Efficient degradation of sulfamethoxazole by the Fe(II)/HSO₅⁻ process enhanced by hydroxylamine: Efficiency and mechanism

Guifang Liu ^{a,b,*}, Xuchun Li ^{c,**}, Bangjun Han ^{d,e}, Liwei Chen ^f, Linan Zhu ^a, Luiza C. Campos ^b

ABSTRACT

Fenton or Fenton-like processes have been regarded as feasible methods to degrade a wide variety of contaminants by generating reactive species, but the efficiency is still challenged by the slow transformation from Fe(III) to Fe(II) and pH. This study employed hydroxylamine (HA) to improve the oxidation efficiency of Fe(II)/HSO₅⁻ (Fe(II)/PMS) process, by selecting sulfamethoxazole (SMX) as the target compound. The degradation efficiency and mechanism of SMX by the HA/Fe(II)/PMS process were elucidated for the first time. Compared with Fe(II)/PMS process, the HA/Fe(II)/PMS process showed about 4 times higher degradation efficiency of SMX at pH 3.0. The analysis of steady-state concentration of Fe species indicated that HA enhanced the transformation of Fe(III) to Fe(II), sustaining the rapid Fenton-like reactions. Both sulfate radicals and hydroxyl radicals accounted for the degradation of SMX, with the latter regarded as the dominant reactive species. Degradation intermediates of SMX were further analyzed, and three main transformation pathways were thus proposed. The HA/Fe(II)/PMS process was also effective in the removal of SMX and total organic carbon from real pharmaceutical wastewater. This work would broaden the scope of application of Fenton and Fenton-like processes enhanced by HA in contaminants treatment.

Keywords: Sulfate radical; Hydroxyl radical; Peroxomonosulfate; Hydroxylamine; Sulfamethoxazole

1. Introduction

An increasing number of antibiotics are environmentally widespread and routinely found in aquatic environment [1], and they are of great concern for their toxicity and potential to induce resistance of drug acting on aquatic ecosystems and human health [2]. Industrial pharmaceutical wastewater treatment plants without effective treatment of antibiotics have become a significant threat for aquatic environment [3].

Conventional treatment processes exhibit poor removal for antibiotics from pharmaceutical wastewater [4]. Advanced oxidation processes based on hydroxyl radical ($\text{HO}^\bullet$) oxidation have indicated a certain success in the degradation of antibiotics [5,6]. Recently, increasing attention has been paid to the catalytic peroxymonosulfate (HSO_5^- , PMS) oxidation based on sulfate radicals ($\text{SO}_4^{\bullet-}$) due to its high efficiency of selection and degradation for some refractory organic contaminants [7]. Having a comparable oxidizing ability of $\text{HO}^\bullet$ ($E^0 = 1.9\text{-}2.7\text{V}$) [8], $\text{SO}_4^{\bullet-}$ with E^0 of $2.5\text{-}3.1\text{V}$ [7] presents a powerful oxidation capacity of antibiotics, e.g., destruction of antibiotics in pure water, underground water, domestic wastewater, and swine wastewater [9-12]. However, little information is currently available with regard to the remediation of antibiotics in pharmaceutical wastewater based on $\text{SO}_4^{\bullet-}$ oxidation.

Generally, generation efficiency of $\text{SO}_4^{\bullet-}$ controls the oxidation of antibiotics. Activated approaches of PMS or persulfate (PS) by such as photons [10], heat [13,14], organic compound [15], metal-based catalyst [16], transition metals [12,17] have been used to produce more $\text{SO}_4^{\bullet-}$ to eliminate organic contaminants. Among these activated methods, ferrous iron (Fe(II)) has the superiority of low cost, high activity, and environmental-friendly nature. Nonetheless, as Fenton and

60 other Fenton-like processes have shown, some intrinsic drawbacks of Fe(II)/PMS oxidation process
61 have been gradually exposed. The slow conversion from Fe(III) back to Fe(II) is considered to be the
62 major drawback of Fe(II)/PMS process [18]. Chen et al. [19] reported that hydroxylamine (NH_2OH ,
63 HA) could effectively accelerate the redox cycle of Fe(III) to Fe(II). Owing to the low rate constants
64 with $\text{SO}_4^{\cdot-}$ [7] and $\text{HO}^{\cdot}$ [8], protonated HA can improve the degradation of benzoic acid [18],
65 trichloroethylene [20], diuron [21], and Orange G [22], as well as reducing the dosage of Fe(II) in
66 Fe(II)/PMS or Fe(II)/PS system. To the best of our knowledge, few literature reported the
67 enhancement of HA on the capacity of Fe(II)/PMS process applied in the pollution remediation of
68 antibiotics.

69 Considering the bioactivity and potential risk arising from the toxicity of oxidation products of
70 antibiotics, attention has to be paid to the degradation pathways of typical antibiotics in oxidation
71 processes in order to assess the safety of treatment methods. Previous researches indicated the
72 degradation products and pathways for same targets (e.g., Sulfamethoxazole, SMX) were different in
73 various $\text{SO}_4^{\cdot-}$ -based on oxidation processes [9,13,16,23]. Qi et al. [14] reported the nitro derivative of
74 SMX as an intermediate in microwave-activated persulfate process, but the same product were not
75 found in ferrous-activated persulfate process [12]. However, the lack of that information in the
76 HA/Fe(II)/PMS process necessitates the study about degradation pathways and mechanism of
77 antibiotics in the aqueous systems.

78 Therefore, the objective of this study was to investigate the efficiency and mechanism of the
79 HA/Fe(II)/PMS process in degradation of typical antibiotics. Sulfamethoxazole, one of the most
80 widely used sulfonamide antibiotics, was selected as the probe compound due to its frequent

detection in the aquatic environment [24]. The study focused specifically on, (i) the degradation efficiency of SMX; (ii) the role of HA; (iii) the role of the reactive species involved; (iv) the identification of degradation products and possible transformation pathways in the HA/Fe(II)/PMS process; and (v) the degradation efficiency of SMX in real pharmaceutical wastewater by the proposed process.

2. Materials and methods

2.1. Materials

All chemicals were obtained from commercial sources and are listed in Text S1. The raw pharmaceutical wastewater was collected from the Fuhe Pharmaceutical Wastewater Treatment Plant located in Zhaodong, China. More details about the chemicals and raw wastewater are given in Text S1.

2.2. Experimental procedure

All experiments were performed in 100 mL triangular flasks at 25°C. The samples were covered with aluminum foil to avoid possible photodegradation. Reaction solution with desired concentrations of SMX or benzoic acid (BA) or SMX and BA, Fe(II), and HA, was prepared with ultrapure water or pharmaceutical wastewater and adjusted to the initial desired pH. Before the experiments were started, the reaction system was blown 15 min by high purity N₂ to eliminate the shadow of dissolved oxygen. Each run was switched on by adding PMS. Samples were withdrawn at set time intervals and quenched with excess pure methanol. The quenching experiments employed methanol and tert-butyl alcohol (TBA) as the quenchers, which were performed by adding desired alcohols into the reaction system and induced immediately after the addition of PMS. All

experiments were repeated independently at least two times, and average values along with one standard deviation ($\pm$ SD) were presented.

2.3. Analytical methods

The concentrations of SMX, BA, and p-hydroxybenzoic acid (*p*-HBA) were determined by a high-performance liquid chromatography (HPLC, Waters e2695, Milford, Massachusetts, USA), and the detailed parameters are shown in Text S2. Solution pH was measured by a pH meter (PHS-3C, Shanghai Rex, Shanghai, China). The concentration of ferric iron was measured at 300 nm [25] with an UV-vis spectrometer (SP-752, Shanghai Spectrum, Shanghai, China), and the detailed procedure is shown in Text S3. The concentration of total ferrous iron was determined using a phenanthroline spectrophotometry method (APHA, 2012) with an UV-vis spectrometer (SP-752, Shanghai Spectrum, Shanghai, China). The degradation intermediates of SMX were detected by ultra-performance liquid chromatography coupled with electrospray ionization quadrupole time-of-flight mass spectrometry (UPLC-ESI-QTOFMS, Waters, Milford, Massachusetts, USA), and the details are shown in Text S4. The analysis of water quality of real pharmaceutical wastewater is given in Text S5. HA samples were measured by a gas chromatograph (Agilent 7890B, Santa Clara, CA, USA) [26], whose detailed procedure is shown in Text S6. The NO_2^- and NO_3^- concentrations were measured with an ion chromatograph (Dionex ICS-900, CA, USA), and more details refer to Text S7. The dissolved N_2O concentration was analyzed using a gas chromatograph (Agilent 7890B, Santa Clara, CA, USA) [27], and more details refer to Text S8.

3. Results and discussion

3.1. Degradation efficiency of SMX in the HA/Fe(II)/PMS process

Fig. 1 shows the degradation of SMX in the HA/Fe(II)/PMS process (more details refer to Fig. S1).

Less than 20% of SMX was degraded within 15 min in Fe(II)/PMS process, similar to that in only PMS process. The low degradation efficiency could be due to the low Fe(II) concentration [28]. Surprisingly, HA (0.4 mM) improved the efficiency greatly and approximately 80% of SMX was degraded within 15 min in the HA/Fe(II)/PMS process. In comparison, HA in the PMS process inhibited the degradation of SMX and only 10% of SMX was degraded within 15 min in HA/PMS process. It is possible that HA competed for and consumed PMS directly [22]. Therefore, both HA and Fe(II) should play a role in accelerating removal of SMX in the HA/Fe(II)/PMS process [21]. The incomplete degradation of SMX in the HA/Fe(II)/PMS process might be due to the depletion of PMS [18]. It should be pointed out that the HA/Fe(II)/PMS process exhibited an equivalent or even higher degradation efficiency of SMX, compared to reported catalytic PS oxidation processes (Table S1), e.g., Fe(II)/PS [12], thermo/PS [13], and Fe⁰/PS [16].

Fig. 1. Degradation of SMX in the HA/Fe(II)/PMS process. Conditions: [HA]₀ = 0.4 mM (no addition in PMS and Fe(II)/PMS process), [Fe(II)]₀ = 10 μM for HA/Fe(II)/PMS and Fe(II)/PMS process, [PMS]₀ = 0.3 mM, [SMX]₀ = 20 μM, pH₀ = 3.0, 25 °C. Error bars represent the standard deviation from the duplicate experiments.

3.2. Effect of pH on SMX degradation in the HA/Fe(II)/PMS process

Solution pH determines the speciation distribution of HA, Fe(II), and Fe(III), and the self-decomposition kinetics of PMS. Fig. 2 shows the effect of initial pH on the degradation of SMX in the HA/Fe(II)/PMS process. No buffering agents were added to stabilize the solution pH in the

experiments, and the variation of pH is given in the Fig. S2.

Fig. 2. Effect of initial pH on SMX degradation in the HA/Fe(II)/PMS process. Conditions: $[HA]_0 = 0.40$ mM, $[Fe(II)]_0 = 10$ μ M, $[PMS]_0 = 0.3$ mM, $[SMX]_0 = 20$ μ M, $pH_0 = 2.0-9.0$, 25 $^{\circ}$ C and reaction time (T) = 15 min. Error bars represent the standard deviation from the duplicate experiments.

From Fig. 2, the degradation of SMX was obviously promoted by increasing the initial pH from 2.0 to 3.0, reflecting the yield of reactive species could be improved greatly. The variation tendency could be mainly attributed to the formation and increase of $Fe(OH)_2$ with increasing solution pH. $Fe(OH)_2$ has been demonstrated to be more effective than Fe(II) iron to activate peroxide and PMS [18,29]. The optimal initial pH range for degradation of SMX was 3.0 to 6.0 (the final balanced range of pH from 2.9 to 3.7 as shown in Fig. S2). And with further increase of initial pH from 6.0 to 9.0 (the final balanced range of pH from 6.5 to 7.3 as shown in Fig. S2), the degradation of SMX was greatly inhibited. The decrease in SMX degradation efficiency implies the inhibited generation of reactive species accordingly. Within the initial range of pH (3.0-9.0), on one hand, the yield of $Fe(OH)_2$ decreased by the increase of ferric oxyhydroxides precipitation above pH 3.0 [30], and the self-decomposition of PMS increased with the increase of solution pH [31], which were bound to reduce the yield of reactive species directly. On the other hand, the primary form of HA is NH_2OH ($pK_a = 5.96$ and 13.74) [32] at pH values in the range of 6.0 to 9.0. NH_2OH has high reaction rate constants with reactive radicals ($k_1 = 8.5 \times 10^8$ $M^{-1} s^{-1}$ for $SO_4^{\bullet-}$ [7], $k_2 = 9.5 \times 10^9$ $M^{-1} s^{-1}$ for $HO^{\bullet}$ [8]), which are comparable to that of SMX ($k_3 = 1.6 \times 10^{10}$ $M^{-1} s^{-1}$ for $SO_4^{\bullet-}$, $k_4 = 7.0 \times 10^9$ $M^{-1} s^{-1}$ for $HO^{\bullet}$)

[33]. From the perspective of competition and consumption of radicals, NH_2OH would also decrease the contribution of reactive species to degrade SMX. Therefore, the speciation distribution of the involved species including HA, Fe(II), and Fe(III), and also the self-decomposition of PMS would be the dominant factors to influence the generation of reactive species and the degradation of SMX at different pH ranging from 2.0 to 9.0.

3.3. Role of HA in the HA/Fe(II)/PMS Process

The aforementioned data and analysis suggest that HA plays an important role in improving the degradation efficiency of SMX in the HA/Fe(II)/PMS process. So, the effect of HA concentration on SMX degradation was investigated and the results are shown in Fig. 3. With the increase of HA concentration from 0.0 to 0.4mM, the degradation efficiency of SMX obviously increased considerably. Then further increasing HA concentration from 0.4 to 1.0mM, the improvement on the removal of SMX was found to be insignificant. Authors [18,19] reported that HA could effectively promote the redox cycle of Fe(III) to Fe(II), improve the generation of reactive species and increase the removal of organic pollutants at pH 3.0. However, excess HA could quench the reactive species (e.g., $\text{SO}_4^{\bullet-}$ and $\text{HO}^{\bullet}$) with a high reaction rate [7,8] in the HA/Fe(II)/PMS process at pH 3.0. Here, 0.4 mM of HA was optimum for SMX degradation and thus was used in the following experiments.

Fig. 3. Effect of HA concentration on SMX degradation in the HA/Fe(II)/PMS Process. Conditions: $[\text{HA}]_0 = 0.0\text{-}1.0\text{ mM}$, $[\text{Fe(II)}]_0 = 10\text{ }\mu\text{M}$, $[\text{PMS}]_0 = 0.3\text{ mM}$, $[\text{SMX}]_0 = 20\text{ }\mu\text{M}$, $\text{pH}_0 = 3.0$, $25\text{ }^\circ\text{C}$. Error bars represent the standard deviation from the duplicate experiments.

186 To further understanding the role of HA, the variation of Fe(III) concentrations in Fe(II)/PMS
187 process with/without SMX and HA/Fe(II)/PMS process with/without SMX were measured
188 respectively (Fig. 4). The interference of HA and PMS on the measurement could be ignored at the
189 experimental concentration [18,19]. However, due to the obvious absorption of SMX and its
190 degradation products at 300 nm, methanol was used to consume the reactive radicals (i.e., $\text{SO}_4^{\bullet-}$ and
191 $\text{HO}^{\bullet}$) in the processes without SMX.

192

193 **Fig. 4.** Effect of HA on Fe(III) concentration in the HA/Fe(II)/PMS process. Conditions: $[\text{HA}]_0 = 0.40 \text{ mM}$ (no
194 addition for Fe(II)/PMS process), $[\text{Fe(II)}]_0 = 100 \text{ }\mu\text{M}$, $[\text{PMS}]_0 = 0.3 \text{ mM}$, $[\text{SMX}]_0 = 20 \text{ }\mu\text{M}$ or $[\text{methanol}]_0 = 10 \text{ mM}$,
195 $\text{pH}_0 = 3.0$, $25 \text{ }^\circ\text{C}$. Error bars represent the standard deviation from the duplicate experiments.

196

197 Almost all Fe(II) was transformed into Fe(III) within 10 s and kept relatively steady throughout
198 the runs in the Fe(II)/PMS processes without SMX and with SMX (Fig. 4). This might be attributed
199 to the fast reaction between Fe(II) and PMS via Eqs. (1) and (2) [34] and the slow transformation
200 from Fe(III) to Fe(II). In the HA/Fe(II)/PMS processes without SMX and with SMX, the similar
201 phenomenon about the generation of Fe(III) occurred within 10 s as the Fe(II)/PMS processes;
202 however, the concentration of Fe(III) rapidly decreased after 10 s and then kept relatively steady
203 after 300 s with the runs of reaction. It should be noted that the concentration of Fe(III) was reduced
204 from approximately $100 \text{ }\mu\text{M}$ to less than $42 \text{ }\mu\text{M}$ and $27 \text{ }\mu\text{M}$ in the HA/Fe(II)/PMS system with and
205 without SMX, respectively. Moreover, the steady-state concentration of Fe(III) could be attributed to
206 dynamic equilibrium of the iron ion circulation given in Eqs. (3) to (5) [19,22]. The higher

207 steady-state concentration of Fe(III) in the system with SMX was probably due to the influence of
 208 target organics and intermediates on the UV absorption of solution at 300 nm. However, the decrease
 209 of Fe(III) concentration in both systems supports that the addition of HA promoted intensively the
 210 redox cycle of Fe(III) to Fe(II) and thus improved the removal of SMX in the HA/Fe(II)/PMS
 211 process.

217 3.4. Role of reactive radicals in the HA/Fe(II)/PMS Process

218 It was reported that three reactive radicals (i.e., $\text{SO}_4^{\bullet-}$, $\text{HO}^{\bullet}$, and $\text{SO}_5^{\bullet-}$) could be generated during
 219 the catalyst-mediated decomposition of PMS [26,34]. Among these radicals, $\text{SO}_4^{\bullet-}$ and $\text{HO}^{\bullet}$ are
 220 commonly known as the dominant reactive species for degrading aqueous organic contaminants in
 221 catalytic PMS oxidation processes [13,18,23]. Based on the radical reaction characteristics, methanol
 222 and TBA were selected as quenching compounds to investigate their inhibition effects on SMX
 223 degradation, and thus explore the degradation mechanism of SMX in the HA/Fe(II)/PMS process.

224 Fig. 5 shows the inhibitory effects of methanol and TBA on the degradation of SMX in the
 225 HA/Fe(II)/PMS process. From Fig. 5, it is apparent that $\text{HO}^{\bullet}$ and $\text{SO}_4^{\bullet-}$ could be the responsible
 226 reactive species. The difference of inhibition effects between methanol and TBA were less than 10%
 227 in terms of SMX degradation, strongly suggesting a relatively weak contribution of $\text{SO}_4^{\bullet-}$ to the SMX

degradation. Therefore, $\text{HO}^\bullet$ should be the dominant reactive species for the degradation of SMX. The results agreed with previous report [18] which suggested the major role of $\text{HO}^\bullet$ in the degradation of BA in the similar system. In addition, considering the relative inertia of alcohols toward $\text{SO}_5^{\bullet-}$ ($k \leq 10^3 \text{ M}^{-1} \text{ s}^{-1}$) [35], approximately 25% of SMX degradation in non-alcohol system could be attributed to the rapid degradation in the initial reaction or the contribution of $\text{SO}_5^{\bullet-}$ which is similar to the degradation of BA in HA/Fe(II)/PMS process [18].

Fig. 5. Inhibition effect of radical scavengers on SMX degradation in the HA/Fe(II)/PMS process. Conditions: $[\text{HA}]_0 = 0.40 \text{ mM}$, $[\text{Fe(II)}]_0 = 10 \text{ }\mu\text{M}$, $[\text{PMS}]_0 = 0.3 \text{ mM}$, $[\text{SMX}]_0 = 20 \text{ }\mu\text{M}$, $[\text{TBA}]_0 = 10 \text{ mM}$ or $[\text{methanol}]_0 = 10 \text{ mM}$, $\text{pH}_0 = 3.0$, $25 \text{ }^\circ\text{C}$. Error bars represent the standard deviation from the duplicate experiments.

In order to further confirm the major reactive species in the HA/Fe(II)/PMS process, the competition kinetics between SMX and BA were carried out and the results are shown in Fig. 6. Theoretically, the degradation of SMX and BA should agree with Eqs. (6) or (7) assuming that either $\text{HO}^\bullet$ or $\text{SO}_4^{\bullet-}$ causes the degradation. The data of competition degradation of SMX and BA within 30 min in the HA/Fe(II)/PMS process (Fig. S3) was used considering the degradation trend of BA and SMX.

Fig. 6. Competition kinetics between SMX and BA with reactive species in the HA/Fe(II)/PMS process. Conditions: $[\text{HA}]_0 = 0.4 \text{ mM}$, $[\text{Fe(II)}]_0 = 10 \text{ }\mu\text{M}$, $[\text{PMS}]_0 = 0.3 \text{ mM}$, $[\text{SMX}]_0 = 20 \text{ }\mu\text{M}$, $[\text{BA}]_0 = 20 \text{ }\mu\text{M}$, $\text{pH} = 3.0$, $25 \text{ }^\circ\text{C}$.

$$\frac{\ln(\frac{C_{t,BA}}{C_{0,BA}})}{\ln(\frac{C_{t,SMX}}{C_{0,SMX}})} = \frac{k_1}{k_2} \quad (6)$$

$$\frac{\ln(\frac{C_{t,BA}}{C_{0,BA}})}{\ln(\frac{C_{t,SMX}}{C_{0,SMX}})} = \frac{k_1'}{k_2'} \quad (7)$$

Here, k_1 and k_2 are the rate constants of $\text{HO}^\bullet$ with BA and SMX, respectively; k_1' and k_2' are the rate constants of $\text{SO}_4^{\bullet-}$ with BA and SMX, respectively. At pH 3.0, $k_1 = 4.3 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [8], $k_2 = 7.0 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [33], $k_1' = 1.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [7], and $k_2' = 1.6 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ [33]. Thus, $k_1 / k_2 = 0.614$, and $k_1' / k_2' = 0.075$.

The slope in Fig. 6 for the competition kinetics is about 0.4756, approaching k_1 / k_2 , but deviating far from k_1' / k_2' . This agreement indeed validated the dominant role of $\text{HO}^\bullet$ in the degradation system. Furthermore, the formation of *p*-HBA (Fig. S4) also confirmed the contribution of $\text{HO}^\bullet$ to the degradation of BA and SMX [36]. It was noted that the formation ratio of *p*-HBA didn't agree with the reported one of about 1/5.87 [37], possibly ascribed to the attack of HBA or their intermediate precursors by Fe(III) and persulfate [38].

3.5. Degradation products and pathways of SMX in the HA/Fe(II)/PMS process

To further study the degradation mechanism of SMX in the HA/Fe(II)/PMS process, UPLC-ESI-QTOFMS was employed to identify the formed intermediates. The ion chromatograms of major degradation products are shown in Fig. S5. Eight oxidation products including **P-93**, **P-98**, **P-155**, **P-189**, **P-267**, **P-269**, **P-270**, and **P-283**, were identified. The empirical formulas of these products were proposed according to the corresponding MS/MS spectra and fragmentation patterns, and the MS spectra of degradation products of SMX are shown in Fig. S6.

Fig. S7 shows the MS/MS spectra of **P-98** (m/z 99 for MH^+), which has fragments of m/z 30, m/z 44, m/z 55, m/z 71, and m/z 72. Based on the fragmentation patterns and reasonable formation pathways of those fragments as shown in Fig. S7, **P-98** was identified as 3-amino-5-methylisoxazole, which was attributed to the cleavage of S-N bond in SMX. **P-98** had also been detected in other oxidation processes based on sulfate radical oxidation [9,12,13,16]. Accompanying with **P-98**, another product **P-155** (m/z 156 for MH^+) would also be yielded and be transformed to **P-189** (m/z 190 for MH^+) partially. The former has the fragments of m/z 65, m/z 92, m/z 108, and the latter of m/z 107, m/z 126, as shown in Fig. S8 and Fig. S9. The fragmentation patterns and the pathways of bond cleavage support that **P-155** and **P-189** were 4-sulfonylcyclohexa-2,5-dien-1-imine and hydroxysulfanilic acid, respectively. **P-189** was identified in various catalytic PS processes [14,23], nevertheless, **P-155** was only found in ozonation process [39]. In addition, **P-155** could be further transformed into aniline (**P-93**, m/z 94 for MH^+) to some degree (Fig. S6) [13,23].

The fragment **P-283** (m/z 284 for MH^+) was another primary product, and its ion fragments (m/z 98, m/z 122, m/z 138, m/z 178, m/z 193, m/z 203 and m/z 220) were detected as shown in Fig. S10. Studies have reported ion fragments of m/z 122 and m/z 138 were identified as nitro benzene [40] and nitro phenol [41], respectively. According to possible fragmentation pathways and structures of daughter ions of **P-283**, it was thus proposed as nitro SMX [9,13] as shown in Fig. S10. In addition, **P-267** (m/z 268 for MH^+) and **P-269** (m/z 270 for MH^+) were both detected during the degradation of SMX in the HA/Fe(II)/PMS process. The MS/MS spectra of **P-267** and the fragmentation pattern (daughter ion fragments at m/z 107, m/z 160, m/z 146, m/z 188, and m/z 204) as shown in Fig. S11 suggests that **P-267** was the nitroso derivative of SMX [9], which was ultimately oxidized as nitro

group (-NO₂) and conformed to **P-283** (Fig. S10). The identification of **P-267** and **P-283** suggested the amino group (-NH₂) on the aromatic ring of SMX was susceptible to be attacked by reactive radicals. Thus, the hydroxylamine derivative of SMX (**P-269**) should be yielded before the conformation of **P-267** and **P-283**. **P-269**, as an intermediate, was also found during the oxidation of SMX in heat/PS process [23].

Two primary ion fragments (m/z 99 and m/z 175 for MH⁺) occurred in the daughter ion spectrum of **P-270** (m/z 271 for MH⁺) (Fig. S12) indicate the formation of a hydroxylated derivative of SMX (i.e., **P-270**). Furthermore, the loss of methyl group to yield the fragment with m/z 256 and the losses of methyl group and oxygen to yield the fragment with m/z 230 also confirmed the addition of hydroxyl group to the benzene ring of SMX. Considering the fragmentation pattern (fragments of m/z 99, m/z 109, m/z 175, m/z 207, m/z 230, and m/z 256) and possible pathways of fragment formation as shown in Fig. S12, **P-270** was regarded as hydroxylated derivative of SMX, with the molecular structure and the substitution position of OH group shown in Fig. S12. **P-270** was also reported as an intermediate of the degradation of SMX by processes such as Fe(II)/PS [12], Cobalt(II)/PMS [9], thermo/PS [13], and microwave/PS [14].

Combined with the identification of oxidation intermediates, three major transformation pathways (A, B, and C) are thus proposed in Fig. 7. The reactive species (HO[•] and SO₄^{•-}) could attack the sites of S-N bond, amine group on the aromatic ring, and benzene ring in SMX, respectively. As aforementioned, HO[•] was the predominant reactive species for the degradation of SMX in the HA/Fe(II)/PMS process. Therefore, HO[•] definitely played a key role in the proposed pathways of SMX degradation. In general, HO[•] likely react with organic compounds by addition reaction,

hydrogen atom abstraction, and single electron transfer [42]. In pathway **A**, S-N bond cleavage occurred, and 3-amino-5-methylisoxazole (**P-98**) and 4-sulfonylcyclohexa-2,5-dien-1-imine (**P-155**) were thus formed when the S-N bond on the molecular structure of SMX broke due to the attack by HO[•]. Subsequently, the addition of HO[•] to the reaction sites of -SO₂ and benzene ring on **P-155** resulted in the formation of hydroxysulfanilic acid (**P-189**), an aniline (**P-93**) was also generated via release of SO₄²⁻ due to the reactivity of sulfonated moiety with HO[•] [5]. For the pathway **B**, oxidation of the amine group at the benzene ring took place, and hydroxylamine derivative of SMX (**P-269**) was produced by the attack of HO[•] and/or SO₄^{•-} via abstracting the hydrogen of -NH₂ to form hydroxylamine moiety [43]. The hydroxylamine moiety of **P-269** could be further oxidized by HO[•] and/or SO₄^{•-} to yield nitroso-SMX (**P-267**) and nitro-SMX (**P-283**) [44]. In pathway **C**, hydroxylation of the benzene ring happened, and the direct addition of HO[•] to benzene ring of SMX formed hydroxylated SMX (**P-270**) [45]. The δ-cleavage of S-N bond on **P-270** led to formation of **P-189** and **P-98** [13].

Fig. 7. Proposed transformation pathways for SMX degradation in the HA/Fe(II)/PMS process.

However, considering the existence of SO₄^{•-} in the HA/Fe(II)/PMS system, to some extent, the degradation products of SMX could also be generated by the attack of SO₄^{•-} on the above-mentioned sites of SMX through electron-transfer mechanism [46]. Especially, as a preferred reactive site of SO₄^{•-}, the amino and imino moiety was easily to be oxidized by SO₄^{•-} and transformed as **P-189** [14] and **P-269** [23]. Ji et al. [13] and Yan et al. [47] also noted that SO₄^{•-} could result in the formation of

hydroxylated SMX.

3.6. Degradation of SMX in real pharmaceutical wastewater

To examine the oxidation efficiency of the HA/Fe(II)/PMS process in actual wastewater, experiments were performed with real pharmaceutical wastewater (the water quality is shown in Table S2). Fig. 8 shows the degradation of SMX in the wastewater sample by the HA/Fe(II)/PMS process. The process still exhibited good capacity to remove SMX and total organic carbon (TOC). Approximately 70% of SMX (Fig. 8) and 50% of TOC (Fig. S13) were removed within 15 min at PMS dosage of 2.0 mM and Fe(II) dosage of 20.6 μ M, respectively. The efficiency was comparable to that of Cobalt(II)/PMS [9] (Compiled in Table S1). Although the removal rates of SMX were reduced with the decreased dosage of PMS, the degradation of SMX almost finished within 4 min. The similar phenomenon was also reported in a previous study about the degradation of SMX in swine wastewater by Fenton process [11], and it was probably due to the fast generation of and attack from the reactive species (e.g., $\text{HO}^\bullet$ and $\text{SO}_4^{\bullet-}$) in the initial period of fast reaction.

Fig. 8. Effect of PMS concentration on the degradation of SMX in real pharmaceutical wastewater in the HA/Fe(II)/PMS process. Conditions: $[\text{HA}]_0 = 0.4 \text{ mM}$, $[\text{Fe(II)}]_0 = 20.6 \text{ }\mu\text{M}$, $[\text{PMS}]_0 = 0.3\sim 2.0 \text{ mM}$, $[\text{SMX}]_0 = 31.3 \text{ }\mu\text{M}$, $\text{pH} = 5.0$, $25 \text{ }^\circ\text{C}$. Error bars represent the standard deviation from the duplicate experiments.

Furthermore, compared with the Milli-Q water sample (Fig. S14), the coexisting water components in the wastewater sample inhibited approximately 7% of SMX degradation within 15min at PMS dosage of 0.3 mM and Fe(II) dosage of 20.6 μ M. Although a high concentration of

chloride (6.7 mM) was detected in the pharmaceutical wastewater, the degradation of SMX was hardly influenced by the chloride (Fig. S14). Therefore, the other coexisting components (especially organic contaminants) in the real wastewater could be responsible for the reduced SMX removal rate.

4. Engineering Implications

In the HA/Fe(II)/PMS process, the transformation of Fe(III) to Fe(II) was strongly promoted by HA, so that much lower amount of Fe was needed to achieve the high oxidation efficiency, e.g., several micromolar (μM) used to remove approximately 70% of SMX (Fig. 8) and 50% of TOC (Fig. S13) from actual wastewater at pH 5.0. Such a low concentration of Fe(II) could significantly alleviate the formation and accumulation of iron sludge (Fig. S15 and Fig. S16) in the presence of HA, which ensures the steady concentration of iron ion (Fig. S17). Although HA is a toxic compound, it could be transformed into N_2O , NO_2^- , NO_3^- and N_2 (Fig. S18) under ambient conditions. And residual HA could also be decomposed completely by oxygen or air catalyzed by transition metals at ambient temperature with environmentally benign by-products (nitrogen and water) [48,49]. Considering the efficient generation of powerful oxidants like $\text{HO}\cdot$ and the more selective oxidant like $\text{SO}_4^{\cdot-}$, the HA/Fe(II)/PMS process might be a promising process to remove antibiotics and refractory organic contaminants from wastewater.

5. Conclusions

The HA/Fe(II)/PMS process was adopted to degrade SMX and exhibited an effective degradation capacity. The enhanced degradation efficiency by the HA/Fe(II)/PMS process in a wider range of solution pH (3.0-6.0) was attributed to the enhancement of HA through accelerating the conversion from Fe(III) back to Fe(II). The optimum dosage of HA depended on the concentration of PMS and

pH, and the excess HA inhibited the SMX degradation by reacting with PMS and quenching the reactive species. The degradation of SMX was initiated by $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$, although $\text{HO}^{\cdot}$ played the dominant role. Eight intermediates of SMX were produced via the cleavage of S-N bond, oxidation of amine group on the aromatic ring and hydroxylation of the benzene ring in the system. The process also exhibited an effective removal of SMX and other coexisting organic pollutants (i.e., TOC) from the real pharmaceutical wastewater.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (21307057), the China Scholarship Council (201406685037), the Postdoctoral Science Foundation of Heilongjiang Province (LBH-Z13062), the Natural Science Foundation of Jiangsu Province (BK20130577, BK20140966), the Specialized Research Fund for the Doctoral Program of Higher Education of China (SRFDP, 20130091120014), the National Science Foundation of the Higher Education Institutions of Jiangsu Province of China (14KJB610006), and the Fundamental Research Funds for the Central Universities (20620140128). The authors sincerely thank Jingyun Fang, Jimin Shen, Jing Zou, Yahong Han, and Anting Wang for technical help and useful discussion of our work.

References

- [1] K. Kümmerer, Antibiotics in the aquatic environment - A review - Part I, *Chemosphere* 75 (2009) 417-434.
- [2] C. Marx, V. Mühlbauer, P. Krebs, V. Kuehn, Environmental risk assessment of antibiotics including synergistic and antagonistic combination effects, *Sci. Total Environ.* 524-525 (2015) 269-279.
- [3] D.G.J. Larsson, C. de Pedro, N. Paxeus, Effluents from drug manufactures contains extremely high levels of pharmaceuticals, *J. Hazard. Mater.* 148 (2007) 751-755.

- 394 [4] I. Michael, L. Rizzo, C.S. McArdell, C.M. Manaia, C. Merlin, T. Schwartz, C. Dagot, D. Fatta-Kassinos,
395 Urban wastewater treatment plants as hotspots for the release of antibiotics in the environment: A review,
396 Water Res. 47 (2013) 957-995.
- 397 [5] A.G. Gonçalves, J.J.M. Órfão, M.F.R. Pereira, Catalytic ozonation of sulphamethoxazole in the presence of
398 carbon materials: Catalytic performance and reaction pathways, J. Hazard. Mater. 239-240 (2012) 167-174.
- 399 [6] C.C. Ryan, D.T. Tan, W.A. Arnold, Direct and indirect photolysis of sulfamethoxazole and trimethoprim in
400 wastewater treatment plant effluent, Water Res. 45 (2011) 1280-1286.
- 401 [7] P. Neta, R.E. Huie, A.B. Ross, Rate constants for reactions of inorganic radicals in aqueous solution, J. Phys.
402 Chem. Ref. Data. 17 (1988) 1027-1284.
- 403 [8] G.V. Buxton, C.L. Greenstock, W.P. Helman, A.B. Ross, Critical-review of rate constants for reactions of
404 hydrated electrons, hydrogen-atoms and hydroxyl radicals ($\bullet\text{OH}/\bullet\text{O}^-$) in aqueous solution, J. Phys. Chem. Ref.
405 Data. 17 (1988) 513-886.
- 406 [9] M.M. Ahmed, S. Barbati, P. Doumenq, S. Chiron, Sulfate radical anion oxidation of diclofenac and
407 sulfamethoxazole for water decontamination, Chem. Eng. J. 197 (2012) 440-447.
- 408 [10] M.M. Ahmed, M. Brienza, V. Goetz, S. Chiron, Solar photo-Fenton using peroxymonosulfate for organic
409 micropollutants removal from domestic wastewater: Comparison with heterogeneous TiO_2 photocatalysis,
410 Chemosphere 117 (2014) 256-261.
- 411 [11] W. Ben, Z. Qiang, X. Pan, M. Chen, Removal of veterinary antibiotics from sequencing batch reactor (SBR)
412 pretreated swine wastewater by Fenton's reagent, Water Res. 43 (2009) 4392-4402.
- 413 [12] Y. Ji, C. Ferronato, A. Salvador, X. Yang, J. Chovelon, Degradation of ciprofloxacin and sulfamethoxazole by
414 ferrous-activated persulfate: Implications for remediation of groundwater contaminated by antibiotics, Sci.

415 Total Environ. 472 (2014) 800-808.

416 [13] Y. Ji, Y. Fan, K. Liu, D. Kong, J. Lu, Thermo activated persulfate oxidation of antibiotic sulfamethoxazole
 417 and structurally related compounds, Water Res. 87 (2015) 1-9.

418 [14] C. Qi, X. Liu, C. Lin, X. Zhang, J. Ma, H. Tan, W. Ye, Degradation of sulfamethoxazole by
 419 microwave-activated persulfate: Kinetics, mechanism and acute toxicity, Chem. Eng. J. 249 (2014) 6-14.

420 [15] Y. Zhou, J. Jiang, Y. Gao, J. Ma, S. Pang, J. Li, X. Lu, L. Yuan, Activation of peroxymonosulfate by
 421 benzoquinone: A novel nonradical oxidation process, Environ. Sci. Technol. 49 (2015) 12941-12950.

422 [16] A. Ghauch, G. Ayoub, S. Naim, Degradation of sulfamethoxazole by persulfate assisted micrometric Fe^0 in
 423 aqueous solution, Chem. Eng. J. 228 (2013) 1168-1181.

424 [17] G.P. Anipsitakis, D.D. Dionysiou, Degradation of organic contaminants in water with sulfate radicals
 425 generated by the conjunction of peroxymonosulfate with cobalt, Environ. Sci. Technol. 37 (2003) 4790-4797.

426 [18] J. Zou, J. Ma, L. Chen, X. Li, Y. Guan, P. Xie, C. Pan, Rapid acceleration of ferrous iron/peroxymonosulfate
 427 oxidation of organic pollutants by promoting Fe(III)/Fe(II) cycle with hydroxylamine, Environ. Sci. Technol.
 428 47 (2013) 11685-11691.

429 [19] L. Chen, J. Ma, X. Li, J. Zhang, J. Fang, Y. Guan, P. Xie, Strong Enhancement on fenton oxidation by
 430 addition of hydroxylamine to accelerate the ferric and ferrous iron cycles, Environ. Sci. Technol. 45 (2011)
 431 3925-3930.

432 [20] C. Tan, N. Gao, W. Chu, C. Li, M.R. Templeton, Degradation of diuron by persulfate activated with ferrous
 433 ion, Sep. Purif. Technol. 95 (2012) 44-48.

434 [21] X. Wu, X. Gu, S. Lu, Z. Qiu, Q. Sui, X. Zang, Z. Miao, M. Xu, Strong enhancement of trichloroethylene
 435 degradation in ferrous ion activated persulfate system by promoting ferric and ferrous ion cycles with

hydroxylamine, Sep. Purif. Technol. 147 (2015) 186-193.

[22] D. Han, J. Wan, Y. Ma, Y. Wang, M. Huang, Y. Chen, D. Li, Z. Guan, Y. Li, Enhanced decolorization of Orange G in a Fe(II)-EDDS activated persulfate process by accelerating the regeneration of ferrous iron with hydroxylamine, Chem. Eng. J. 256 (2014) 316-323.

[23] Y. Gao, N. Gao, Y. Deng, D. Yin, Y. Zhang, W. Rong, S. Zhou, Heat-activated persulfate oxidation of sulfamethoxazole in water, Desalin. Water Treat. 56 (2015) 2225-2233.

[24] M. Al Aukidy, P. Verlicchi, A. Jelic, M. Petrovic, D. Barcelò, Monitoring release of pharmaceutical compounds: Occurrence and environmental risk assessment of two WWTP effluents and their receiving bodies in the Po Valley, Italy, Sci. Total Environ. 438 (2012) 15-25.

[25] K. Scharf, Spectrophotometric measurement of ferric ion concentration in the ferrous sulphate (Fricke) dosimeter, Phys. Med. Biol. 16 (1971) 77-86.

[26] S. X. Peng, M. J. Strojnowski, J. K. Hu, B. J. Smith, T. H. Eichhold, K. R. Wehmeyer, S. Pikul, N. G. Almstead, Gas chromatographic-mass spectrometric analysis of hydroxylamine for monitoring the metabolic hydrolysis of metalloprotease inhibitors in rat and human liver microsomes, J. Chromatogr. B. 724 (1999) 181-187.

[27] L. Chen, X. Li, J. Zhang, J. Fang, Y. Huang, P. Wang, J. Ma, Production of hydroxyl radical via the activation of hydrogen peroxide by hydroxylamine, Environ. Sci. Technol. 49(2015) 10373-10379.

[28] G.P. Anipsitakis, D.D. Dionysiou, Radical generation by the interaction of transition metals with common oxidants, Environ. Sci. Technol. 38 (2004) 3705-3712.

[29] C.F. Wells, M.A. Salam, The effect of pH on the kinetics of the reaction of iron (II) with hydrogen peroxide in perchlorate media, J. Chem. Soc. A. (1968) 24-29.

- 457 [30] A. Stefánsson, Iron (III) hydrolysis and solubility at 25 °C, *Environ. Sci. Technol.* 41 (2007) 6117-6123.
- 458 [31] D.L. Ball, J.O. Edwards, The kinetics and mechanism of the decomposition of Caro's acid, *J. Am. Chem. Soc.*
- 459 78 (1956) 1125-1129.
- 460 [32] M.N. Hughes, H.G. Nicklin, K. Shrimanker, Autoxidation of hydroxylamine in alkaline solutions. Part II.
- 461 Kinetics. The acid dissociation constant of hydroxylamine, *J. Chem. Soc. A.* (1971) 3485-3487.
- 462 [33] R. Zhang, P. Sun, T.H. Boyer, L. Zhao, C. Huang, Degradation of pharmaceuticals and metabolite in synthetic
- 463 human urine by UV, UV/H₂O₂, and UV/PDS, *Environ. Sci. Technol.* 49 (2015) 3056-3066.
- 464 [34] C. Brandt, R. Van Eldik, Transition metal-catalyzed oxidation of sulfur(IV) oxides. Atmospheric-relevant
- 465 processes and mechanisms, *Chem. Rev.* 95 (1995) 119-190.
- 466 [35] E. Hayon, A. Treinin, J. Wilf, Electronic spectra, photochemistry, and autoxidation mechanism of the
- 467 sulfite-bisulfite-pyrosulfite systems. SO₂⁻, SO₃⁻, SO₄⁻, and SO₅⁻ radicals, *J. Am. Chem. Soc.* 94 (1972) 47-57.
- 468 [36] G.W. Klein, K. Bhatia, V. Madhavan, R.H. Schuler, Reaction of •OH with benzoic acid. Isomer distribution in
- 469 the radical intermediates, *J. Phys. Chem.* 79 (1975) 1767-1774.
- 470 [37] X. Zhou, K. Mopper, Determination of photochemically produced hydroxyl radicals in seawater and
- 471 freshwater, *Mar. Chem.* 30 (1990) 71-88.
- 472 [38] C.K. Duysterberg, T.D. Waite, Kinetic modeling of the oxidation of p-Hydroxybenzoic acid by Fenton's
- 473 reagent: Implications of the role of quinones in the redox cycling of iron, *Environ. Sci. Technol.* 41 (2007)
- 474 4103-4110.
- 475 [39] M.M. Gómez-Ramos, M. Mezcua, A. Agüera, A.R. Fernández-Alba, S. Gonzalo, A. Rodríguez, R. Rosal,
- 476 Chemical and toxicological evolution of the antibiotic sulfamethoxazole under ozone treatment in water
- 477 solution, *J. Hazard. Mater.* 192 (2011) 18-25.

- 478 [40] S. Gao, Z. Zhao, Y. Xu, J. Tian, H. Qi, W. Lin, F. Cui, Oxidation of sulfamethoxazole (SMX) by chlorine,
479 ozone and permanganate - A comparative study, *J. Hazard. Mater.* 274 (2014) 258-269.
- 480 [41] M.N. Abellán, W. Gebhardt, H.Fr. Schröder, Detection and identification of degradation products of
481 sulfamethoxazole by means of LC/MS and $-MS^n$ after ozone treatment, *Water Sci. Technol.* 58 (2008)
482 1803-1812.
- 483 [42] T. An, Y. Gao, G. Li, P.V. Kamat, J. Peller, M.V. Joyce, Kinetics and mechanism of $(\bullet)\text{OH}$ mediated
484 degradation of dimethyl phthalate in aqueous solution: experimental and theoretical studies, *Environ. Sci.*
485 *Technol.* 48 (2014) 641-648.
- 486 [43] A. Dirany, I. Sirés, N. Oturan, A. Özcan, M.A. Oturan, Electrochemical treatment of the antibiotic
487 sulfachloropyridazine: Kinetics, reaction pathways, and toxicity evolution, *Environ. Sci. Technol.* 46 (2012)
488 4074-4082.
- 489 [44] C. Kim, V.R. Panditi, P.R. Gardinali, R.S. Varma, H. Kim, V.K. Sharma, Ferrate promoted oxidative cleavage
490 of sulfonamides: Kinetics and product formation under acidic conditions, *Chem. Eng. J.* 279 (2015) 307-316.
- 491 [45] L. Hu, P.M. Flanders, P.L. Miller, T.J. Strathmann, Oxidation of sulfamethoxazole and related antimicrobial
492 agents by TiO_2 photocatalysis, *Water Res.* 41 (2007) 2612-2626.
- 493 [46] P. Neta, V. Madhavan, H. Zemel, R.W. Fessenden, Rate constants and mechanism of reaction of sulfate radical
494 anion with aromatic compounds, *J. Am. Chem. Soc.* 99 (1977) 163-164.
- 495 [47] J. Yan, M. Lei, L. Zhu, M.N. Anjum, J. Zou, H. Tang, Degradation of sulfamonomethoxine with
496 Fe_3O_4 magnetic nanoparticles as heterogeneous activator of persulfate, *J. Hazard. Mater.* 186 (2011)
497 1398-1404.
- 498 [48] E. Gomez, J.M. Estela, V. Cerda, Thermometric determination of Cu^{II} based on its catalytic effect on the

499 oxidation of hydroxylamine by dissolved oxygen, *Thermochim. Acta.* 165 (1990) 255-260.

500 [49] W. Song, J. Li, J. Liu, W. Shen, Production of hydrogen peroxide by the reaction of hydroxylamine and

501 molecular oxygen over activated carbons, *Catal Commu.* 9 (2008) 831-836.

502

503

504

505

506

507

508

509

510

511

512

513

514

515

516

517

518

519

520 **Figure captions**

521 **Fig. 1.** Degradation of SMX in the HA/Fe(II)/PMS process.

522 **Fig. 2.** Effect of initial pH on SMX degradation in the HA/Fe(II)/PMS process.

523 **Fig. 3.** Effect of HA concentration on SMX degradation in the HA/Fe(II)/PMS Process.

524 **Fig. 4.** Effect of HA on Fe(III) concentration in the HA/Fe(II)/PMS process.

525 **Fig. 5.** Inhibition effect of radical scavengers on SMX degradation in the HA/Fe(II)/PMS process.

526 **Fig. 6.** Competition kinetics between SMX and BA with reactive species in the HA/Fe(II)/PMS
527 process.

528 **Fig. 7.** Proposed transformation pathways for SMX degradation in the HA/Fe(II)/PMS process.

529 **Fig. 8.** Effect of PMS concentration on the degradation of SMX in real pharmaceutical wastewater in
530 the HA/Fe(II)/PMS process.

531

532

533

534

535

536

537

538

539

540

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

Fig. 6

Fig. 7

Fig. 8