Optimizing the parameters of amoxicillin removal in a photocatalysis/ozonation process using Box–Behnken response surface methodology

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ABSTRACT

Concerns about environmental pollution from antibiotics such as amoxicillin have received increasing attention. These compounds should be eliminated from discharged effluents to avoid their possible negative effects on humans and animals, as well as on the environment. Recently, advanced oxidation techniques have been used to remove antibiotics. This work aims to study the removal of amoxicillin using a photocatalysis/ozonation process for treating pharmaceutical waste-water loaded with this type of refractory pollutants. The removal process was carried out using different pH values (3–11), catalyst dosages (250–750 mg/L), and reaction times (30–90 min), at an ozonation rate of 200 mg/h. Statistical analysis indicated that a quadratic model was suitable for modeling amoxicillin degradation by the photocatalytic process and that all studied parameters had statistically significant critical levels. Under optimum conditions (pH 11, a catalyst dose of 500 mg/L, and a reaction time of 90 min), the amoxicillin degradation efficiency of the photocatalytic process was 78.7%. The results of the photocatalysis/ozonation process indicated that after 90 min of ozone injection, an amoxicillin degradation efficiency of 98.7% was obtained. Therefore, it was concluded that the combined ozonation process and photocatalytic process could be used to remove amoxicillin effectively.

Keywords: Amoxicillin; Photocatalysis/ozonation reaction; Optimization; Box–Behnken; RSM

1. Introduction

Antibiotics are used extensively in human and veterinary medicine for disease control, as well as in aquaculture to prevent or treat microbial infection [1,2]. Amoxicillin is a broad-spectrum β-lactam antibiotic that belongs to the penicillin class, and is used as a veterinary medicine for the treatment of bacterial infections in the gastrointestinal tract and systemic infections [3]. Recent studies have shown that 65 percent of all antibiotics used worldwide are β-lactam type [4]. Antibiotics enter the aquatic environment from various sources, such as the pharmaceutical industry, hospital

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effluents, and laboratory activities, as well as via excretion from humans and livestock, as 30%–90% of these compounds are not metabolized completely by humans or animals [5,6]. These materials have undesirable effects, including toxicity in living beings, antibiotic resistance in pathogenic bacteria, and digestive disorders and genotoxicity in humans. Accordingly, a variety of pharmaceuticals have been detected in many environmental samples, including wastewater treatment plant effluents, surface water sources, groundwater sources, seawater, soil, sediments, and even drinking water owing to their resistant nature [2,5]. Therefore, antibiotics should be removed from wastewater effluents before they are discharged to the environment [7].

In water and wastewater industries, methods available for the removal of pharmaceutical compounds include the use of membrane filters, adsorption, and advanced oxidation processes (AOPs) such as ozonation, UV irradiation, and photo-Fenton processes [5,7–9]. Among these methods, AOPs processes are generally recognized as being the most effective for the removal of hazardous, refractory, and non-biodegradable organic pollutants because of their low-cost, convenient operation, high efficiency, and mineralization capability [10–12]. One of the advanced oxidation processes is the ozonation process, in ozonation processes, ozone attacks organic compounds and oxidizes them directly at low pH and/or indirectly via a chain reaction mechanism to produce the $^\bullet$HO radical at high pH.

In AOPs, the catalyst increases the generation of hydroxyl radicals ($^\bullet$OH), the reaction rate, and the removal of pollutants, while they decreases the amount of toxic intermediates in solution [13]. A variety of metal oxides, including TiO_2, ZnO, and MgO, have been used as catalyst in AOPs [14–17]. Magnesium oxide (MgO) is a heterogeneous catalyst that is known to be useful in the treatment of water and wastewater owing to its potential for removing a variety of organic contaminants, low cost, nontoxicity, environment-friendly properties, and high concentration of active sites [14,18].

Recently, the combination of ozone with photocatalysis (photocatalysis/ozonation) has been considered to be one of the most promising methods for the elimination of pollutants. In photocatalytic ozonation, excited electrons interact with ozone molecules to generate ozonide radicals, or with oxygen to generate $^\bullet O_2^-$ and ozonide radicals. Finally, these radicals undergo chain reactions to produce $^\bullet$HO radicals and degrade the organic pollutants.

Lately, statistical models have been used to optimize different processes in many fields. Statistical models used in the field of environmental health engineering include the response level statistical model. Response surface methodology (RSM) is a powerful statistical technique to investigate the interactive effects of several factors at different levels. RSM also decreases the number of experimental runs needed, thus reducing the consumption of energy and materials [19,20]. Thus far, no study has been reported on the photocatalysis/ozonation of amoxicillin using MgO through RSM. In this work, an MgO-based photocatalysis process was used to remove the antibiotic amoxicillin from aqueous solution, and the optimum conditions were determined using RSM based on a Box–Behnken Design (BBD). The effect of ozonation in the photocatalysis/ozonation process was then investigated.

2. Materials and methods

2.1. Materials

MgO nanoparticles and the antibiotic amoxicillin (analytical grade) were purchased from Sigma-Aldrich and used as received without any further purification. Sodium hydroxide and sulfuric acid were purchased from Merck.

2.2. Preparation of the synthetic solution and experimental procedure

All experiments were performed at the laboratory bench scale at constant temperature (25°C) with 250 ml of amoxicillin solution in a 500 ml tubular glass reactor. A 1,000 mg/L amoxicillin stock solution was prepared by dissolving 1 g amoxicillin powder in 1,000 ml distilled water. Solutions with the required amoxicillin concentration (100 mg/L) were then prepared by diluting the amoxicillin stock solution with distilled water. The desired amount (250–750 mg/L) of MgO powder and the amoxicillin solution were added to the laboratory bench scale reactor. The pH values of the amoxicillin solution were then adjusted using diluted sulfuric acid and sodium hydroxide and were measured using a pH meter (Denver Ultrabasic-UB10).

After adjusting the initial pH, but prior to UV irradiation, the suspension was magnetically stirred for 30 min in the dark to ensure that the adsorption/desorption equilibrium of amoxicillin on the catalyst surface had been reached (efficiency 6% ± 2%). For the photocatalytic reaction, the suspension was irradiated with UV light using a 6 W low-pressure mercury lamp (OSRAM), which was placed in the center of the reactor inside a quartz tube for protection. In the photocatalytic ozonation process, ozone was generated by an ozone generator (Denali Ozone Generator, Pasargad) with a flow rate of 5 L/min and bubbled into the reactor to achieve a dosage of 200 mg/h. After the desired reaction time had elapsed, 5 ml aliquots of the suspension were withdrawn at regular intervals and centrifuged at 6,000 RPM for 20 min to separate the catalysts using a centrifuge (Hettich, Germany). The analysis of amoxicillin was carried out using a UV–vis spectrophotometer (Shimadzu UV 1700, Japan) at a maximum absorbance wavelength of 228 nm. After determining the optimal parameters for the photocatalytic degradation of amoxicillin via response surface methodology, ozone was injected into the reactor to evaluate the impact of ozonation on the elimination of amoxicillin. The degradation efficiency of amoxicillin was obtained using Eq. (1):

$$\text{Degradation}\% = \frac{C_i - C_f}{C_i} \times 100 \qquad (1)$$

In Eq. (1) R, C_i, and C_f are the efficiency of the process and the initial and final amoxicillin concentration, respectively.

2.3. Statistical design of the experiments

The software program Design Expert 6.0.7 (Stat-Ease Inc., Minneapolis, USA) was used for the design, mathematical modeling and optimization of experiments. RSM based on the BBD was employed for the experimental design,

calculating the interaction effects between various factors, and determining the optimum conditions for the photocatalytic degradation of amoxicillin. In this study, the pH value (A, 3–11), catalyst dose (B, 250–750 mg/L), and reaction time (C, 30–90 min) were considered experimental variables to evaluate the photocatalytic degradation of amoxicillin (Table 1). A total of 17 experiments were carried out according to Eq. (2):

$$N = 2X(X-1) + Y = 2 \times 3(3-1) + 5 = 17 \tag{2}$$

In Eq. (2), X, Y, and N are the number of variables, the number of repeats at the center point, and the total number of experiments, respectively.

After the experimental design, to carry out the photocatalytic activity, we implemented it according to the mentioned protocol in Table 2. But before doing any work (the photo-catalytic and ozonation processes), we put the nanoparticles and pollutants in contact with each other about 30 min to carry out the adoption/desorption, and then the samples were placed under the photocatalytic and ozonation processes.

3. Results and discussion

3.1. Model fitting and statistical analysis

Using the RSM, experiments of design of three variables and five central points, a total of 17 runs (experiments) was obtained according to Eq. (2). The results of the photocatalytic degradation of amoxicillin in each experimental stage are given in Table 2. The obtained data were analyzed and interpreted using analysis of variance (ANOVA).

3.1.1. Analysis of variance (ANOVA)

Analysis of variance was used to evaluate the raw experimental data, and the adequacy of the quadratic model was examined via the F-value, p-value, and R^2 value. The results of the variance analysis are shown in Table 3, and significant parameters with a p-value < 0.05 have been indicated for the input response variables. According to the analysis, the computed F-value (30.11), p-value (<0.0001), and R^2 (0.97) of the model indicated significance with low probability (lower than 0.05). Moreover, the obtained R^2 value was found to be 0.97, which has a logical fit with R^2 adjusted value of 0.97, indicating a good fit. The validity of the proposed model was confirmed by the insignificance of the p-value for lack of fit, which was found to be 0.61, which was greater than the upper limit of 0.05 for significance.

Hence, by applying the Box–Behnken response surface methodology and analysis of variance, the following regression equation was obtained from the experimental results:

$$Y = 75.36 + 1.92A + 0.54B + 0.014C + 0.16AB + 0.092AC - 0.23BC + 0.98A^2 + 0.2B^2 + 0.34C^2 \tag{3}$$

where Y represents amoxicillin degradation (%), and A, B, and C are the coded values for the pH, catalyst dose, and reaction time, respectively.

The normal probability graph of the residuals from the least-squares fitting for the percentage of amoxicillin degradation response is shown in Fig. 1. As shown, the points on the plot form a reasonably straight line, and the residuals follow a normal distribution pattern. Fig. 2 is a scatter plot of the actual values and predicted results for the amoxicillin degradation efficiency. As shown, both the predicted and actual results were randomly scattered around the straight line at 45°, which confirms that the error between the actual and predicted values was very low. According to these findings, the proposed model exhibited a high correlation and adequacy to predict the degradation process of amoxicillin via photocatalysis.

3.2. Response surface plotting and optimization of the experimental conditions

3.2.1. Effect of the initial solution pH

The solution pH plays an important role in the degradation of amoxicillin in AOPs processes. The effect of the solution pH on the degradation efficiency of amoxicillin in

Table 1
Variables and levels of the Box–Behnken experimental design

Independent variables	Coded symbol	Code levels		
		–1	0	+1
pH	A	3	7	11
Catalyst dose (mg/L)	B	250	500	750
Reaction time (min)	C	30	60	90

Table 2
Steps of the experimental design using Box–Behnken response surface methodology

Run	pH	Nanocatalyst dose (mg/L)	Reaction time (min)	Efficiency (%)
1	11	250	60	77.3
2	3	500	30	74.55
3	7	500	60	75.05
4	11	500	30	78.42
5	3	500	90	74.76
6	7	250	30	74.85
7	3	250	60	74.0
8	3	750	60	74.66
9	7	750	30	76.5
10	7	500	60	74.92
11	7	500	60	75.4
12	7	500	60	75.63
13	7	750	90	75.7
14	7	250	90	74.97
15	11	750	60	78.6
16	11	500	90	79.0
17	7	500	60	75.81

Table 3
Results of the analysis of variance for the degradation of amoxicillin via photocatalytic reaction

Source	Sum of squares	df	Mean square	F-value	p-value
Model	36.91	9	4.10	30.11	<0.0001
pH	29.45	1	29.45	216.23	<0.0001
Nanocatalyst dose	8.35	1	8.35	17.29	0.0043
Time	5.3	1	5.3	9.11	0.008
pH × nanocatalyst dose	3.11	1	3.11	0.75	0.021
pH × time	1.34	1	1.34	0.25	0.041
Nanocatalyst dose × time	0.8	1	0.8	1.55	0.009
pH^2	4.03	1	4.03	29.55	0.001
Nanocatalyst dose^2	1.07	1	1.07	1.23	0.019
Time^2	0.5	1	0.5	3.63	0.035
Residual	0.95	7	0.14		
Lack of fit	0.39	3	0.13	0.91	0.61
Pure error	0.57	4	0.14	–	–
Cor. total	37.86	16	–	–	–
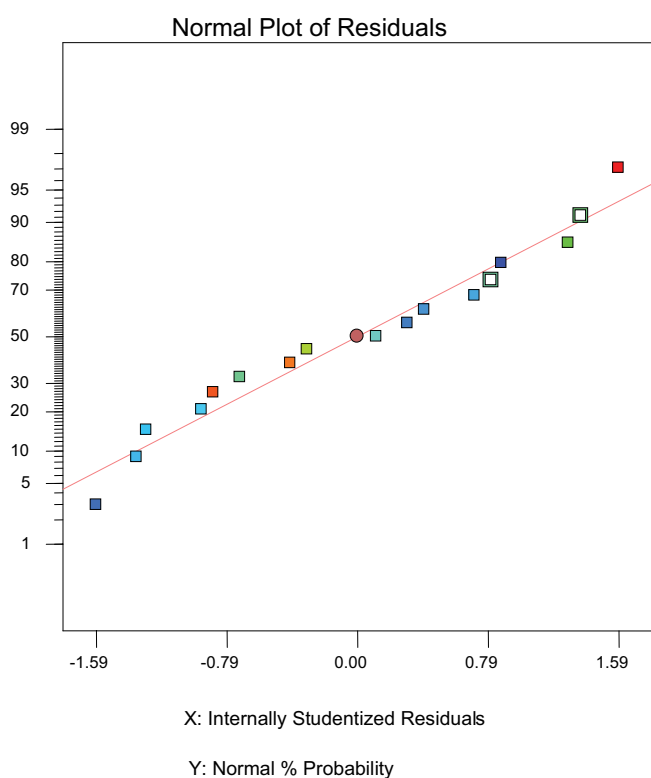
Fig. 1. Normal probability plot of the residuals.

Fig. 2. Scatter plot of the actual vs. predicted values.

the MgO photocatalytic process was evaluated by conducting experiments at pH values of 3, 7, and 11 (Figs. 3a and b). As can be seen from Fig. 3, amoxicillin degradation strongly depended on the solution pH in this photocatalytic process. According to the obtained results, increasing the pH from 3 to 11 increased the efficiency of antibiotic degradation, with the highest degradation percentages of amoxicillin being
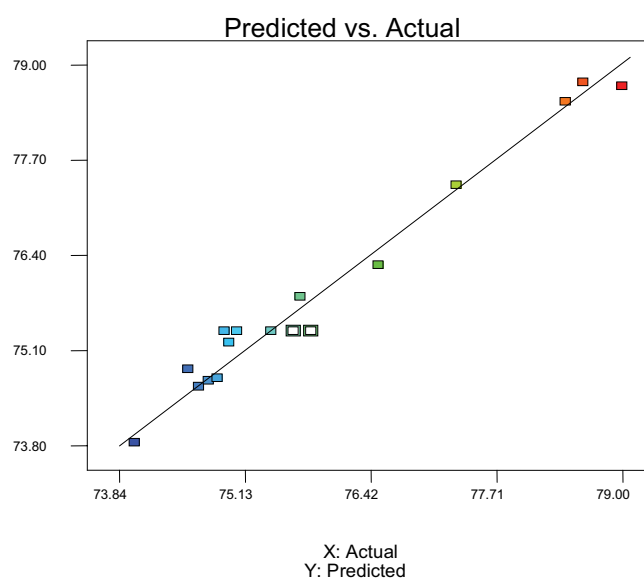
observed at alkaline pH (pH = 11). The effect of the pH on amoxicillin degradation can be explained by considering the properties of both the catalyst and the antibiotic at different pH values. Amoxicillin is a zwitterionic molecule with both basic and acidic groups and has three pKa values (3, 7, and 11). The pH at the potential of zero point charge (pH$_{zpc}$) of the catalyst is 12.4. In solutions with a pH less than the pH$_{zpc}$, the catalyst is positively charged, while at a pH higher than the pH$_{zpc}$, it has a negative charge. Therefore, at pH values less than pH$_{zpc}$ and higher than pKa, electrostatic adsorption occurs between the negative amoxicillin ions and the positively charged MgO nanoparticles, increasing the efficiency of removal [21]. The increased removal rate of amoxicillin at high pH can also be related to the presence of hydroxyl
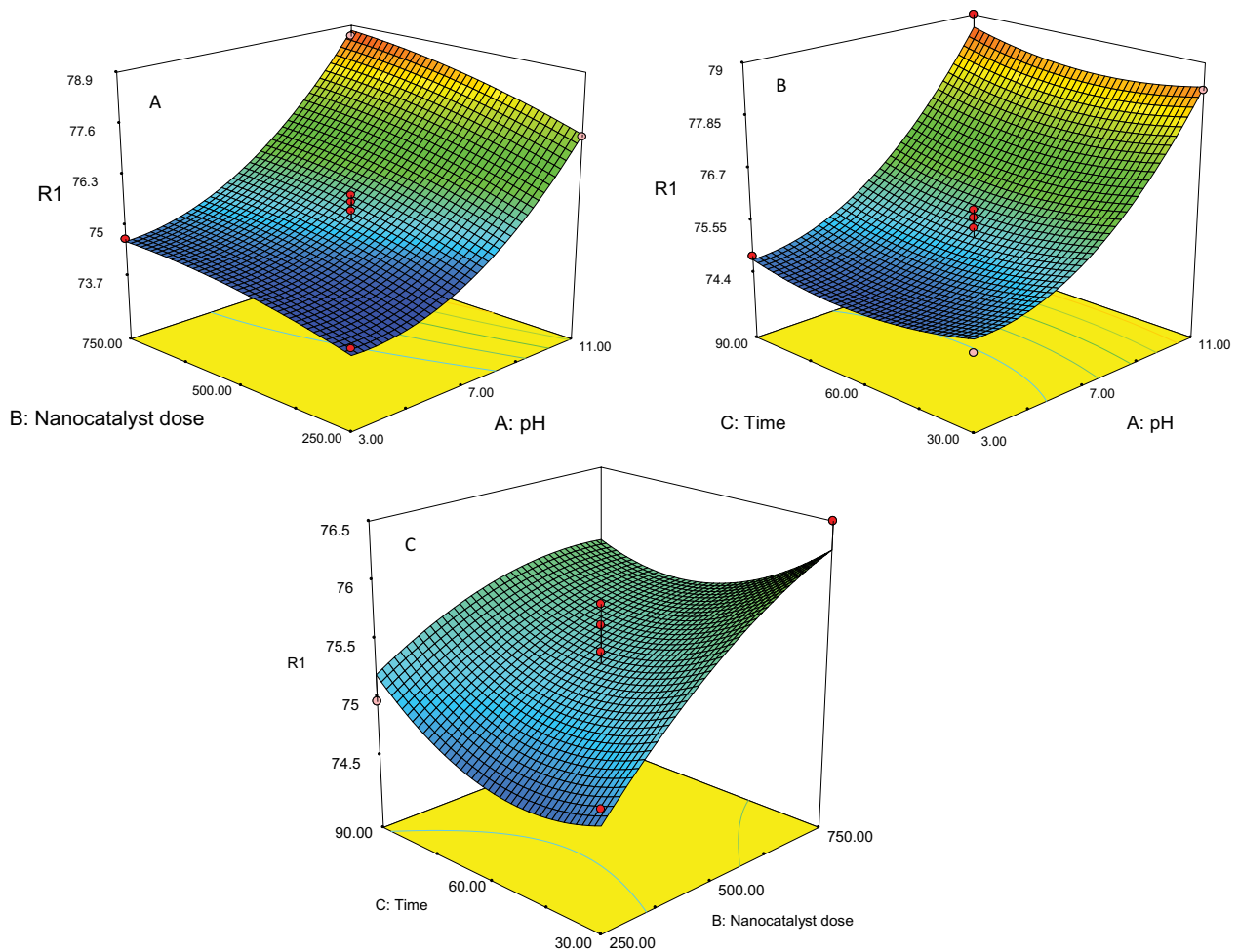
Fig. 3. Three-dimensional plots of the effects of the parameters on the photocatalytic process.

radicals (•OH) and the reaction of the generated holes (h⁺) with the antibiotic. The decreased degradation of amoxicillin at pH 3 can also be explained in terms of the pH_{zpc} and pKa values. When the pH is reduced from 7 to 3, both the catalyst and amoxicillin are positively charged, which creates a repulsive force between them, thereby reducing the removal efficiency.

3.2.2. Effect of catalyst loading

The dosage of MgO nanoparticles is another important parameter that affects the performance of photocatalytic processes. Increasing the catalyst dosage leads to an increase in the number of available uptake sites; as a result, the UV adsorption capacity and production of hydroxyl radicals increases. As shown in Figs. 3a and c, the influence of MgO nanoparticle dosages from 250 to 750 mg/L on the amoxicillin removal performance of the UV/MgO process were investigated. The results indicated that the removal efficiency of amoxicillin increased with increasing catalyst dose from 250 to 500 mg/L, but increasing the catalyst dose above 500 mg/L resulted in reduced efficiency (Fig. 4). The reduced efficiency at doses above 500 mg/L was attributed

to the reduced penetration of UV irradiation into the solution because of the presence of the nanocatalyst; in other words, increasing the quantity of MgO nanoparticles made the solution turbid, which blocked the UV irradiation. These results were in agreement with the findings of photocatalytic studies conducted by other researchers involving the photocatalytic elimination of tetracycline (TC) [22], 2-chlorophenol [23], phenolic compounds [24], and amoxicillin and ampicillin [5].

3.2.3. Effect of reaction time

Reaction time is one of the most important parameters in the design and performance of any chemical reaction, including adsorption and oxidation processes. The reaction time must be sufficiently long for the goals of the treatment process to be achieved. Figs. 3b and c show the effect of the ozonation time (30–90 min) on the amoxicillin removal efficiency. The amoxicillin removal percentage increased with increasing reaction time. This phenomenon was attributed to longer reaction time allowing for the generation of more hydroxyl radicals, which in turn led to the degradation of more amoxicillin molecules.
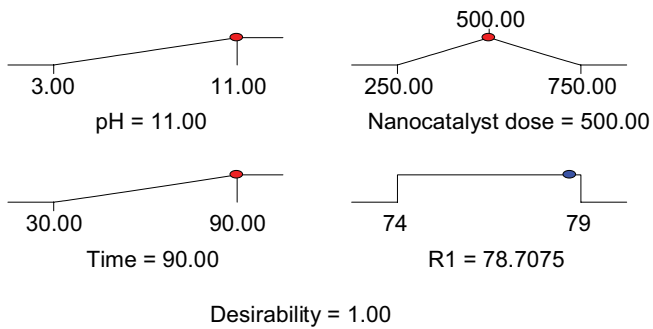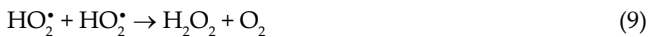
Fig. 4. Plot of optimal conditions using the RSM design.

3.2.4. Optimization of photocatalytic activity

The purpose of the optimization study was to find the combination of levels of variables that resulted in the greatest elimination of the antibiotic amoxicillin. The response surface methodology was used to select and predict the best operating parameters within the ranges of the variables used. The model estimated that 78.7% amoxicillin degradation could be achieved under optimal conditions (pH = 11, catalyst dose = 500 mg/L, and reaction time = 90 min); the desirability factor of these conditions was 1.00, where a value of 1 is ideal (Fig. 4). In the photocatalytic process using MgO nanoparticles, the MgO is excited and generates holes and electrons. The generated holes electrons react with H_2O and produce $^{\bullet}OH$ radicals. On the other hand, the excited electron reacts with O_2 molecule, and then produces $^{\bullet}O^-$ radicals, which oxidize amoxicillin directly [Eqs. (4)–(11)].

$$PC \rightarrow h^+ + e^- \tag{4}$$

$$H_2O + h^+ \rightarrow OH^{\bullet} + H^+ \tag{5}$$

$$OH^- + h^+ \rightarrow OH^{\bullet} \tag{6}$$

$$O_2 + e^- \rightarrow O_2^{\bullet-} \tag{7}$$

$$O_2^{\bullet-} + H^+ \rightarrow HO^{\bullet} \tag{8}$$

$$HO_2^{\bullet} + HO_2^{\bullet} \rightarrow H_2O_2 + O_2 \tag{9}$$

$$O_2^{\bullet-} + HO_2^{\bullet} \rightarrow HO_2^- + O_2 \tag{10}$$

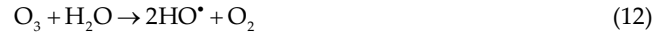$$HO_2^- + H^+ \rightarrow H_2O_2 \tag{11}$$

3.3. Effect of ozonation on photocatalysis/ozonation process

After the determination of the optimum parameters in the photocatalytic process, the ozonation process was added in order to study its effect on the amoxicillin degradation. The ozonation process was carried out using optimum conditions (pH = 11, catalyst dose = 500 mg/L, and reaction time 90 min); ozone was injected to the solution using an ozone generator with a flow rate of 5 L/min and bubbled into the reactor to achieve a dosage of 200 mg/h.

After 90 min, an approximately 20% increase in efficiency was achieved, increasing the efficiency of the photocatalysis/ ozonation process to 98.7%. The increased efficiency can be related to the synergistic effect between the ozonation and photocatalytic process [Eqs. (12)–(15)]. In this situation, the electrons excited in the photocatalytic process react quickly with the ozone molecules in solution to generate active radicals, which break down antibiotics in solution.

$$O_3 + H_2O \rightarrow 2HO^{\bullet} + O_2 \tag{12}$$

$$O_3 + OH^- \rightarrow O_2^{\bullet-} + HO_2^{\bullet} \tag{13}$$

$$O_3 + HO^{\bullet} \rightarrow O_2 + HO_2^{\bullet} \tag{14}$$

$$O_3 + HO_2^{\bullet} \xrightleftharpoons[b]{a} 2O_2 + {}^{\bullet}OH \tag{15}$$

Huang et al. [25] investigated the removal of perfluorooctanoic acid by photocatalysis/ozonation; their results showed that the efficiency of the combined photocatalysis/ ozonation process was higher than that of the individual photocatalytic and ozonation processes owing to synergistic effects.

4. Conclusion

The results of the present study showed that the response surface methodology is an appropriate statistical method for the optimization of amoxicillin removal experiments, which allows the effects of variables on process efficiency to be investigated using the least number of experiments. According to statistical analysis, the proposed quadratic model was suitable for the degradation of amoxicillin by the studied photocatalytic process. In other words, the proposed quadratic model successfully predicted the degradation of amoxicillin; all studied parameters were found to be statistically significant. The amoxicillin degradation efficiency of 78.7% was achieved under the optimum conditions (pH = 11, catalyst dose = 500 mg/L, and reaction time = 90 min). The results of the photocatalytic/ozonation process indicated that using the optimum conditions above in conjunction with ozonation at a flow rate of 5 L/min, 98.7% amoxicillin degradation efficiency was obtained after 90 min. These results suggest that the photocatalysis/ozonation process is an effective method for the degradation of amoxicillin from aqueous solutions.

Acknowledgments

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