Comparison of metoprolol degradation by Fe^{III}-NTA modified Fenton-like reaction in the absence and presence of manganese: Efficiency and intermediates

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[a] K L   w R   H   R   ⚡   E   P   C   , M   E   , H   K   L   E   P   C   ,
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[b]   K   L   G   C   E   ,   C   E   E   , C   C   , C   E   M   ,
     w   ,   , J   215123, PR C

HIGHLIGHTS

- Metoprolol degradation by Fe^{III}-NTA/H$_2$O$_2$ was enhanced in the presence of Mn^{II}.
- Rapid degradation of metoprolol was obtained by Fe^{III}-NTA/H$_2$O$_2$-Mn at pH 4.0–8.0.
- Fe^{III}-NTA/H$_2$O$_2$-Mn led to more efficient degradation of metoprolol and intermediates.
- Degradation pathways of metoprolol were proposed.

GRAPHICAL ABSTRACT
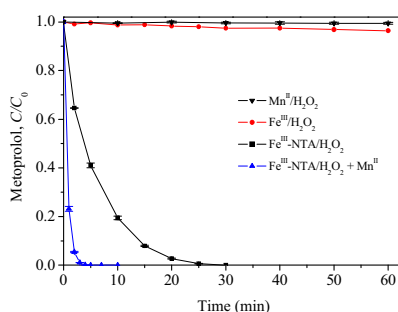
ABSTRACT

The degradation of metoprolol in aqueous solutions by traditional Fenton-like reaction (Fe^{III}/H$_2$O$_2$), and Fe^{III}-NTA modified Fenton-like reaction (Fe^{III}-NTA/H$_2$O$_2$) in the absence and presence of Mn^{II} (Fe^{III}-NTA/H$_2$O$_2$-Mn) have been investigated. The results show that Fe^{III}-NTA/H$_2$O$_2$ is able to degrade metoprolol at initial neutral pH. In particular, the presence of Mn^{II} greatly improved the degradation rate of metoprolol by Fe^{III}-NTA/H$_2$O$_2$ over a wide pH range of 4.0–8.0. Under the same conditions, the degradation rate constants of metoprolol ( ) obtained in Fe^{III}-NTA/H$_2$O$_2$-Mn system were typically 7–9-fold larger than those obtained in Fe^{III}-NTA/H$_2$O$_2$ system. The involved reactions in Fe^{III}-NTA/H$_2$O$_2$-Mn system were proposed on the basis of important parameters analysis including ferrous ion concentration, dissolved oxygen (DO) concentration, and the quenching experiments for hydroxyl radial (HO·) and superoxide anion radical (O$_2^-$). Several intermediates have been identified by mass spectrometry. Our results suggest that the degradation of metoprolol in both Fe^{III}-NTA/H$_2$O$_2$ and Fe^{III}-NTA/H$_2$O$_2$-Mn systems were caused by HO· attack. The degradation pathways of metoprolol were proposed on the basis of the identified intermediates. Fe^{III}-NTA/H$_2$O$_2$-Mn system led to more efficient degradation of metoprolol and its intermediates.

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1.

Metoprolol, a selective β1 receptor blocking drug, is widely used in the therapy of hypertension and angina. In the past decade, metoprolol and its metabolites have been detected in sewage treatment plant effluents, surface water, groundwater, and even

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in drinking water, which pose a potential risk to human health [1,2]. The degradation rate of metoprolol in water by the direct photolysis is small, e.g., the extrapolated half-lives of metoprolol in central Europe and the U.S. were reported at 28–95 d in summer and 190–449 d in winter [3]. Thus, metoprolol is most likely to be pseudo-persistent in natural waters if do not consider the indirect photolysis effects. In addition, the efficiency of metoprolol removal is lower than 30% in traditional sewage treatment plant [4]. There is an urgent need to improve the removal efficiencies of pharmaceuticals in water.

A far more effective method is the so-called advanced oxidation processes (AOPs), involving the generation of hydroxyl radical (HO·) [5–7], have been widely applied in water treatment for harmful organic compounds removal. Efficient degradation of metoprolol has been obtained by photocatalysis, UV/H_2O_2 and Fenton-related processes [8–10]. Two decades ago, research by Sun and Pignatello [11] showed the successful degradation of 2,4-dichlorophen-oxyacetic acid at pH 6.0 by chelates modified Fenton-like reaction. Chelating agents modified Fenton-like reaction has been receiving increasing attention because it can work at neutral pH conditions, which overcomes the limitation of acidic pH (e.g., optimal pH 2.8–3.0) by using traditional Fenton and/or Fenton-like reaction. S,S-ethylenediamine-N,N′-disuccinic acid (EDDS) modified Fenton reaction (i.e., Fe^{II}-EDDS/H_2O_2) and Fenton-like reaction (i.e., Fe^{III}-EDDS/H_2O_2) are capable of degrading 4-chlorophenol, bisphenol A, naphthenic acid, and 4-tert-butylphenol at near neutral or basic pH conditions [12–15]. The use of Fe^{III}-EDDS for photo-Fenton reaction at neutral pH is also successful in degrading micro-pollutants in wastewater treatment plant effluents [16–18]. In addition, nitrilotriacetic acid (NTA) and ethylenediaminetetraacetic acid (EDTA) modified Fenton-like reactions (i.e., Fe^{III}-NTA/H_2O_2 and Fe^{III}-EDTA/H_2O_2) have also been proved to be highly effective in degrading atrazine, carbamazepine, fenuron, naphthenic acid, parachlorobenzoic acid and sulfamethoxazole at neutral or slightly basic pH conditions [19–22]. In particular, our recent finding suggested that the presence of manganese (Mn^{II}) could greatly enhance the Fenton-like catalytic activity of Fe^{III}-NTA/H_2O_2 [23]. The potential mechanism may involve an enhanced generation of superoxide anion radical ($O_2^{·-}$) by the Mn^{II}, which can accelerate the reduction of Fe^{III}-NTA to Fe^{II}-NTA and indirectly improve the generation of HO· [23]. The Mn^{II}/Fe^{III}-NTA catalytic system would be very promising since Fe^{III} and Mn^{II} are quite ubiquitous in the environment and can be used as natural Fenton-like catalyst in the presence of NTA (or natural Fe^{III} complexing agents) and H_2O_2. However, little research on this system has been reported.

The purpose of this study is to demonstrate the potential effectiveness of Fe^{III}-NTA/H_2O_2-Mn for water treatment. In the present study, we choose metoprolol as a target compound, to evaluate the efficiency and intermediates generated from metoprolol degradation by Fe^{III}-NTA/H_2O_2 in the absence and presence of Mn^{II}. The degradation kinetics of metoprolol in both systems were compared under various conditions. The involved reactions in Fe^{III}-NTA/H_2O_2-Mn system were proposed on the basis of certain important parameters analysis such as ferrous ion concentration, dissolved oxygen (DO) concentration, and the quenching experiments for HO· and $O_2^{·-}$. The intermediates were identified by liquid chromatography/mass spectrometry.

2.

2.1. C

Ferric chloride hexahydrate, hydrogen peroxide (30% H_2O_2, w/w), sodium hydroxide and sulfuric acid were purchased from Sino-pharm Chemical Reagent Co., Ltd. Metoprolol tartrate (purity ≥ 98%) was purchased from LKT Laboratories, Inc. NTA was purchased from Acros Organics. Formic acid and manganese nitrate tetrahydrate were purchased from Sigma-Aldrich. HPLC-grade methanol, 2-propanol and water were purchased from Fisher Scientific. Chloroform was purchased from Chinasun Specialty Products Co., Ltd. All chemicals were of reagent grade or better, and used as received without further purification. Milli-Q water was used to prepare solutions.

2.2. E

All experiments were performed in 125 ml glass Erlenmeyer flasks. Briefly, 100 ml of metoprolol aqueous solution and an appropriate amount of freshly prepared Fe^{III}-NTA solution were added into the flask. The flask was then placed in a water-jacketed glass vessel water bath (25 ± 1 °C) under a magnetic stirring condition. After that, an appropriate amount of Mn^{II} was added to the solution. The pH of the solution was then adjusted to the desired value using 1.0/0.1 M NaOH or 1.0/0.1 M H_2SO_4. Finally, Fenton-like reaction was started by the addition of an appropriate amount of H_2O_2. It is worth noting that the water-jacketed glass vessel was covered with aluminum foil to prevent the effect of light on the Fenton-like reaction. Samples (1 ml) were withdrawn at different time intervals and mixed with 0.1 ml of methanol immediately to quench the reaction.

2.3. A

The concentration of metoprolol was determined by a high performance liquid chromatography (HPLC, Agilent 1100) with fluorescence detection. An Ultra C-18 column (5 μm, 250 × 4.6 mm) was used for the chromatographic separation. The mobile phase consisted of methanol and 0.1% formic acid aqueous solution (35:65, v/v) at a flow rate of 0.9 ml min^{-1}. The column temperature was 30 °C. The injection volume was 20 μl, and the fluorescence detection was performed at 275 nm of excitation and 298 nm of emission.

The degradation intermediates were identified by an Agilent 1200 HPLC system coupled to a 6130 quadrupole mass spectrometer. The MS detector was performed for a full scan range of / 30–600 under an ESI + APCI positive mode. The MS operating conditions were as follows: Fragmentor 90, drying gas flow rate 6 L min^{-1}, nebulizer pressure 45 psi, dry gas temperature 300 °C, vaporizer temperature 250 °C, capillary voltage 3500 V, corona current 4.0 μA and charging voltage 2000 V.

The concentration of ferrous ion in the aqueous solutions was determined by using the 1,10-phenathroline method. The concentration of H_2O_2 was determined by the iodide method [24]. The dissolved oxygen (DO) concentration in the aqueous solutions during the reaction time was monitored by a dO_2 sensor (Model Z010023525, AppliSens).

3.

3.1. C F^{III}/H_2O_2, F^{III}-N A/ H_2O_2 F^{III}-N A/H_2O_2-M

Fig. 1 shows a comparison of metoprolol degradation by Fe^{III}/ H_2O_2, Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems at initial neutral pH. A minimum degradation of metoprolol was observed in Fe^{III}/H_2O_2 system, with 3.61% degradation efficiency of metoprolol after 60 min of the reaction time. This result was expected because of the precipitation of ferric ion at pH 7.0 in the absence of chelator. In contrast, Fe^{III}-NTA complex is able to catalyze

Fenton-like reaction at pH 7.0, resulted in 100% degradation efficiency of metoprolol after 30 min of the reaction time in Fe^{III}-NTA/H_2O_2 system. In particular, Fe^{III}-NTA/H_2O_2-Mn system led to a very fast degradation of metoprolol, with 100% degradation efficiency of metoprolol after 7 min of the reaction time. The result is consistent with our recent finding that the presence of Mn^{II} could enhance Fe^{III}-NTA-catalyzed Fenton-like reaction [23].

The effects of Mn^{II} concentration on the degradation kinetics of metoprolol in Fe^{III}-NTA/H_2O_2-Mn system were shown in Fig. 2. An increase in Mn^{II} concentration from 0.01 to 0.1 mM, corresponding to Mn:Fe molar ratios of 0.1:1 to 1:1, had a positive effect on metoprolol degradation. The apparent degradation rate constant of metoprolol ( ) increased from 0.7547 to 1.6048 min^{-1}. However, further increasing Mn^{II} concentration from 0.2 to 1.0 mM led to a slight inhibitory effect on the degradation rate of metoprolol, e.g., the   value of metoprolol decreased from 1.6289 to 1.1103 min^{-1}. This is because when Mn^{II} concentration was larger than 0.2 mM, hydrous manganese dioxide could form from free Mn^{II} in excess

from the reaction of Fe^{III}-NTA with H_2O_2 in Fe^{III}-NTA/H_2O_2 system (i.e., R7), thus the generation rate of Fe^{II}-NTA in Fe^{III}-NTA/H_2O_2 system is much slower than that in Fe^{III}-NTA/H_2O_2-Mn system.

$$Mn^{II}\text{-NTA} + 2H_2O_2 \leftrightarrow Mn^{II}\text{-NTA-}2H_2O_2 \qquad \text{(R1)}$$

$$Mn^{II}\text{-NTA-}2H_2O_2 \rightarrow Mn^{III}\text{-NTA-}H_2O_2\text{-HO}^{\cdot} + OH^{-} \qquad \text{(R2)}$$

$$Mn^{III}\text{-NTA-}H_2O_2\text{-HO}^{\cdot} \rightarrow Mn^{III}\text{-NTA} +$$
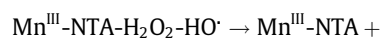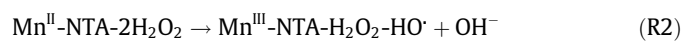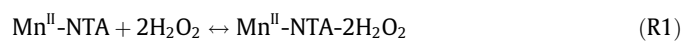
the range of NTA:Fe molar ratios tested, the values of metoprolol in Fe^{III}-NTA/H_2O_2-Mn system were 7–17-fold larger than those in Fe^{III}-NTA/H_2O_2 system. An increase in NTA/Fe molar ratio from 0.5:1 to 2:1 had positive effects on the degradation rates of metoprolol in both Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems. The values of metoprolol increased from 0.0311 to 0.1754 min^{-1} in Fe^{III}-NTA/H_2O_2 system and increased from 0.3450 to 1.6048 min^{-1} in Fe^{III}-NTA/H_2O_2-Mn system, respectively. When NTA/Fe molar ratio was larger than 2:1, however, a slight decrease in the values of metoprolol was observed in either Fe^{III}-NTA/H_2O_2 or Fe^{III}-NTA/H_2O_2-Mn system. This can be explained by the fact that the free NTA in excess scavenges HO·. Although the reaction rate constant of metoprolol with HO· ($5.2–8.4 \times 10^9$ M^{-1} s^{-1}) [32,33] is larger than that of Fe^{III}-NTA/free NTA with HO·, it is believed that the competitive consumption of HO· by the free NTA in excess can slightly limit the degradation of metoprolol.

3.4. E H_2O_2:F^{III}

Fig. 6 shows the effects of H_2O_2/Fe^{III} molar ratios on the degradation kinetics of metoprolol by Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems at initial neutral pH. Without the addition of H_2O_2, no degradation of metoprolol was observed in both systems. Over the range of H_2O_2/Fe^{III} molar ratios tested, the values of metoprolol in Fe^{III}-NTA/H_2O_2-Mn system were 5–9-fold larger than those in Fe^{III}-NTA/H_2O_2 system. With increasing H_2O_2/Fe^{III} molar ratio from 10:1 to 200:1, the values of metoprolol continuously increased from 0.0598 to 0.2276 min^{-1} in Fe^{III}-NTA/H_2O_2 system. In Fe^{III}-NTA/H_2O_2-Mn system, the values of metoprolol increased greatly from 0.3384 to 1.6048 min^{-1} and reached a plateau with increasing H_2O_2/Fe^{III} molar ratio from 10:1 to 100:1. It is expected that the use of higher molar ratio of H_2O_2/Fe^{III} led to higher rate of HO· generation, by which faster degradation of metoprolol could be obtained. No inhibitory effect of H_2O_2 on the degradation kinetics of metoprolol was observed even at H_2O_2/Fe^{III} molar ratio of 200:1. This is because the reaction rate constant of H_2O_2 with HO· (($1.2–4.5) \times 10^7$ M^{-1} s^{-1}) [34] is much smaller than those of metoprolol, Fe^{III}-NTA and free NTA with HO·.

3.5. E F^{III}

Fe^{III} acts as the catalyst to initiate Fenton-like reaction, a high rate of HO· generation might be obtained at high concentration of Fe^{III}-NTA. The effects of Fe^{III} dosages on the degradation kinetics of metoprolol by Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems at
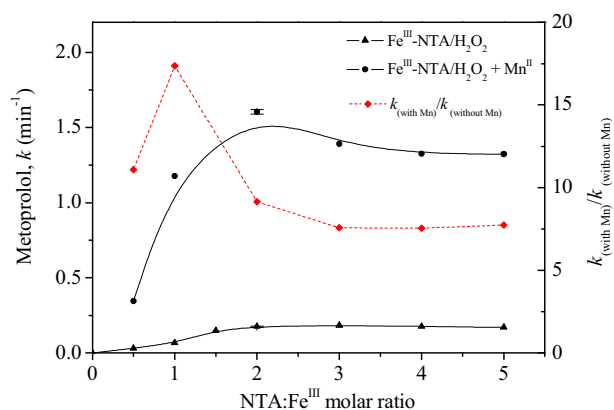

. . Effects of H_2O_2/Fe^{III} molar ratios on the degradation kinetics of metoprolol by Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems. Experimental conditions: 29.2 µM of metoprolol, 0.1 mM of Fe^{III}, NTA/Fe^{III} molar ratio of 2:1, H_2O_2/Fe^{III} molar ratio of 5:1–200:1, Mn^{II}/Fe^{III} molar ratio of 1:1, and initial pH of 7.0.
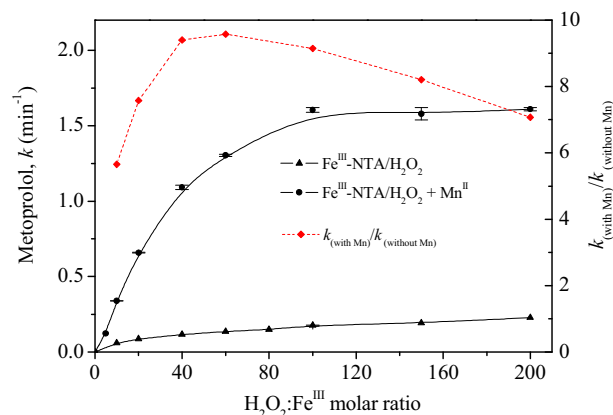

. . Effects of Fe^{III} dosages on the degradation kinetics of metoprolol by Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems. Experimental conditions: 29.2 µM of metoprolol, 0.01–0.15 mM of Fe^{III}, NTA/Fe^{III} molar ratio of 2:1, H_2O_2/Fe^{III} molar ratio of 100:1, Mn^{II}/Fe^{III} molar ratio of 1:1, and initial pH of 7.0.
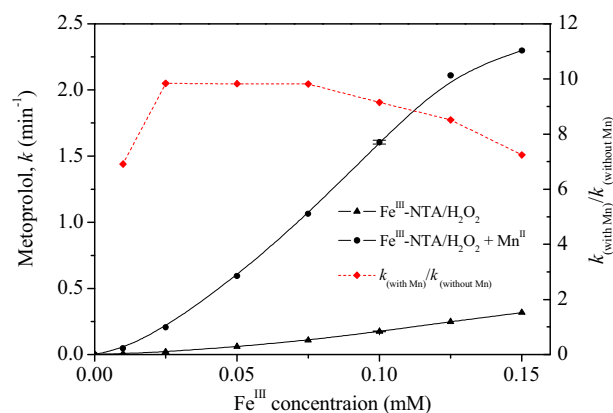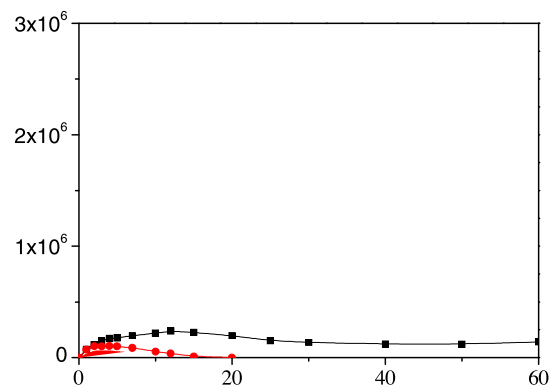

. . Effects of NTA/Fe^{III} molar ratios on the degradation kinetics of metoprolol by Fe^{III}-NTA/H_2O_2 and Fe^{III}-NTA/H_2O_2-Mn systems. Experimental conditions: 29.2 µM of metoprolol, 0.1 mM of Fe^{III}, NTA/Fe^{III} molar ratio of 0.5:1–5:1, H_2O_2/Fe^{III} molar ratio of 100:1, Mn^{II}/Fe^{III} molar ratio of 1:1, and initial pH of 7.0.

initial neutral pH were shown in Fig. 7. No degradation of metoprolol was observed in the absence of Fe^{III}, which suggests that HO· is generated from the Fenton-like reaction of $Fe^{III/II}$-NTA/H_2O_2. Over

the range of Fe^{III} concentrations tested, the values of metoprolol in Fe^{III}-NTA/H$_2$O$_2$-Mn system were 7–9-fold larger than that in Fe^{III}-NTA/H$_2$O$_2$ system. An increase in Fe^{III} concentrations from 0 to 0.15 mM has positive effects on the degradation rate of metoprolol in both systems. The values of metoprolol increased from 0 to 0.3174 min^{-1} in Fe^{III}-NTA/H$_2$O$_2$ system and to 2.2988 min^{-1} in Fe^{III}-NTA/H$_2$O$_2$-Mn system, respectively. The results indicate that the rate of HO$^{\cdot}$

Fe^{III}-NTA would increase the generation rate of Fe^{II}-NTA (R5) and (R7), which in turn reacts with H$_2$O$_2$

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