Chemical Engineering Journal 221 (2013) 446–451

Contents lists available at SciVerse ScienceDirect

Chemical Engineering Journal

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

Oxidation of β-lactam antibiotics by ferrate(VI)

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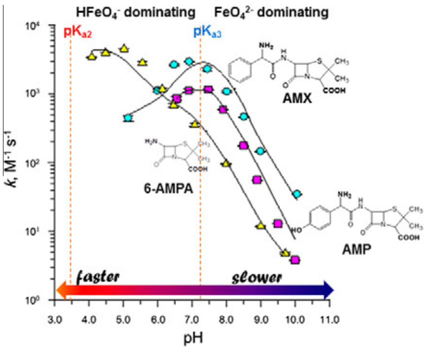
HIGHLIGHTS

- β-Lactams, amoxicillin (AMX) and ampicillin (AMP) were oxidized by ferrate(VI).
- Kinetics for AMX and AMP oxidation by ferrate(VI) were second-order.
- Second-order rate constants were pH dependent.
- Ferrate(VI) likely reacting with the amine moiety of β-lactams under study.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 23 November 2012
Received in revised form 4 February 2013
Accepted 6 February 2013
Available online 13 February 2013

Keywords:
Ferrate
β-Lactam removal
Amoxicillin
Ampicillin
Advanced oxidation
Stoichiometry

ABSTRACT

Amoxicillin (AMX) and ampicillin (AMP), penicillin class β-lactam antibiotics, have been detected in wastewater effluents and their release into the environment may involve long-term risks such as toxicity to aquatic organisms and endocrine disruption in higher organisms. This paper demonstrates the removal of AMX and AMP by ferrate(VI) (Fe(VI)) by performing kinetics and stoichiometric experiments. The dependence of the second-order rate constants of the reaction between Fe(VI) and AMX (or AMP) on pH was explained using acid–base equilibria of Fe(VI) and organic molecules. The kinetics study with the model compound, 6-aminopencillanic acid and the pH dependence behavior suggested that Fe(VI) reacted with the amine moieties of the studied β-lactams. The reactivity of different oxidants with AMX have been shown to follow the sequence: $^{\cdot}OH \approx SO_4^{\cdot-}$ > bromine > ozone > chlorine > Fe(VI). The required molar stoichiometric ratios ([Fe(VI)]:[β-lactam]) for the complete removal of AMX and AMP by Fe(VI) were about 4.5 and 3.5, respectively. The Fe(VI) is able to eliminate AMX and AMP and hence is likely to also oxidize other β-lactams effectively.

1. Introduction

Pharmaceuticals in the aquatic environment pose long-term risks such as toxicity to aquatic organisms and the disruption of endocrine systems of higher organisms [1,2]. As pharmaceuticals, antibiotics are highly consumed as both human and veterinary medicines and their presence in water is of concern due to the development of antibiotic resistant bacteria [3]. β-Lactams can efficiently block the biosynthetic enzymes that are needed to synthesize cell walls of bacteria and thus are able to destroy Gram-positive and Gram-negative bacteria [4]. They are biorefractory and are incompatible with biological treatment technologies [5,6]. β-Lactams have been found at concentrations up to μg L^{-1} in wastewater effluent [1] and therefore suitable alternate water treatment methods are needed to degrade these non-biodegradable molecules in water sources.

Advanced oxidation processes (AOPs) have been shown to be promising in the treatment of β-lactams. AOPs studied with respect to β-lactam removal include UV/H_2O_2, Fenton, photo-Fenton,

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http://dx.doi.org/10.1016/j.cej.2013.02.024

electro-Fenton, O_3, UV/O_3, $\cdot SO_4^-$, and photocatalysis [7–19]. The effectiveness of AOPs is generally related to the hydroxyl radical, which reacts with organic molecules by addition and hydrogen abstraction pathways [15]. Mixtures of phenolic (and quinolic) compounds have been observed as intermediate products in the case of oxidation of aromatic compounds. Chemical oxidants studied include bromine, chlorine, and chlorine dioxide [20–22]. These oxidants were found to have high reactivity with β-lactams and achieved complete elimination of the parent molecules. The current paper is the first report on the oxidation of the β-lactams amoxicillin (AMX) and ampicillin (AMP), by the green oxidant, ferrate(VI) ($Fe^{VI}O_4^{2-}$, Fe(VI)).

In the last few years, several researchers have demonstrated the potential of Fe(VI) as an oxidant, coagulant, and disinfectant in treating water and wastewater [23–26]. Studies have been performed on the kinetics of the reactions of Fe(VI) with endocrine disruptors, estrogens, and pharmaceuticals [27–50]. However, no kinetics studies on the oxidation of β-lactam antibiotics by Fe(VI) have been published in the scientific literature. In the current paper, the kinetics of the reactions of Fe(VI) with amoxicillin (AMX) and ampicillin (AMP) is reported. The chemical structures of AMX and AMP are given in Fig. 1. The reaction of Fe(VI) with the model compound, 6-aminopencillanic acid (6-AMPA) (see Fig. 1), of the studied β-lactam antibiotics was also investigated. The objectives of the paper are to: (i) determine the species-specific rate constants for the kinetics of the reaction of Fe(VI) and β-lactams as a function of pH, (ii) compare the kinetics with other chemical oxidants (chlorine, bromine, and ozone), and (iii) demonstrate removal of β-lactams by Fe(VI) in water.

2. Materials and methods

2.1. Reagents

Amoxicillin, the sodium salt of AMP, and 6-AMPA were obtained from Sigma–Aldrich (St. Louise, MO, USA), Fisher-Scientific (Austin, TX, USA), and Acros Organics (Geel, Belgium), respectively, and were used without any further purification. Solid potassium ferrate (K_2FeO_4) of ~98% purity was synthesized by the wet technique [51]. Fe(VI) solutions were prepared by the addition of solid K_2FeO_4 to 1 mM $Na_2B_4O_7{\cdot}10H_2O$/5 mM Na_2HPO_4 at pH 9.0, the pH at which Fe(VI) solutions are most stable. Phosphate in the solution acts as a complexing agent for Fe(III), which otherwise precipitates rapidly as a hydroxide that instantly interferes with the optical monitoring of the reaction and also accelerates the spontaneous decomposition of Fe(VI). All solutions were prepared using doubly distilled water that had been passed through an 18 MΩ Milli-Q (Millipore, Waters Alliance, Milford, MA, USA) water purification system. Stock solutions of target β-lactams were prepared by dissolving solid compounds in 10 mM Na_2HPO_4 buffer solution. The solution pH was adjusted to the desired pH by adding either phosphoric acid or sodium hydroxide. Concentrations of Fe(VI) were determined by performing spectral measurements of the solutions at 510 nm using a UV–Vis spectrophotometer (Agilent 8453 UV–Vis spectrophotometer, Santa Clara, CA, USA). A molar absorption coefficient, $\varepsilon_{510\,nm} = 1150\ M^{-1}\ cm^{-1}$ was used to determine Fe(VI) concentrations at pH 9.0 [51]. HPLC-grade methanol was purchased from Fisher-Scientific for use in HPLC experiments.

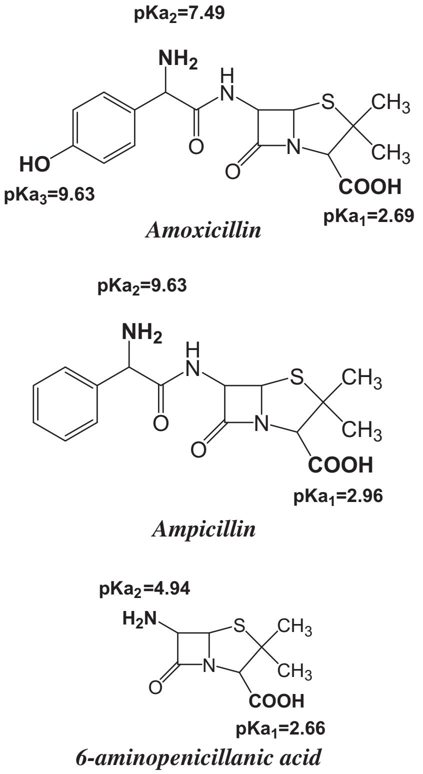

Fig. 1. Chemical structures of β-lactams under study and a model compound, the 6-AMPA.

2.2. Kinetic studies

A stopped-flow spectrophotometer (SX-18 MV, Applied Photophysics, Surrey, UK) with a photomultiplier detector was used to carry out kinetic studies under pseudo-order conditions in which concentrations of AMX, AMP, and 6-AMPA were in excess compared to Fe(VI). The Fe(VI) concentration used was 0.1 mM. The pseudo-first-order rate constants were determined by collecting kinetic traces at a wavelength of 510 nm. The analysis of the data was done using the nonlinear least-square algorithm of the SX-18MV Global Software (Applied Photophysics, Surrey, UK). Rate constants obtained represent the average of six replicate runs.

2.3. Removal study

The oxidations of AMX and AMP by Fe(VI) were carried out by mixing equal solution volumes of 10 mL and the pH of the reaction mixture was maintained at pH 7.0. The concentration of AMX and AMP in the reaction mixtures were kept at 0.1 mM and the concentrations of Fe(VI) varied from 0.1 to 10 mM. The concentrations of AMX and AMP were analyzed until no residual Fe(VI) was detectable. The solutions were filtered using 0.45 μm nylon filters into HPLC vials. The concentrations of AMX and AMP in the resulting reaction mixtures were quantified by the use of an HPLC (Waters Alliance 2695, Milford, MA, USA) with a d-C_{18} column (5 μm; 150 mm × 4.6 mm; Atlantis, Milford, MA, USA) at wavelengths of 230 and 268 nm, respectively. Analyses were carried out under isocratic elution conditions. For AMX, a binary mobile phase consisting of 25% Solvent A (methanol) and 75% Solvent B (0.1% HCOOH in water) at a flow rate of 0.6 mL min^{-1} and an injection volume of 50 μL were used in an isocratic elution mode. For AMP, a binary mobile phase consisting of 35% Solvent A (methanol) and 65% Solvent B (0.1% HCOOH in water) at a flow rate of 1.0 mL min^{-1} and an injection volume of 50 μL were used also in an isocratic elution mode.

3. Results and discussion

3.1. Kinetics

Initially, the kinetic studies were carried out for the reaction between Fe(VI) and AMX at pH 6.0 and 25 °C to determine the rate law of the reaction in an aqueous acidic medium. The rate expression for the reaction of Fe(VI) with AMX can be expressed as in the following equation:

$$-d[\mathrm{Fe(VI)}]/dt = k[\mathrm{Fe(VI)}]^m[\mathrm{AMX}]^n \tag{1}$$

where [Fe(VI)] and [AMX] are the concentrations of Fe(VI) and AMX, m and n are the orders of the reaction with respect to the concentrations of Fe(VI) and AMX respectively and k is the overall reaction rate constant. For kinetic studies being carried out under pseudo-order conditions with AMX in excess, Eq. (1) can be re-written as:

$$-d[\mathrm{Fe(VI)}]/dt = k_1[\mathrm{Fe(VI)}]^m \tag{2}$$

where $k_1 = k\,[\mathrm{AMX}]^n$. The decrease in absorbance of Fe(VI) as a function of time could be fitted nicely to single exponential decay, which indicates that the rate is first-order with respect to the concentration of Fe(VI), i.e., $m = 1$. Different values of k_1 were determined at various concentrations of AMX. The values of k_1 increased linearly with [AMX] (SM-1). The plot of log k_1 versus log [AMX] was linear ($R^2 = 0.99$) and a slope of 0.96 ± 0.11 (SM-1) was obtained. Similar results were obtained in the kinetics study in basic media (SM-1). These results indicate that the reaction between Fe(VI) and AMX is first-order with respect to the [AMX] in both acidic and basic media, i.e., $n = 1$ (SM-1). Kinetic studies were then extended to AMP and 6-AMPA, which also showed first-order kinetics with respect to the concentrations of Fe(VI) and AMP (or 6-AMPA). The rate law for the reaction between Fe(VI) and the β-lactams can then be expressed as:

$$-d[\mathrm{Fe(VI)}]/dt = k[\mathrm{Fe(VI)}][\mathrm{B}] \tag{3}$$

where k is the second-order rate constant and [B] = [AMX], [AMP], or [6-AMPA].

Plots of the values of second-order rate constants, k, as a function of pH are presented in Fig. 2a. The rate constants for the oxidation of AMX by Fe(VI) were higher than those for AMP for all pH conditions studied. This indicates that the phenolic moiety in the AMX may be influencing the reactivity with Fe(VI). With respect to the pH dependence behavior for the oxidation of the β-lactams, rates decreased with increase in pH ⩾ 7.5. Rate constants decreased in the acidic media for these compounds from a maximum at ~pH 7.0. This trend appears to be similar to the general trend of variation of k with pH for oxidation of primary (glycine, $\mathrm{NH_3^+CH_2COOH}$) and secondary (dimethylamine, $\mathrm{(CH_3)_2NH}$) amines (Fig. 2b) [31,52,53]. This similarity allows one to suggest that the oxidation of β-lactams by Fe(VI) may involve the amine moieties. The rate constants for the oxidation of the model compound (i.e., 6-AMPA), were lower than those of the studied β-lactams at high pH values (see Fig. 2a). The model compound had a similar trend in pH dependence of the rate constants as that seen for the reactivity of Fe(VI) with aniline (Fig. 2a and b). It seems that the 6-aminopencillanic moiety had a minor role in determining the reactivity of Fe(VI) with β-lactams.

Finally, the pH dependence behavior of rate constants were analyzed quantitatively using acid–base equilibria of Fe(VI), AMX, AMP, and 6-AMPA:

Fe(VI) [54] :

$$\mathrm{H_3FeO_4^+} \rightleftharpoons \mathrm{H^+} + \mathrm{H_2FeO_4} \quad \mathrm{p}Ka1 = 1.6$$

$$\mathrm{H_2FeO_4} \rightleftharpoons \mathrm{H^+} + \mathrm{HFeO_4^-} \quad \mathrm{p}Ka2 = 3.5$$

$$\mathrm{HFeO_4^-} \rightleftharpoons \mathrm{H^+} + \mathrm{FeO_4^{2-}} \quad \mathrm{p}Ka3 = 7.23$$

AMX [55] :

$$\mathrm{H_3AMX^+} \rightleftharpoons \mathrm{H^+} + \mathrm{H_2AMX} \quad \mathrm{p}Ka1 = 2.69$$

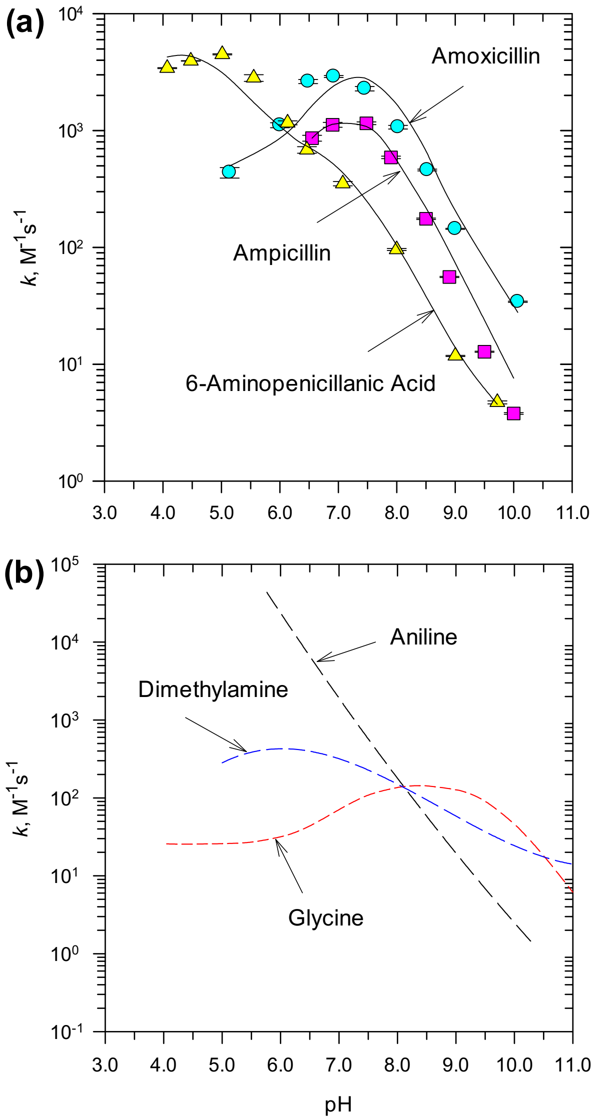

Fig. 2. Effect of pH on the second-order rate constants for the oxidation of (a) β-lactams and a model compound and (b) amines by Fe(VI) at 25 °C.

$$\mathrm{H_2AMX} \rightleftharpoons \mathrm{H^+} + \mathrm{HAMX^-} \quad \mathrm{p}Ka2 = 7.49$$

$$\mathrm{HAMX^-} \rightleftharpoons \mathrm{H^+} + \mathrm{AMX^{2-}} \quad \mathrm{p}Ka3 = 9.63$$

AMP [4] :

$$\mathrm{H_2AMP^+} \rightleftharpoons \mathrm{H^+} + \mathrm{HAMP} \quad \mathrm{p}Ka1 = 2.96$$

$$\mathrm{HAMP} \rightleftharpoons \mathrm{H^+} + \mathrm{AMP^-} \quad \mathrm{p}Ka2 = 9.63$$

6-AMPA [56] :

$$\mathrm{H_2(6\text{-}AMPA)^+} \rightleftharpoons \mathrm{H^+} + \mathrm{H(6\text{-}AMPA)} \quad \mathrm{p}Ka1 = 2.66$$

$$\mathrm{H(6\text{-}AMPA)} \rightleftharpoons \mathrm{H^+} + \mathrm{(6\text{-}AMPA)^-} \quad \mathrm{p}Ka2 = 4.94$$

Considering the pH range studied for the reaction between Fe(VI) and AMX, the four species of Fe(VI) (i.e., $\mathrm{H_3FeO_4^+}$, $\mathrm{H_2FeO_4}$, $\mathrm{HFeO_4^-}$, and $\mathrm{FeO_4^{2-}}$) with the four species of AMX could possibly react with each other. The pH dependence can therefore be modeled by the following equation:

$$k[\mathrm{Fe(VI)}]_{tot}[\mathrm{B}]_{tot} = \Sigma k_{ij}\alpha_i\beta_j[\mathrm{Fe(VI)}]_{tot}[\mathrm{AMX}]_{tot} \quad i = 1,2,3,4, \quad j = 1,2,3,4 \tag{4}$$

where $[\mathrm{Fe(VI)}]_{tot} = [H_3FeO_4^+] + [H_2FeO_4] + [HFeO_4^-] + [FeO_4^{2-}]$; $[\mathrm{AMX}]_{tot} = [H_3AMX^+] + [H_2AMX] + [HAMX^-] + [AMX^{2-}]$; α_i and β_j represent the species of Fe(VI) and AMX, respectively; *i* and *j* are each of the species of Fe(VI) and AMX, respectively and k_{ij} is the species-specific second-order rate constant for the reaction between the Fe(VI) species i and the AMX species *j*. While there are sixteen possible reactions which could contribute to Eq. (4), only three of the following four reactions (Eqs. (5)–(8)) were needed to fit the experimentally observed rate constants using the kinetic model (Eq. (4)).

$$HFeO_4^- + H_2AMX \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_5 = (4.5 \pm 0.5) \times 10^2\ M^{-1}\ s^{-1} \tag{5}$$

$$HFeO_4^- + HAMX^- \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_6 = (1.5 \pm 0.2) \times 10^4\ M^{-1}\ s^{-1} \tag{6}$$

$$FeO_4^{2-} + H_2AMX \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_7 = (8.3 \pm 0.1) \times 10^3\ M^{-1}\ s^{-1} \tag{7}$$

$$FeO_4^{2-} + AMX^- \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_8 = (3.0 \pm 0.5) \times 10^1\ M^{-1}\ s^{-1} \tag{8}$$

Reaction Eqs. (6) and (7) introduce proton ambiguity and thus the experimental values of *k* could be fitted reasonably well by using either reactions Eqs. (5), (6), and (8) or reactions Eqs. (5), (7), and (8) (solid line in Fig. 2a). The rate constant of the reaction for Eq. (7) (k_7) is much greater than the rate constant of reaction Eq. (5) (k_5), which is contradictory with the results of numerous studies on oxidation reactions of Fe(VI), which have shown that the protonated form of Fe(VI), $HFeO_4^-$ reacts faster than the un-protonated species (FeO_4^{2-}) [27,57]. Therefore, reaction Eqs. (5), (6), and (8) would be the most likely contributors to the rates of the reaction of Fe(VI) and AMX at different pH values.

A similar analysis of the rate constants was performed for the reactions of Fe(VI) with AMP. The kinetic model given in Eq. (4) was applied to fit the rate constants as a function of pH. The observed rate constants could be fitted nicely using only two of the following reactions (Eqs. (9)–(11)) (Fig. 2a). Since reaction Eqs. (10) and (11) had proton ambiguity, rate constants could be fitted using either reaction Eqs. (9) and (10) or the reactions below:

$$HFeO_4^- + HAMP \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_9 = (3.0 \pm 0.9) \times 10^2\ M^{-1}\ s^{-1} \tag{9}$$

$$FeO_4^{2-} + AMP^- \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_{10} = (4.5 \pm 0.2) \times 10^3\ M^{-1}\ s^{-1} \tag{10}$$

$$FeO_4^{2-} + HAMP \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_{11} = (4.6 \pm 0.2) \times 10^2\ M^{-1}\ s^{-1} \tag{11}$$

In the case of the oxidation of 6-AMPA, reactions (Eqs. (12)–(14)) were needed to fit the experimental data (a solid line, Fig. 2a).

$$H_2FeO_4 + 6\text{-}AMPA^- \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_{12} = (1.7 \pm 0.2) \times 10^5\ M^{-1}\ s^{-1} \tag{12}$$

$$HFeO_4^- + 6\text{-}AMPA^- \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_{13} = (7.0 \pm 0.1) \times 10^2\ M^{-1}\ s^{-1} \tag{13}$$

$$FeO_4^{2-} + 6\text{-}AMPA^- \rightarrow Fe(OH)_3 + \mathrm{Product(s)} \quad k_{14} = 2.2 \pm 0.2\ M^{-1}\ s^{-1} \tag{14}$$

3.2. Comparison with other oxidants

Fig. 3 compares the second-order rate constants for the oxidation of AMX by different oxidants. The pH dependence profiles for chlorine and bromine were drawn using known species-specific rate constants (Table 1) [20,21]. In the case of ozone, specific rate constants were estimated earlier using only two dissociation constants of AMX (pK_a = 2.8 and 7.2) [12], hence the experimental values shown in Fig. 3 (square symbols) were re-evaluated in the present study using all three p*K*a values (see Fig. 1). The estimated species-specific rate constants for the oxidation of AMX by ozone are also given in Table 1. The estimated values fitted nicely to the experimental values of the rate constants (solid line in Fig. 3). Rate constants for the oxidation of AMX by both bromine and ozone increased with increase in pH. The increase in the reactivity of AMX with ozone, with increase in pH, had a similar trend, which could be related to the acid/base equilibria of amines. Protonated amines had almost no reactivity while the deprotonated form reacted rapidly with ozone; hence increase in pH would be expected to increase the rates for oxidation of AMX by ozone. Both chlorine and Fe(VI) had similar pH dependence patterns with respect to rate constants. Protonated species of chlorine (i.e., HOCl) and Fe(VI) (i.e., $HFeO_4^-$) had much higher reactivity than those of un-protonated forms (i.e., OCl^- and FeO_4^{2-}); therefore, the observed decrease in rate constants with increase in pH were expected (Fig. 3). Significantly, diprotonated species of AMX (H_2AMX) reacted more slowly with HOCl and $HFeO_4^-$ than did monoprotonated AMX ($HAMX^-$) (see Table 1) and, therefore, decreases in rates were seen in the acidic pH region (pH 5–7).

Several studies have shown high effectiveness of the oxidation of AMX by ${}^{\cdot}OH$, produced by a variety of AOPs [1,5,10,12,55,58]. These results are consistent with observed diffusion-controlled rate constants for the reaction of AMX with ${}^{\cdot}OH$ radical (see Fig. 3). Similarly, $SO_4^{\cdot-}$ was very efficient at removing AMX [17]. However, oxidation by $SO_4^{\cdot-}$ occurred adjacent to the β-lactam moiety whereas ${}^{\cdot}OH$ attacks at the peripheral aromatic-ring of AMX [15,17]. Fig. 3 suggests the following order of reactivity for oxidation of AMX at neutral pH:

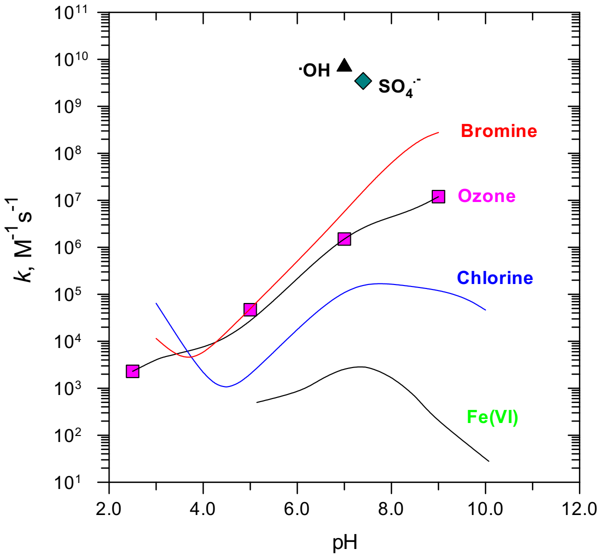

Fig. 3. The second-order rate constants for the oxidation of AMX by different oxidants at 25 °C (solid lines were drawn using species-specific rate constants given in Table 1).

Table 1
The species-specific rate constant (k, $M^{-1}\ s^{-1}$) for the oxidation of amoxicillin by different oxidant species.

Oxidant species	H_3AMX^+	H_2AMX	k, $M^{-1}\ s^{-1}$ $HAMX^-$	AMX^{2-}	Reference
HOCl	$(2.6 \pm 0.4) \times 10^4$ $1.7 \times 10^8\ [H^+]$	$(2.6 \pm 0.4) \times 10^4$	$(3.8 \pm 0.3) \times 10^5$	$(2.0 \pm 0.4) \times 10^7$	[21]
HOBr	$(2.4 \pm 0.4) \times 10^4$ $<1 \times 10^7\ [H^+]$	$(2.4 \pm 0.4) \times 10^4$	$(9.9 \pm 1.5) \times 10^6$	$(3.8 \pm 1.2) \times 10^9$	[20]
O_3[a]	–	$(5.9 \pm 0.2) \times 10^3$	$(4.4 \pm 0.9) \times 10^6$	$(5.1 \pm 0.5) \times 10^7$	This study
$HFeO_4^-$	–	$(4.5 \pm 0.5) \times 10^2$	$(1.5 \pm 0.2) \times 10^4$		This study
FeO_4^{2-}	–	–	–	$(3.0 \pm 0.5) \times 10^1$	

[a] Experimental data were taken from [12].

$\cdot OH \approx SO_4^{\cdot-}$ ($k \sim 5 \times 10^9\ M^{-1}\ s^{-1}$) > bromine ($k = 5.7 \times 10^6\ M^{-1}\ s^{-1}$) > ozone ($k = 1.5 \times 10^6\ M^{-1}\ s^{-1}$) > chlorine ($k = 1.1 \times 10^4\ M^{-1}\ s^{-1}$) > Fe(VI) ($k = 3.0 \times 10^3\ M^{-1}\ s^{-1}$). Chlorination of AMX resulted in elimination of AMX, but the formation of trihalomethanes was detected [21]. In addition, the presence of Br^- in treated water can form hypobromous acid upon chlorination ($HOCl + Br^- \rightarrow HOBr + Cl^-$, $k = 1.55 \times 10^3\ M^{-1}\ s^{-1}$) [20], which may accelerate the oxidation of AMX due to the much higher reactivity of bromine as compared to chlorine (see Fig. 3). However, brominated by-products may be among the oxidized products of AMX. The presence of Br^- during ozonation is also of concern due to the potential formation of carcinogenic bromate ions [59]. Comparatively, the treatment of water by Fe(VI) does not yield bromate ion due to non-reactivity with Br^- [60]. A half-life of ~5 s, using a dose of 10 mg L^{-1} K_2FeO_4, was determined for the oxidation of AMX by Fe(VI). This suggests that Fe(VI) has enormous potential as a means of removing AMX from water.

3.3. Removal study

Results of the removal experiments demonstrated that Fe(VI) is effective at oxidizing AMX and AMP at neutral pH (Fig. 4). The required stoichiometric ratios of Fe(VI) to β-lactams ([Fe(VI)]/[β-lactam]) for complete removal of AMX and AMP were ~4.5 and ~3.5, respectively. The AMX has a phenolic group, not present in AMP (see Fig. 1) and Fe(VI) may be simultaneously reacting with this group in addition to the amines, resulting in a higher Fe(VI) dose needed for AMX relative to that required for the removal of AMP by Fe(VI). Previous studies also report similar Fe(VI) dose requirements for the elimination of sulfamethoxazole (SMX) and trimethoprim (TMP) [45,46]. Complete removal of the antibiotics SMX and TMP required stoichiometric ratios of ~4 and ~5, respectively, as previously reported [45,46]. In the case of TMP, the oxidized products had no antibacterial activity against *Escherichia coli* [45]. In a recent study, complete removal of a number of antibiotics by Fe(VI) was also demonstrated for secondary wastewater effluents [61]. However, the dosage of Fe(VI) needed would depend on the water chemistry. Dissolved organic matter should increase the demand for Fe(VI) since it would also consume Fe(VI). Fe(VI) is a promising oxidant for the removal of antibiotics from water, and the required dose will vary with the concentration of antibiotics and the chemistry of the water.

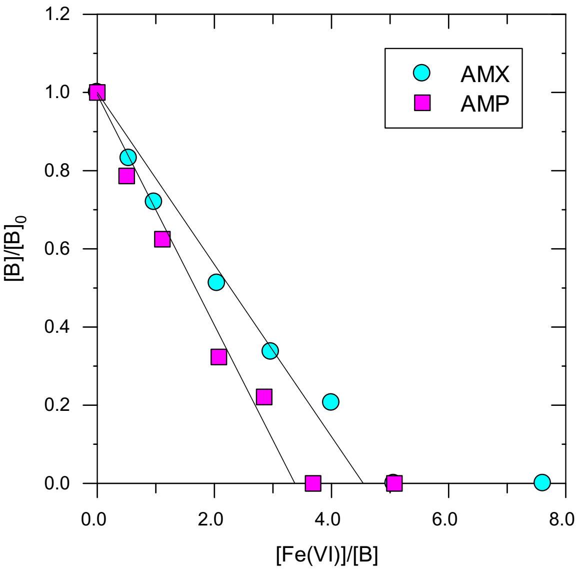

Fig. 4. Removal of AMX and AMP by Fe(VI) at pH 7.0.

4. Conclusions

The oxidation reaction between Fe(VI) and AMX (or AMP) followed second-order kinetics and the dependence of the second-order rate constant on pH was successfully explained using the species-specific rate constants of the reactions of Fe(VI) with the β-lactam antibiotics. The trend in the pH dependence suggests that Fe(VI) may likely be attacking the amine moieties of the organic molecules. The determination of oxidized products would confirm preferential attack(s) of Fe(VI) on the β-lactams. At neutral pH, complete removal of target β-lactams by Fe(VI) was achieved, however, tests of the products of the reaction are needed to confirm no antibiotic activity after complete elimination of β-lactams by Fe(VI).

Acknowledgment

This work was supported by a grant from the R&D Program of MKE/KEIT (10037331, Department of Core Water Treatment Technologies based on the Intelligent BT-NT-IT Fusion Platform).

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.cej.2013.02.024.

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