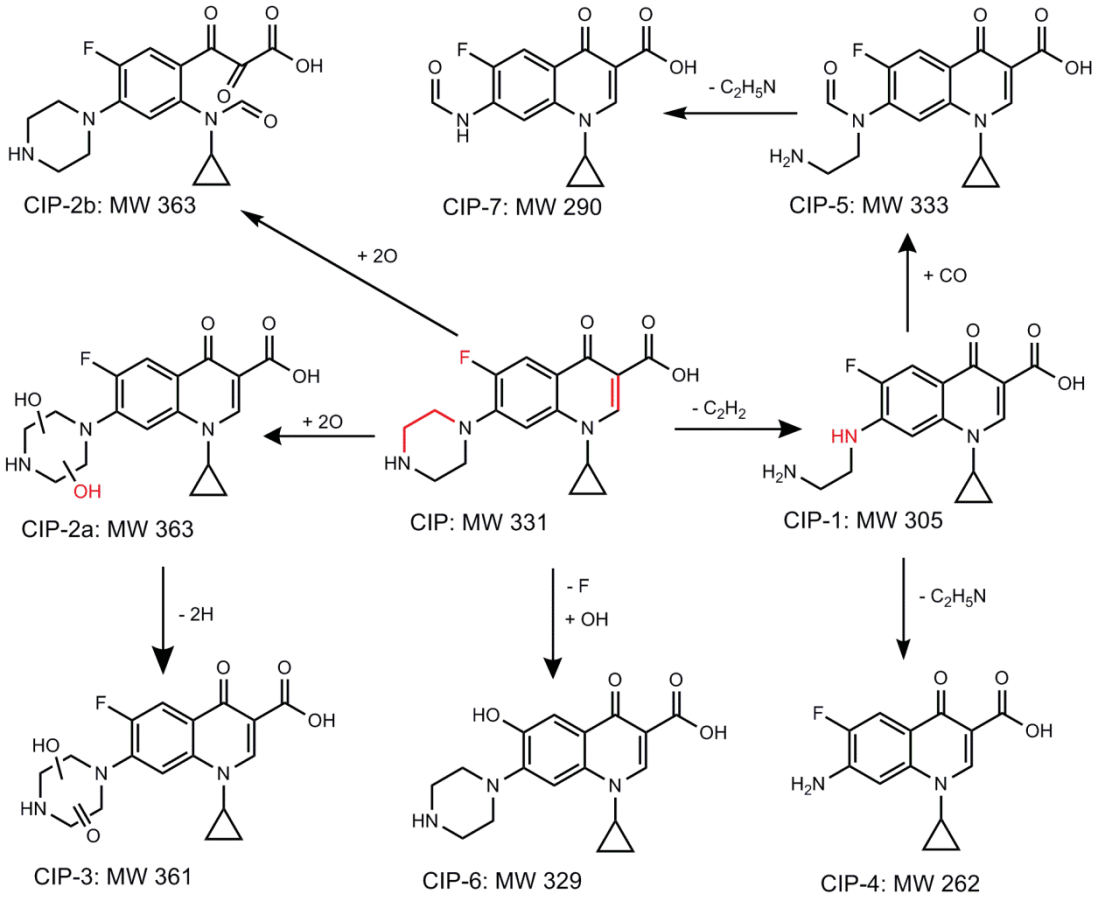
433



434

435 **Fig. 4** *k*' values versus [CIP] at pH 9

436

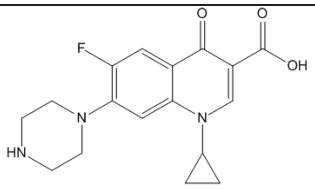
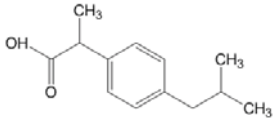


437

438 **Fig. 5** Pathways of CIP degradation by ferrate (VI)

439

440 **Table 1** Information about CIP and IBU

Compound	CAS NO.	Chemical structure	MW (g·mol^{-1})	pKa	Kow
CIP	85721-33-1		331.35	6.09	0.28
IBU	15687-27-1		206.29	4.91	3.97

441 From SRC PhysProp Database

442 **Table 2** Self-decomposition rates of ferrate (VI) at pH 8 and pH 9

Solvent	$k'_{self\text{-}decomposition}$, s^{-1}	
	pH 8	**pH 9**
Water	3.24×10^{-4}	3.8×10^{-5}

443

444 **Table 3** Apparent second-order rate constants of CIP and IBU at pH 8 and pH 9

Compound	k_{app}, (M^{-1} s^{-1})	
	pH 8	**pH 9**
CIP	113.689 ± 6.345	64.131 ± 0.982
IBU	0.122 ± 0.006	0.0150 ± 0.0002

445

446 **Table 4** Removal of CIP and IBU by 5 mg/L and 10 mg/L ferrate (VI)

Compound	Ferrate (VI)	
	5 mg/L	**10 mg/L**
CIP	61%	100%
IBU	2%	6%

447 **Table 5** Response of selected OPs of CIP in the MS.

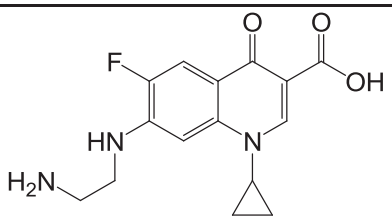
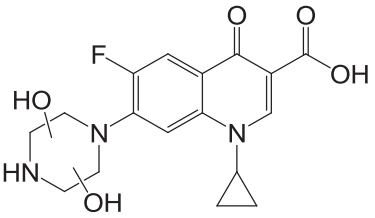
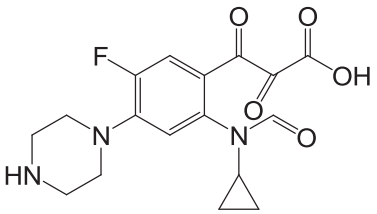
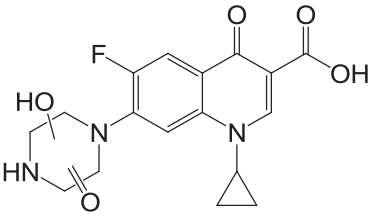
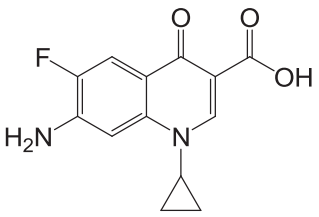
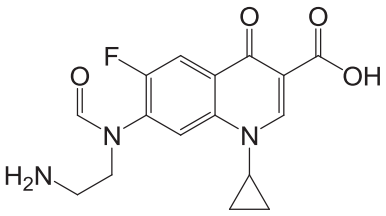
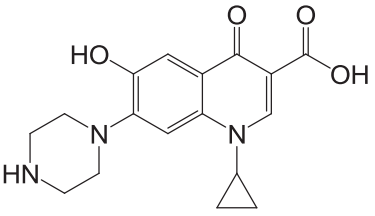
Dosage	m/z=262.7	m/z = 305.7	m/z=329.7	m/z = 333.7	m/z=363.7
5 mg/L	1.7×10^7	5.0×10^5	8.1×10^6	1.9×10^8	7.2×10^6
10 mg/L	1.4×10^8	7.2×10^6	1.8×10^7	1.0×10^8	2.6×10^7

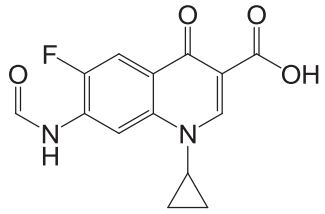
448

449 **Table 6** OPs formation from the CIP degradation and detected by LC-MS in ESI

450 positive mode

OP	*m/z*	Molecular	Molecular	Probable structure

		Weight	**formula**	
CIP-1	305.7	305	$C_{15}H_{16}FN_3O_3$	
CIP-2a	363.7	363	$C_{17}H_{18}FN_3O_5$	
CIP-2b				
CIP-3	361.6	361	$C_{17}H_{16}FN_3O_5$	
CIP-4	262.7	262	$C_{13}H_{11}FN_2O_3$	
CIP-5	333.7	333	$C_{16}H_{16}FN_3O_4$	
CIP-6	329.7	329	$C_{17}H_{19}N_3O_4$	

CIP-7	290.7	290	$C_{14}H_{11}FN_2O_4$	

451

452