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Advanced oxidation of amoxicillin by Fenton's reagent treatment

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ABSTRACT

Advanced oxidation of amoxicillin was realized in aqueous solution by using Fenton's reagent treatment. Box–Behnken statistical experiment design was used to determine the effects of reagent concentrations on amoxicillin degradation and mineralization. Amoxicillin (10–200 mg L^{-1}), hydrogen peroxide (10–500 mg L^{-1}) and Fe(II) (0–50 mg L^{-1}) concentrations were considered as independent variables in batch oxidation experiments. Percent amoxicillin and total organic carbon (TOC) removals (mineralization) were considered as the objective functions to be maximized. Required reaction times were 2.5 min and 15 min, respectively for degradation and mineralization of amoxicillin. Both peroxide and amoxicillin concentrations affected the extent of amoxicillin degradation and mineralization. Complete amoxicillin degradation was obtained within 2.5 min while 37% mineralization took place within 15 min. The optimum peroxide/Fe/amoxicillin ratio resulting in complete amoxicillin degradation and 37% mineralization was 255/25/105 mg L^{-1}.

1. Introduction

Human and veterinary drugs represent more than 10,000 specialized products and are the main sources of pharmaceutical contamination in natural water systems [1–6]. Presence of antibiotics in aquatic environment constitutes a major environmental pollution. The emerging pollution issue in aquatic environment caused by pharmaceutically active compounds (PhACs) has been reported by Heberer [4]. Amoxicillin is one of the widely used human and veterinary medicine of environmental concern. Amoxicillin is a semi-synthetic penicilin with a beta-lactam ring inhibiting synthesis of bacterial cell wall [7].

Fenton's reagent consisting of H_2O_2 and Fe(II) is one of the most effective advanced oxidation agent used for degradation of recalcitrant organic compounds. The following mechanism is accepted for the Fenton's reagent activity [8].

$$Fe(II) + H_2O_2 \rightarrow Fe(III) + OH^- + {}^{\bullet}OH \quad (1)$$

$$Fe(II) + {}^{\bullet}OH \rightarrow Fe(III) + OH^- \quad (2)$$

Due to the high oxidation potential (2.8 V) of hydroxyl radicals ($^{\bullet}OH$), Fenton's reagent has been commonly used for degradation of non-biodegradable chemicals after biological treatment [9,10]. Fenton's reagent may used to treat micropollution caused by residual pharmaceuticals in surface waters as well as industrial effluents.

A number of studies were reported in literature on advanced oxidation of various antibiotics. Ben et al. [11] investigated degradation of six selected antibiotics by Fenton's reagent and the optimum reagent ratio was found to be $[H_2O_2]/[Fe(II)] = 1.5/1$.

Oxidation by the Fenton's reagent was found quite effective in treatment of aqueous solution containing amoxicillin, ampicillin and cloxacillin. Complete degradation of the antibiotics occurred in 2 min at COD/H_2O_2/Fe(II) molar ratio 1/3/0.30 and pH 3 [12].

Relatively high COD and TOC removals were obtained with the Fenton's reagent (Fe(II)/H_2O_2) at pH 3 as compared with the Fenton-like reagent (Fe(III)/H_2O_2) treating amoxicillin containing aqueous solution. The highest percent TOC removal was obtained by the photo-Fenton oxidation. Aqueous phase amoxicillin was eliminated in 40 min by photo-Fenton oxidation at pH 3 and by alkaline ozonation at pH 11.5 [13].

Photodegradation of amoxicillin (AMX), bezafibrate (BZF) and paracetamol (PCT) in aqueous solutions by photo-Fenton oxidation was investigated under black-light and solar irradiation. Photo-Fenton treatment was successfully applied to degradation of AMX, BZF and PCT in sewage tretament plant effluents [14].

Rizzo et al. [15] investigated degradation and mineralization kinetics of antibiotics present in treated wastewater effluent containing amoxicillin (10 mg L^{-1}), carbamazepine (5 mg L^{-1}) and diclofenac (2.5 mg L^{-1}) using TiO_2 photocatalysis. A pseudo-first order kinetic model was found to be suitable [15].

Zero-valent iron powder (ZVI or Fe^0) and nano-particulate ZVI (nZVI) were used for complete removal of amoxicillin (AMX) and ampicillin (AMP). Kinetic studies indicated first-order decay with half-lives of about 60.3 ± 3.1 and 43.5 ± 2.1 min, respectively for ZVI treatment under oxic conditions [16].

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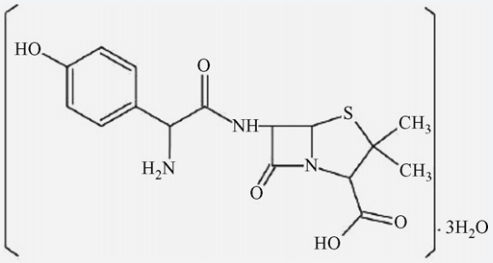
Table 1
Basic characteristics of amoxicilin trihydrate.

Name of the clinical form	Amoxicillin trihydrate
Molecular formula	$C_{16}H_{19}N_3O_5S{\cdot}3H_2O$
Chemical structure	
Molecular weight	419.408 g
Solubility	Slightly soluble in water and in methyl alcohol, and insoluble in carbon tetrachloride, chloroform, and in benzene

Solar photo-Fenton oxidation of sulfamethoxazole (SMX) was investigated by Trovó et al. [17] at pilot plant scale using distilled water (DW) and seawater (SW). Peroxide concentration was found to be more effective in degradation and mineralization of SMX as compared to Fe(II) [18].

Combined polyferric sulfate (PFS) coagulation, Fenton reagent treatment and sedimentation were used for treatment of antibiotic manufacturing wastewater. Nearly 66.6% of antibiotic and 72.4% of chemical oxygen demand (COD) were removed at PFS dosage of 200 mg L^{-1} and pH 4.0. Optimal peroxide and $FeSO_4$ concentrations for Fenton oxidation were 150 mg L^{-1} and 120 mg L^{-1}, respectively [19].

In the light of the literature studies, this study was designed to provide a systematic approach for degradation and mineralization of amoxicillin by the Fenton's reagent oxidation for a large range of reagent concentrations. Box–Behnken statistical experiment design approach was used by considering the amoxicillin, hydrogen peroxide and Fe(II) concentrations as independent variables while percent degradation and mineralization (TOC removal) of amoxicillin were the objective functions to be optimized. The optimal conditions maximizing amoxicillin degradation and mineralization were determined.

2. Materials and methods

2.1. Chemicals

Pure amoxicillin trihydrate was supplied by the Bilim Pharmaceuticals Co., Istanbul, Turkey. Some basic characteristics of amoxicillin trihydrate are summarized in Table 1. The oxidant hydrogen peroxide (35%, w/w, solution), the catalyst ferrous sulfate ($FeSO_4{\cdot}7H_2O$) and sulfuric acid (H_2SO_4) used for pH adjustments were all obtained from Merck. Concentrated stock solution of Fe(II) (5000 mg L^{-1}), stock solution of H_2O_2 (10,000 mg L^{-1}) and sulfuric acid solution (1N) were prepared to obtain desired concentrations by dilutions. Fe(II) stock solution was stored in the dark to prevent oxidation of Fe(II).

HPLC-grade acetonitrile, methanol and KH_2PO_4 (Merck) were used for HPLC analyses. Potassium phthalate solution was used for calibration in TOC measurements. Water used in all experiments was purified using a Mili-Q filtration system.

2.2. Experimental system

A jar test apparatus consisting of four 1 L beakers was used as the experimental system. The beakers were filled with 1 L of the amoxicillin solution and predetermined amounts of oxidant (H_2O_2) and catalyst (Fe(II)) were injected into the agitated reactor (185 rpm) at the beginning of each experiment. The iron salt was mixed well with aqueous amoxicillin solution before addition of hydrogen peroxide solution. The beakers were open to the atmosphere at room temperature (23–25 °C). Temperature changes during reactions were negligible. Initial pHs were adjusted to 3.5 since this was reported to be the most suitable pH for Fenton's reagent treatment [20].

2.3. Analytical methods

Samples (20 mL) were analyzed for TOC and antibiotic removal after filtration through 0.45 μm Millipore filter papers. Antibiotic analyses were carried out using Agilent 1100 Series High Performance Liquid Chromotograph (HPLC) equipped with a Prevail C18 Column (150 mm × 4.6 mm, 5 μm). The mobile phase was composed of acetonitril (40%) at pH 3, and 25 mM of KH_2PO_4 solution (60%) which was fed to HPLC with a flow rate of 1 mL min^{-1}. Under the specified conditions, amoxicillin retention time was 5.5 min. Amoxicillin solutions (0–500 mg L^{-1}) were used as calibration standards.

TOC analyses were carried out using a Teledyne Tekmar, Apollo 9000 Combustion TOC Analyzer. Potassium phthalate solution was used as calibration standard with the concentrations between 0 and 500 mg L^{-1}.

2.4. Design of experiments

Statistical experiment design and response surface methodology (RSM) are widely used methods to determine the effects of multiple variables on objective functions to be optimized [21,22]. Different types of RSM designs include 3-level factorial design, central composite design (CCD) [23,24], Box–Behnken design (BBD) [25] and D-optimal design [26]. Among all response surface methodology (RSM) designs, the Box–Behnken design requires fewer runs than the others [27]. Box–Behnken design is a spherical, revolving design consisting of a central point and the middle points of the edges of the cube circumscribed on the sphere [28]. The method has been applied for optimization of several chemical and physical processes [29]. The Box–Behnken design is a preferred response surface methodology because the method permits: (i) estimation of the parameters of the quadratic model; (ii) building of sequential designs and (iii) detection of lack of fit of the model [30].

The optimization procedure involves studying the response of the statistically designed experiments, estimating the coefficients by fitting the experimental data to the response functions, predicting the response of the fitted model, and checking the adequacy of the model [31]. Three independent variables varied at three levels were amoxicillin (X_1), hydrogen peroxide (X_2), and ferrous ion (X_3) concentrations.

Table 2
Comparison of the experimental and predicted results of Box–Behnken experimental design.

Run No.	Variables			Experimental percent removals		Predicted percent removals	
	Amoxicillin, X_1 (mg L^{-1})	H_2O_2, X_2 (mg L^{-1})	Fe(II), X_3 (mg L^{-1})	Amoxicillin removal (%)	TOC removal (%)	Amoxicillin removal (%)	TOC removal (%)
1	200	10	25	1.97	2.51	0	1.72
2	10	10	25	16.18	14.62	24.02	11.72
3	10	500	25	100	24.82	100	25.61
4	200	500	25	90	21.45	82.16	24.35
5	200	255	0	35	7	44.06	8.97
6	200	255	50	44.61	25.93	53.35	21.86
7	10	255	0	90	5	81.26	9.07
8	10	255	50	85	35	75.94	33.03
9	105	10	0	8.18	2.75	9.08	1.57
10	105	10	50	11.52	5	12.73	9.86
11	105	500	0	100	14.56	98.79	9.7
12	105	500	50	100	37.08	99.19	38.26
13	105	255	25	100	30	100	30
14	105	255	25	100	30	100	30
15	105	255	25	100	30	100	30

The experimental results were correlated with a second order polynomial as described below

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_{12}X_1X_2 + b_{13}X_1X_3 + b_{23}X_2X_3 + b_{11}X_1^2 + b_{22}X_2^2 + b_{33}X_3^2 \quad (3)$$

where Y is the predicted response; b_0 is model constant; X_1, X_2 and X_3 are independent variables; b_1, b_2 and b_3 are linear coefficients; b_{12}, b_{13} and b_{23} are interaction coefficients; and b_{11}, b_{22} and b_{33} are the quadratic coefficients. The quality of fit to the quadratic equation was expressed by the coefficient of determination R^2 [32]. A multiple regression analysis was carried out to obtain the coefficients of the response functions.

3. Results and discussion

In order to determine the required reaction time for maximum amoxicillin and TOC removals several experiments were performed. The results of the experiment at the central point of the Box–Behnken design (peroxide, 255 mg L^{-1}; Fe(II), 25 mg L^{-1}; amoxicillin, 105 mg L^{-1}; pH 3.5) indicated that amoxicillin degradation was completed within 2.5 min with formation of some intermediates. However, TOC removal or mineralization was completed after 15 min of reaction time. For this reason, the reaction time in all experiments was decided to be 15 min. The experimental conditions and results at the end of 15 min reaction time are presented in Table 2. The center point (0, 0, 0) was repeated three times and the nearly the same results were obtained indicating the reproducibility of the data.

The experimental results presented in Table 2 were correlated with the quadratic response functions and the coefficients were determined by regression analysis. A Stat-Ease Design Expert program was used for this purpose. Response functions for percent amoxicillin (Y_1) and TOC (Y_2) removals after 15 min of reaction time are presented in Eqs. (4) and (5) with the determined coefficients

$$Y_1 = 2.69 + 0.25X_1 + 0.42X_2 + 1.25X_3 + 4.52 \times 10^{-5}X_1X_2 + 1.536 \times 10^{-3}X_1X_3 - 1.363 \times 10^{-4}X_2X_3 - 2.17 \times 10^{-3}X_1^2 - 4.722 \times 10^{-4}X_2^2 - 0.0267X_3^2 \quad (R^2 = 0.98) \quad (4)$$

$$Y_2 = -3.327 + 0.10X_1 + 0.081X_2 + 0.79X_3 + 9.388 \times 10^{-5}X_1X_2 - 1.165 \times 10^{-3}X_1X_3 + 8.273 \times 10^{-4}X_2X_3 - 5.96 \times 10^{-4}X_1^2 - 1.46 \times 10^{-4}X_2^2 - 0.01X_3^2 \quad (R_2 = 0.97) \quad (5)$$

Eqs. (4) and (5) were used to predict percent amoxicillin and TOC removals at the experimental points. The observed and predicted amoxicillin and TOC removals are compared in Table 2.

Response function predictions are in good agreement with the experimental results. The analysis of variance (ANOVA) test was used to determine the goodness of the fit. The results of ANOVA test for percent amoxicillin removal are presented in Table 3. The Model F-value of 19.12 implies the model is significant. p-Values less than 0.10 indicate the model terms are significant. Peroxide and amoxicillin concentrations had significant effects on amoxicillin removal.

Table 3
ANOVA test for the response function Y_1 (% amoxicillin removal).

Source	Sum of squares	df	Mean square	F ratio	p-Value Prob > F
Model	22114.39	9	2457.15	19.12	0.0023
A-Antibiotic (mg/L)	1788.02	1	1788.02	13.92	0.0136
B-H_2O_2 (mg/L)	15501.20	1	15501.20	120.64	0.0001
C-Fe^{2+} (mg/L)	7.90	1	7.90	0.061	0.8140
AB	4.43	1	4.43	0.034	0.8600
AC	53.36	1	53.36	0.42	0.5477
BC	2.79	1	2.79	0.022	0.8886
A^2	1420.97	1	1420.97	11.06	0.0209
B^2	2966.54	1	2966.54	23.09	0.0049
C^2	1033.45	1	1033.45	8.04	0.0364
Residual	642.45	5	128.49		
Lack of fit	642.45	3	214.15		
Pure error	0.000	2	0.000		
Cor total	22756.84	14			

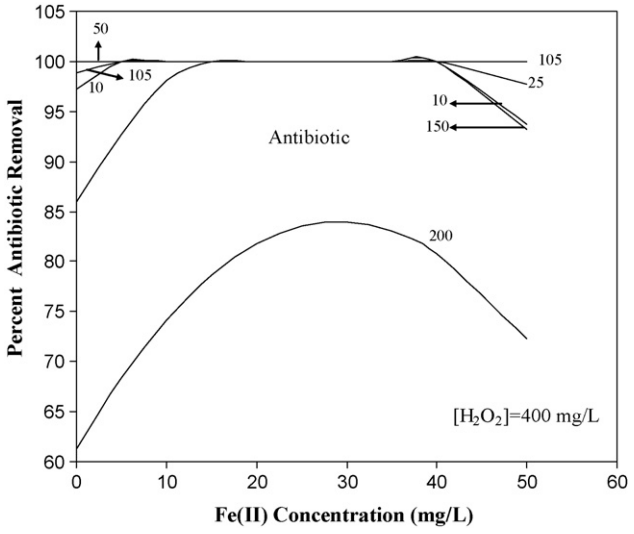


Fig. 1. Variation of percent amoxicillin removal with Fe(II) concentration at different amoxicillin doses and constant H_2O_2 dose of 400 mg L^{-1}. pH 3.5.

The parameters X_1, X_2, X_1^2, X_2^2 and X_3^2 were determined to be significant model terms with p-values less than 0.1. The ANOVA test results for percent mineralization (TOC removal) indicated that the variables X_2, X_3, X_2^2 and X_3^2 were significant model terms with p-values less than 0.1.

Variations of percent antibiotic removals with Fe(II) concentration at different antibiotic concentrations and constant peroxide concentration of 400 mg L^{-1} are depicted in Fig. 1. For all antibiotic doses, antibiotic removal increased with increasing Fe(II) concentration up to 25 mg L^{-1} and then decreased with further increases in Fe(II) dose. Apparently, high Fe(II) doses caused scavenging effect on hydroxyl radicals. This behavior has been reported in literature too [27]. Nearly complete amoxicillin removals were obtained up to 150 mg L^{-1} amoxicillin concentrations at peroxide and Fe(II) doses of 400 mg L^{-1} and 25 mg L^{-1}, respectively. At amoxicillin concentration of 200 mg L^{-1}, the highest antibiotic removal decreased to 83%. High amoxicillin concentrations above 150 mg L^{-1} required high peroxide and Fe(II) doses.

Fig. 2 depicts variation of percent amoxicillin removal with amoxicillin concentration at different H_2O_2 doses and constant Fe(II) dose of 25 mg L^{-1} at pH 3.5. Percent amoxicillin removal increased with increasing peroxide dose up to 255 mg L^{-1}. The results indicated peroxide limitations at peroxide doses below 255 mg L^{-1}. Antibiotic removal also increased with antibiotic concentration up to 60 mg L^{-1} indicating antibiotic limitations at low

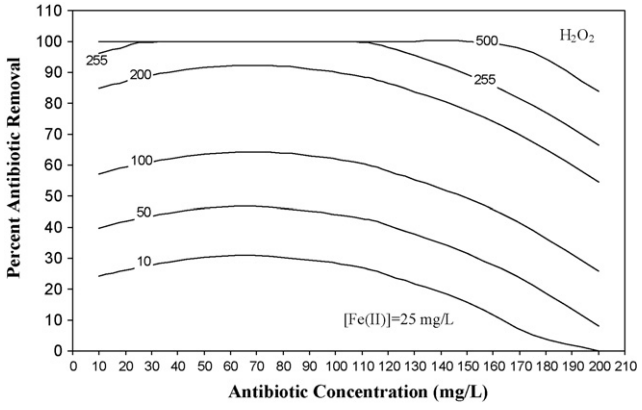


Fig. 2. Variation of percent amoxicillin removal with amoxicillin concentration at different H_2O_2 doses and constant Fe(II) dose of 25 mg L^{-1}. pH 3.5.

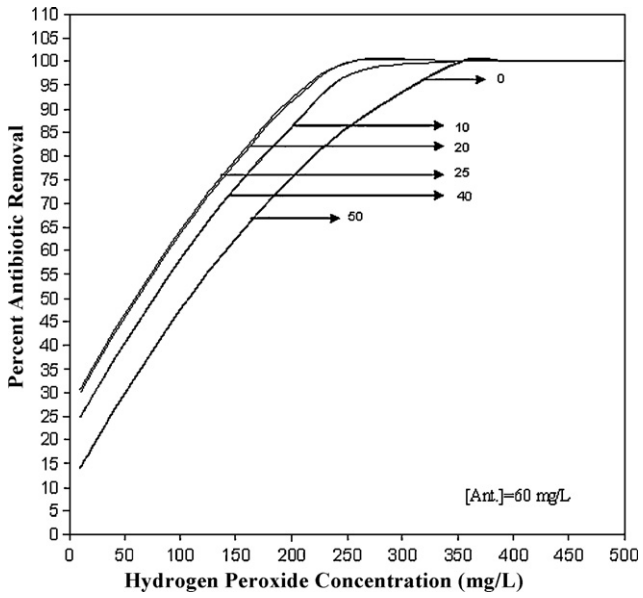


Fig. 3. Variation of percent amoxicillin removal with H_2O_2 concentration at different Fe(II) doses and constant amoxicillin dose of 60 mg L^{-1}. pH 3.5.

concentrations. Further increases in antibiotic concentration above 60 mg L^{-1} resulted in decreases in percent antibiotic removal due to limitations by peroxide and Fe(II). At high amoxicillin concentrations above 150 mg L^{-1}, peroxide concentration must be above 250 mg L^{-1} in order to obtain complete amoxicillin removal. High amoxicillin concentrations required high peroxide doses for effective amoxicillin degradation. At a typical amoxicillin concentration of 100 mg L^{-1}, 25 mg L^{-1} Fe(II), and 230 mg L^{-1} peroxide are required for complete degradation of amoxicillin.

Variations of percent amoxicillin removals with H_2O_2 concentration at different Fe(II) doses and constant amoxicillin dose of 60 mg L^{-1} are depicted in Fig. 3. Amoxicillin removal increased with increasing peroxide dose up to 400 mg L^{-1} indicating limitations by the oxidant concentration at low peroxide doses. Low Fe(II) doses required low peroxide doses for maximum amoxicillin removal. Antibiotic removal also increased with Fe(II) dose up to 25 mg L^{-1} indicating limitations by Fe(II) ions at low concentrations. Further increases in Fe(II) dose to 40 mg L^{-1} resulted in decreases in amoxicillin removal probably due to hydroxyl radical scavenging effects of high Fe(II) doses. In the absence of Fe(II), amoxicillin removal only by peroxide oxidation was lower than that of the Fenton oxidation (peroxide + Fe(II)). The optimum peroxide and Fe(II) doses were 250 mg L^{-1} and 25 mg L^{-1}, respectively for complete degradation of amoxicillin at 60 mg L^{-1} concentration. Preliminary kinetic analysis for amoxicillin degradation indicated nearly first order reaction kinetics with respect to amoxicillin concentration.

Fig. 4 depicts variation of percent TOC removal (mineralization) with Fe(II) concentration at different amoxicillin doses and constant H_2O_2 dose of 400 mg L^{-1} at pH 3.5. Percent TOC removal increased with increasing Fe(II) dose up to 50 mg L^{-1} due to limitations by the catalyst concentration at high peroxide dose of 400 mg L^{-1}. Increases in amoxicillin concentration resulted in slight increases in TOC removal up to 105 mg L^{-1} amoxicillin dose. However, TOC removal decreased at high antibiotic doses above 105 mg L^{-1} due to limitations by peroxide and Fe(II). At 200 mg L^{-1} amoxicillin dose, TOC removal was nearly 25% at peroxide and Fe(II) doses of 400 mg L^{-1} and 50 mg L^{-1}, respectively. The highest TOC removal was 37% at 50 mg L^{-1} amoxicillin, 50 mg L^{-1} Fe(II) and 400 mg L^{-1} peroxide doses. Unlike complete amoxicillin degradation, TOC removals were lower than 40% due to formation of some intermediates which were apparently hard to mineralize. Besides,

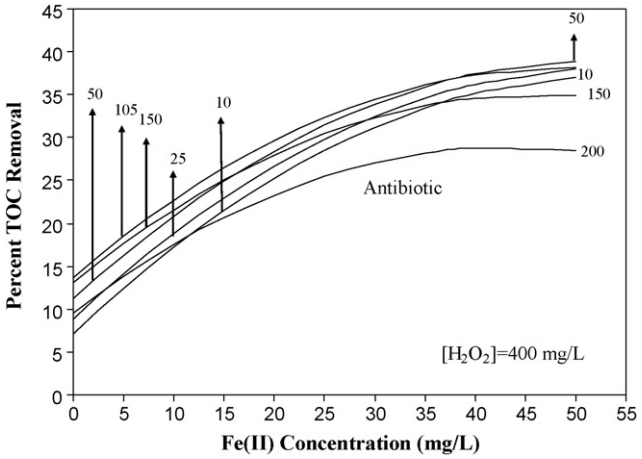


Fig. 4. Variation of percent TOC removal with Fe(II) concentration at different amoxicillin doses and constant H_2O_2 dose of 400 mg L^{-1}. pH 3.5.

mineralization required higher peroxide (400 mg L^{-1}) and Fe(II) doses (50 mg L^{-1}) as compared to amoxicillin degradation.

Variations of percent TOC removals with amoxicillin concentration at different H_2O_2 doses and constant Fe(II) dose of 40 mg L^{-1} are depicted in Fig. 5. Percent TOC removal slightly increased up to 60 mg L^{-1} amoxicillin concentration and then decreased with further increases in amoxicillin dose for all peroxide doses between 10 and 500 mg L^{-1}. High peroxide doses resulted in significant increases in percent TOC removal due to peroxide limitations at low peroxide doses. At amoxicillin and Fe(II) doses of 60 mg L^{-1} and 40 mg L^{-1}, an increase in peroxide dose from 10 to 255 mg L^{-1} resulted in a considerable increase in percent TOC removal. Further increases in peroxide dose to 500 mg L^{-1} resulted in slight increase (from 33% to 35%) in percent TOC removal. High amoxicillin concentrations yielded low TOC removals due to limitations by peroxide and Fe(II) doses. For amoxicillin dose of 100 mg L^{-1} optimum peroxide and Fe(II) doses were 500 mg L^{-1} and 40 mg L^{-1}, respectively yielding nearly 37% mineralization of amoxicillin.

Fig. 6 depicts variation of percent TOC removal with peroxide concentration at different Fe(II) doses and constant amoxicillin dose of 60 mg L^{-1}. Percent TOC removal increased with peroxide concentration up to 400 mg L^{-1} due to limitations by the peroxide dose at low peroxide levels. Further increases in peroxide doses resulted in decreases in TOC removal due to hydroxyl radical scavenging effect of peroxide at high concentrations. The optimum peroxide dose varied depending on Fe(II) dose. Optimum peroxide dose was around 250 mg L^{-1} at low Fe(II) doses below 20 mg L^{-1} which increased with increasing Fe(II) dose and reached nearly 400 mg L^{-1} peroxide dose for Fe(II) doses above 40 mg L^{-1}.

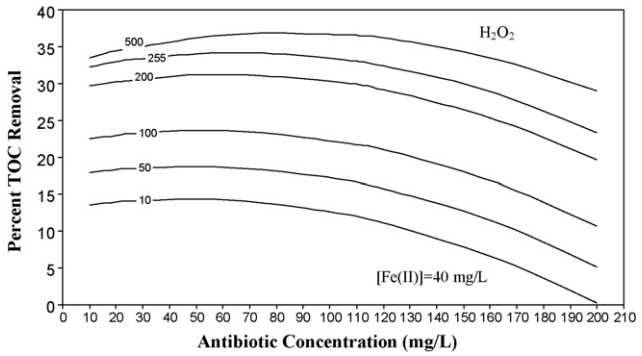


Fig. 5. Variation of percent TOC removal with amoxicillin concentration at different H_2O_2 doses and constant Fe(II) dose of 40 mg L^{-1}. pH 3.5.

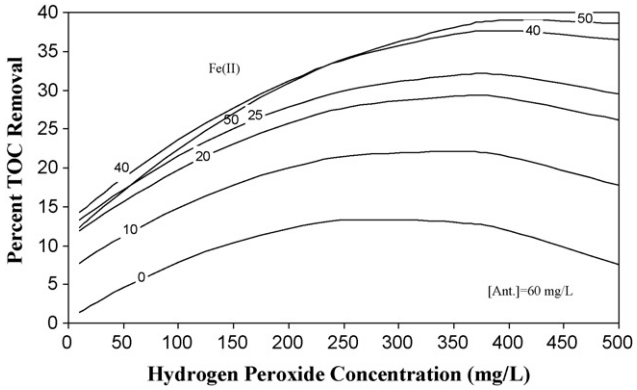


Fig. 6. Variation of percent TOC removal with peroxide concentration at different Fe(II) doses and constant amoxicillin dose of 60 mg L^{-1}. pH 3.5.

TOC removal in the absence of catalyst (Fe(II)) was less than 10% indicating negligible TOC removals by peroxide alone. The highest TOC removal (37%) at an antibiotic dose of 60 mg L^{-1} was obtained with 400 mg L^{-1} peroxide and 50 mg L^{-1} Fe(II) doses. The results indicated that mineralization of amoxicillin required higher concentrations of peroxide and Fe(II) as compared to amoxicillin degradation. The highest percent mineralization was 37% while amoxicillin degradation was 100% indicating formation of some refractory intermediate compounds.

Complete mineralization of amoxicillin by the Fenton reagent can be described by the following reaction

$$C_{16}H_{19}N_3O_5S + 47H_2O_2 + Fe(II) \rightarrow 16CO_2 + 54H_2O + 3HNO_3 + H_2SO_4 + Fe(II) \quad (6)$$

On the basis of complete mineralization reaction stoichiometry, the required peroxide is approximately 4.38 mg H_2O_2/mg amoxicillin. In the absence of intermediate formation, at an amoxicillin concentration of 105 mg L^{-1}, 460 mg L^{-1} H_2O_2 would suffice for complete mineralization of amoxicillin. However, only 37% TOC removal or mineralization was obtained at peroxide and Fe(II) doses of 500 and 50 mg L^{-1} when amoxicillin was 105 mg L^{-1} (Table 2). This difference is due to incomplete mineralization and intermediate formation.

There are limited number of studies on advanced oxidation of amoxicillin [12–15,33]. Different AOPs were used by different investigators for removal of amoxicillin. Andreozzi et al. [33] used ozonation for amoxicillin removal and obtained nearly 90% antibiotic and 18% TOC removal within 20 min. Elmolla and Chaudhuri [12] used Fenton oxidation for removal of a mixture of antibiotics and reported complete degradation of antibiotics in 2 min and nearly 81% COD removal within 60 min. Rizzo et al. [15] used TiO_2 and UV treatment for removal of a mixture of antibiotics from wastewater. More than 90% TOC removal was achieved within 120 min. Alkaline ozonation and photo-Fenton methods were reported to be effective for TOC and COD removals from amoxicillin containing water [13]. As compared to the literature studies, complete antibiotic removal and nearly 37% TOC removals were achieved within 15 min in this study. The extent of amoxicillin and TOC removals obtained in this study are higher than most of the literature studies. However, in real wastewater tretament, percent amoxicillin and TOC removals would probably be lower than that obtained in this study due to presence of other organics.

4. Conclusions

Advanced oxidation of amoxicillin was achieved in aqueous medium by using the Fenton's reagent treatment for a a large

range of reagent doses. Box–Behnken statistical experiment design was used by considering the amoxicillin, peroxide and Fe(II) concentrations as independent variables. Objective functions were percent amoxicillin and TOC removals (mineralization). Complete amoxicillin degradation was obtained at four experimental points. Amoxicillin removal increased with increasing peroxide and amoxicillin doses at a Fe(II) dose of 25 mg L^{-1}. High concentrations of peroxide and Fe(II) resulted in lower antibiotic removals due to hydroxyl radical scavenging effects of high peroxide and Fe(II) doses. The optimum peroxide/Fe/amoxicillin ratio resulting in complete antibiotic removal was 255/25/105 mg L^{-1}.

Unlike complete amoxicillin degradation, TOC removal (mineralization) was not complete in Fenton oxidation due to formation of refractory intermediates. Apparently, some of the intermediate compounds were resistant to mineralization by the Fenton's reagent. The highest TOC removal was 37% at all antibiotic concentrations. Peroxide and Fe(II) requirements increased with increasing antibiotic concentration for effective mineralization. Mineralization required higher concentrations of peroxide and Fe(II) as compared to amoxicillin degradation due to further degradation of intermediates. Percent TOC removal can be improved by using sequential AOPs such as photo-Fenton, ozonation, and TiO_2-UV treatments.

References

[1] J. Beausse, Selected drugs in solid matrices: a review of environmental determination, occurrence and properties of principal substances, Trends Anal. Chem. 23 (2004) 753–761.

[2] D. Bendz, N.A. Paxéus, T.R. Ginn, F.J. Loge, Occurrence and fate of pharmaceutically active compounds in the environment, a case study: Höje River in Sweden, J. Hazard. Mater. 122 (2005) 195–204.

[3] K. Kümmerer, Antibiotics in the aquatic environment – a review – part I, Chemosphere 75 (2009) 417–434.

[4] T. Heberer, Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data, Toxicol. Lett. 131 (2002) 5–17.

[5] K. Fent, A. Weston, D. Caminada, Ecotoxicology of human pharmaceuticals, Aquat. Toxicol. 76 (2006) 122–159.

[6] J. Ikehata, N.J. Naghashkar, M. Gamal El-Din, Degradation of aqueous pharmaceuticals by ozonation and advanced oxidation processes: a review, Ozone Sci. Eng. 28 (2006) 353–414.

[7] Amoxicillin (n.d.). Retrieved on August 5, 2009, from http://www.marvistavet.com/html/body_Amoxicillin.html.

[8] D.F. Bishop, G. Stern, M. Fleischman, L.S. Marshall, Hydrogen peroxide catalytic oxidation of refractory organics in municipal wastewater, Ind. Eng. Chem.: Proc. Des. Develop. 7 (1968) 110–117.

[9] J.A. Zazo, J.A. Casas, A.F. Mohedano, M.A. Gilarranz, J.J. Rodríguez, Chemical pathway and kinetics of phenol oxidation by Fenton's reagent, Environ. Sci. Technol. 39 (2005) 9295–9320.

[10] E.C. Catalkaya, F. Kargi, Effects of operating parameters on advanced oxidation of diuron by the Fenton's reagent: a statistical design approach, Chemosphere 69 (2007) 485–492.

[11] W. Ben, Z. Qiang, X. Pan, M. Chen, Removal of veterinary antibiotics from sequencing batch reactor (SBR) pre-treated swine wastewater by Fenton's reagent, Water Res. 43 (2009) 4392–4402.

[12] E. Elmolla, M. Chaudhuri, Optimization of Fenton process for treatment of amoxicillin, ampicillin and cloxacillin antibiotics in aqueous solution, J. Hazard. Mater. 170 (2009) 666–672.

[13] I. Arslan-Alaton, S. Dogruel, Pre-treatment of penicillin formulation effluent by advanced oxidation processes, J. Hazard. Mater. 112 (2004) 105–113.

[14] A.G. Trovó, A.S.S. Melo, R.F.P. Nogueira, Photodegradation of the pharmaceuticals amoxicillin, bezafibrate and paracetamol by the photo-Fenton process—application to sewage treatment plant effluent, J. Photochem. Photobiol. A: Chem. 198 (2008) 215–220.

[15] L. Rizzo, S. Meric, M. Guida, D. Kassinos, V. Belgiorno, Heterogenous photocatalytic degradation kinetics and detoxification of an urban wastewater treatment plant effluent contaminated with pharmaceuticas, Water Res. 43 (2009) 4070–4078.

[16] A. Ghauch, A. Tuqan, H.A. Assi, Antibiotic removal from water: elimination of amoxicillin and ampicillin by microscale and nanoscale iron particles, Environ. Poll. 157 (2009) 1626–1635.

[17] A.G. Trovó, R.F.P. Nogueira, A. Agüera, A.R. Fernandez-Alba, C. Sirtori, S. Malato, Degradation of sulfomethoxazole in water by solar photo-Fenton. Chemical and toxicological evaluation, Water Res. 43 (2009) 3922–3931.

[18] T.G. Vasconcelos, K. Kümmerer, D.M. Henriques, A.F. Martins, Ciprofloxacin in hospital effluent: degradation by ozone and photoprocesses, J. Hazard. Mater. 169 (2009) 1154–1158.

[19] Z.P. Xing, D.Z. Sun, Treatment of antibiotic fermentation wastewater by combined polyferric sulfate coagulation. Fenton and sedimentation process, J. Hazard. Mater. 168 (2009) 1264–1268.

[20] C.L. Hsueh, Y.H. Huang, C.C. Wang, C.Y. Chen, Degradation of azo dyes using low iron concentration of Fenton and Fenton-like system, Chemosphere 58 (2005) 1409–1414.

[21] E. Balanosky, F. Herrera, J. Kiwi, Optimization in design, testing and construction of reactors by use of statistical modeling of the reaction variables, energy input and reaction time, in: B. Delmon, J. Yates (Eds.), Advances in Surface Science and Catalysis C, vol. 30, Elsevier, Amsterdam, 2000, pp. 2177–2218.

[22] J. Fernandez, J. Kiwi, C. Lizama, J. Freer, H.D. Mansilla, Factorial experimental design of Orange II photocatalytic discolouration, J. Photochem. Photobiol. A Chem. 151 (2002) 213–219.

[23] G.E.P. Box, K.B. Wilson, On the experimental attainment of optimum multifactorial conditions, R. Stat. Soc. 13 (1951) 1–12.

[24] A. Boza, Y. De la Cruz, G. Jordan, U. Jauregui-Haza, A. Aleman, I. Caraballo, Statistical optimization of a sustained-release matrix tablet of lobenzarit disodium, Drug Develop. Ind. Pharm. 26 (2000) 1303–1307.

[25] S.K. Singh, J. Dodge, M.J. Durrani, M.A. Khan, Optimization and characterization of controlled release pellets coated with an experimental latex. I. Anionic drug, Int. J. Pharmaceut. 125 (1995) 243–255.

[26] C. Sanchez-Lafuente, S. Furlanetto, M. Fernandez-Arevalo, Didanosine extended-release matrix tablets: optimization of formulation variables using statistical experimental design, Int. J. Pharmaceut. 237 (2002) 107–118.

[27] F. Ay, E.C. Catalkaya, F. Kargı, A statistical experiment design approach for advanced oxidation of Direct Red azo-dye by photo-Fenton treatment, J. Hazard. Mater. 162 (2009) 230–236.

[28] M. Evans, Optimization of Manufacturing Processes: A Response Surface Approach, Carlton House Terrace, London, UK, 2009.

[29] A. Kumar, B. Prasad, I.M. Mishra, Process parametric study for ethene carboxylic acid removal onto powder activated carbon using Box–Behnken design, Chem. Eng. Technol. 30 (2007) 932–937.

[30] S.L.C. Ferreira, R.E. Bruns, H.S. Ferreira, G.D. Matos, J.M. David, G.C. Brandão, E.G.P. da Silva, L.A. Portugal, P.S. dos Reis, A.S. Souza, W.N.L. dos Santos, Box–Behnken design: an alternative for the optimization of analytical methods, Anal. Chim. Acta 597 (2007) 179–186.

[31] F. Ay, E.C. Catalkaya, F. Kargı, Advanced oxidation of Direct Red (DR 28) by Fenton treatment, Environ. Eng. Sci. 25 (2009) 1455–1462.

[32] C.H. Dong, X.Q. Xie, X.L. Wang, Y. Zhan, Y.J. Yao, Application of Box–Behnken design in optimisation for polysaccharides extraction from cultured mycelium of *Cordyceps sinensis*, Food Bioprod. Proces. 87 (2009) 139–144.

[33] R. Andreozzi, M. Canterino, R. Marotta, N. Paxeus, Antibiotic removal from wastewaters: the ozonation of amoxicillin, J. Hazard. Mater. 122 (2005) 243–250.