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Application of response surface methodology to optimize the treatment of cephems pharmaceutical wastewater by ultrasound/Fenton process

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ABSTRACT

Response surface methodology was utilized to optimize the treatment of wastewater from a production of cephem pharmaceuticals using ultrasound/Fenton processes. Box–Behnken design with four variables (initial pH (3, 4 ,5), Fe^{2+} concentration (0.006, 0.008, 0.010 mol/L), mole ratio of H_2O_2 to Fe^{2+} (1:1, 2:1, 3:1), and ultrasound power (400, 450, 500 W)) was employed in this study to determine the most efficient combination of these variables for COD removal. The optimum conditions of initial pH, Fe^{2+} concentration, mole ratio of H_2O_2 to Fe^{2+}, and ultrasound power were found to be 4.04, 0.008 mol/L, 2:1, and 487 W, respectively, for maximum COD removal efficiency (87.9%). A quadratic model was obtained for COD removal efficiency through this design. The experimental values are in good agreement with predicted values and the model was highly significant with the correlation coefficient of 0.999.

Keywords: Response surface methodology; Box–Behnken design; Cephems pharmaceutical wastewater; Ultrasound/Fenton

1. Introduction

Cefoxitin acid was a raw material of semi-synthetic cephalosporin and it is widely used as an antibiotic intermediate. The disposal of industrial pharmaceutical wastewater containing cefoxitin acid poses major problems to aquatic environment. Due to their complicated components, high organic load, toxicity, and persistent characteristics, traditional treatment methods are not sufficient to completely remove the active pharmaceutical ingredients and other wastewater constituents from these waters. It is therefore a great desire to treat such effluent prior to their discharge into receiving water stream. In recent years, a growing body of evidence suggests that the ultrasound/Fenton hybrid method can be an effective process to reduce the COD and enhance the efficiency and economic feasibility of biological techniques [1–6].

Fenton's oxidation using the mixture of ferrous ion (Fe^{2+}) and hydrogen peroxide (H_2O_2) to induce a free radical chain reaction and produce hydroxyl radicals (Eq. (1)) has been shown to be capable of decomposing

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organic chemicals [7–10]. Meanwhile, the ·OH created from Reaction (1) can also oxidize Fe^{2+} to Fe^{3+} in aqueous solution (Eq. (2)) and decrease effect of Fenton's reagent. Excessive Fe^{2+} can however consume some ·OH (Eq. (2)) and decrease effect of Fenton's reagent [11].

$$H_2O_2 + Fe^{2+} \rightarrow {}^{\cdot}OH + OH^- + Fe^{3+} \quad (1)$$

$$Fe^{2+} + {}^{\cdot}OH \rightarrow Fe^{3+} + OH^- \quad (2)$$

When the ultrasound/Fenton hybrid process is applied, synergistic effects occur. Under the influence of ultrasound, Fe^{3+} can degrade a portion of the hydrogen peroxide to form the complex intermediate FeO_2H^{2+} (Eq. (3)) and FeO_2H^{2+} was decomposed into

Table 1
Independent variables and their levels used in the response surface design

	Range and level of actual and coded values				
Variable	Uncoded	Coded	−1	0	+1
pH value	x_1	X_1	3	4	5
H_2O_2/Fe^{2+}	x_2	X_2	1:1	2:1	3:1
Fe^{2+} conc. (mol/L)	x_3	X_3	0.006	0.008	0.010
US power (W)	x_4	X_4	400	450	500

Table 2
The Box–Behnken design and responses

Exp. #	Variable 1 pH	Variable 2 H_2O_2/Fe^{2+}	Variable 3 $[Fe^{2+}]$ Mol/L	Variable 4 US power (W)	Response (η), %
1	3	1:1	0.008	450	48.85
2	5	1:1	0.008	450	52.40
3	3	3:1	0.008	450	51.16
4	5	3:1	0.008	450	50.89
5	4	2:1	0.006	400	46.34
6	4	2:1	0.01	400	54.06
7	4	2:1	0.006	500	72.49
8	4	2:1	0.01	500	74.56
9	3	2:1	0.008	400	48.78
10	5	2:1	0.008	400	49.02
11	3	2:1	0.008	500	70.23
12	5	2:1	0.008	500	73.12
13	4	1:1	0.006	450	50.44
14	4	3:1	0.006	450	51.13
15	4	1:1	0.01	450	53.89
16	4	3:1	0.01	450	55.10
17	3	2:1	0.006	450	50.02
18	5	2:1	0.006	450	49.87
19	3	2:1	0.01	450	52.11
20	5	2:1	0.01	450	55.66
21	4	1:1	0.008	400	48.23
22	4	3:1	0.008	400	49.12
23	4	1:1	0.008	500	71.56
24	4	3:1	0.008	500	73.08
25	4	2:1	0.008	450	85.04
26	4	2:1	0.008	450	85.23
27	4	2:1	0.008	450	86.24
28	4	2:1	0.008	450	85.46
29	4	2:1	0.008	450	85.36

Table 3
ANOVA results for the quadratic equation obtained from design expert 8.0

Source	Sum of squares	Degree freedom	Mean square	F-value	p-value
Model	5,719.83	14	408.56	2,168.41	<0.0001
X_1	8.02	1	8.02	42.56	<0.0001
X_2	2.18	1	2.18	11.55	0.0043
X_3	52.46	1	52.46	278.42	<0.0001
X_4	1,621.46	1	1,621.46	8,605.79	<0.0001
X_1X_2	3.65	1	3.65	19.36	0.0006
X_1X_3	3.42	1	3.42	18.16	0.0008
X_1X_4	1.76	1	1.76	9.32	0.0086
X_2X_3	0.068	1	0.068	0.36	0.5588
X_2X_4	0.099	1	0.099	0.53	0.4800
X_3X_4	7.98	1	7.98	42.36	<0.0001
X_1^2	1,999.49	1	1,999.49	10,612.17	<0.0001
X_2^2	1,894.42	1	1,894.42	10,054.54	<0.0001
X_3^2	1,632.05	1	1,632.05	8,662.04	<0.0001
X_4^2	389.31	1	389.31	2,066.24	<0.0001
Residual	2.64	14	0.19		
Lack of fit	1.79	10	0.18	0.84	0.6246
Pure error	0.85	4	0.21		
Cor total	5,722.47	28			
R^2 = 0.9995; R^2_{adj} = 0.9991; C.V. = 0.71%					

Table 4
Regression coefficients obtained from statistical analyses

Factor	Coefficient estimate	Degree freedom	Standard error	95% CI low	95% CI high
Intercept	85.47	1	0.19	85.05	85.88
X_1	0.82	1	0.13	0.55	1.09
X_2	0.43	1	0.13	0.16	0.69
X_3	2.09	1	0.13	1.82	2.36
X_4	11.62	1	0.13	11.36	11.89
X_1X_2	−0.96	1	0.22	−1.42	−0.49
X_1X_3	0.93	1	0.22	0.46	1.39
X_1X_4	0.66	1	0.22	0.20	1.13
X_2X_3	0.13	1	0.22	−0.34	0.60
X_2X_4	0.16	1	0.22	−0.31	0.62
X_3X_4	−1.41	1	0.22	−1.88	−0.95
X_1^2	−17.56	1	0.17	−17.92	−17.19
X_2^2	−17.09	1	0.17	−17.46	−16.72
X_3^2	−15.86	1	0.17	−16.23	−15.50
X_4^2	−7.75	1	0.17	−8.11	−7.38

ferrous ion Fe^{2+} and $HO_2^{\bullet}$ (Eq. (4)) [12]. As a result, Fe^{2+} can be reproduced through reactions (Eqs. (1) and (4)), and the efficiency of Fenton chain reactions can be increased.

$$Fe^{3+} + H_2O_2 \rightarrow FeO_2H^{2+} + H^+ \quad (3)$$

$$FeO_2H^{2+} + US \rightarrow Fe^{2+} + HO_2^{\bullet} \quad (4)$$

Because the ultrasound/Fenton is a hybrid process containing multiple variables, it is essential to optimize the reaction conditions to maximize COD removal efficiency. A number of statistically designed experimental models have been applied to optimize the reaction parameters in wastewater treatment systems. Among these methods, response surface methodology (RSM) is a collection of mathematical and statistical techniques based on the fit of a polynomial equation to the experimental data [13–16].

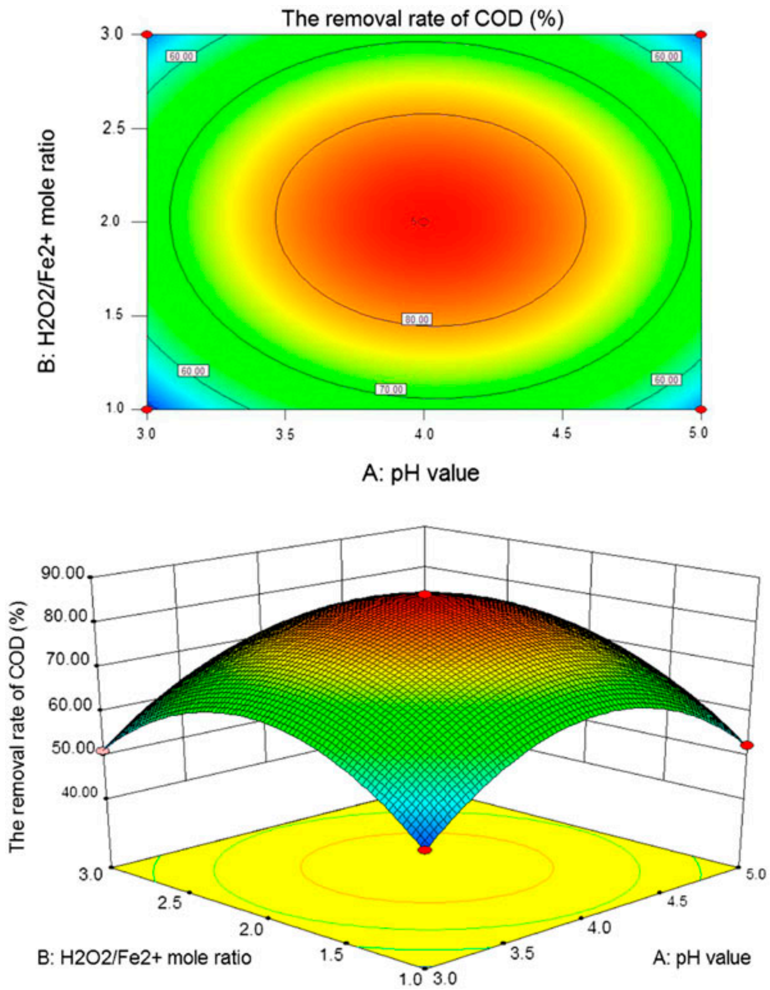

Fig. 1. Contour and response surface plots for initial pH and H_2O_2/Fe^{2+} molar ratio on the COD removal rate.

It has been shown to be an effective approach to investigate the effects of the independent variables and their interactions on the process response [17–19]. RSM has been widely applied for parameter optimization in environmental waste management including dye waste treatments [20], aerobic micro-electrolysis process for mustard wastewater treatment [21], Fenton process on removal of linear alkylbenzene sulfonate [22] and acrylic acid wastewater treatment [23], Fenton/Photo-Fenton process for distillery effluent treatment [24], and ultrasound/Fenton method on dyeing wastewater [25].

To our knowledge, no systematical investigation using RSM has been conducted to optimize the variables of the ultrasound/Fenton process for treatment of cephems pharmaceutical wastewater. In this study, Box–Behnken design with four variables namely initial pH (3, 4, and 5), Fe^{2+} concentration (0.006, 0.008, and 0.010 mol/L), mole ratio of H_2O_2 to Fe^{2+} (1:1, 2:1, and 3:1), and ultrasound power (400, 450, and 500 W) was employed to optimize significant correlation between the effects of these variables on the COD removal efficiency. The model was verified using an experiment quadratic equation, and the agreement between the model predicted values and actual experiment values was evaluated.

2. Materials and methods

2.1. Chemicals and sample preparation

Ferrous sulfate ($FeSO_4{\cdot}7H_2O$) was purchased from Sigma-Aldrich (>99.5% purity). Hydrogen peroxide (H_2O_2) was purchased from Fisher Scientific (30% purity; density 1.13 kg/L). Sulfuric acid (H_2SO_4) and Sodium hydroxide (NaOH) were supplied by Merck (AR).

The wastewater used in this study was obtained from Heibei Jiubai Pharmaceutical Plant, Heibei Province, China. The main components of the

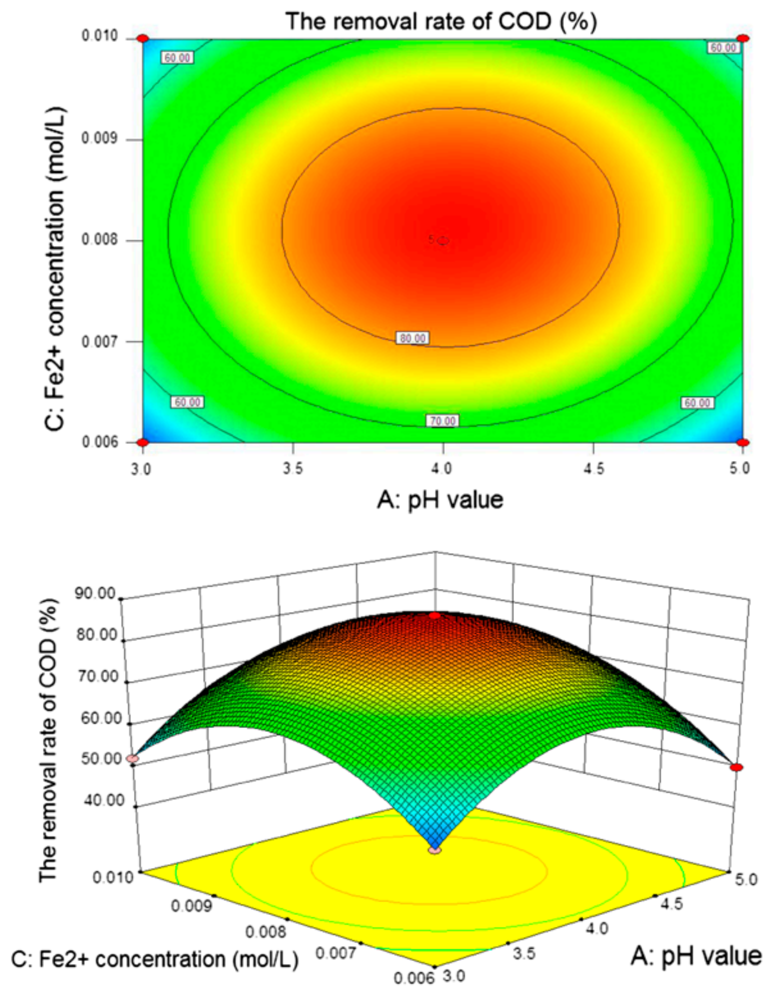

Fig. 2. Contour and response surface plots for Fe^{2+} concentration and initial pH on the COD removal rate.

wastewater were semi-synthesis second-generation cephalosporin and their intermediates, but the original productive materials were also present. Initial characteristic of the wastewater are as follows: yellow color, pH 3.60, extremely high COD value (92.10 g/L). The originated wastewater samples were diluted 200 times using distilled water with the final COD of 460.5 mg/L and were prepared for optimization experiments at ambient room temperature.

2.2. Experimental procedure

A hybrid treatment method was applied to the diluted pharmaceutical wastewater by combining Fenton reaction and ultrasound (US/Fenton). The relative influence of the four test variables initial pH (3, 4, 5), Fe^{2+} concentration (0.006, 0.008, 0.010 mol/L), mole ratio of H_2O_2 to Fe^{2+} (1:1, 2:1, 3:1), and ultrasound power (400, 450, 500 W) on the COD removal efficiency of US/Fenton's oxidation was investigated. The variables and numerical ranges were selected according to our preliminary single factor screening.

Samples' COD was measured according to EPA Method 5220C for the COD range of 1–1,500 mg/L with a 5B-3C instrument (Lianhua Technology, Lanzhou, China), pH measurements were conducted using a pH digital meter (Model PHS-3C, Shanghai Lei-Ci Co., Ltd., China). Suspended solid levels were determined according to EPA Method 2540D.

2.3. RSM optimization and experiment conditions

In this study, we selected Box–Behnken design for the optimization of the ultrasound/Fenton process for the treatment of the cephems pharmaceutical wastewater. This design was applied using Design Expert Software (version 8.0, Stat-Ease Inc., Minneapolis, MN, USA) with four variables at three levels.

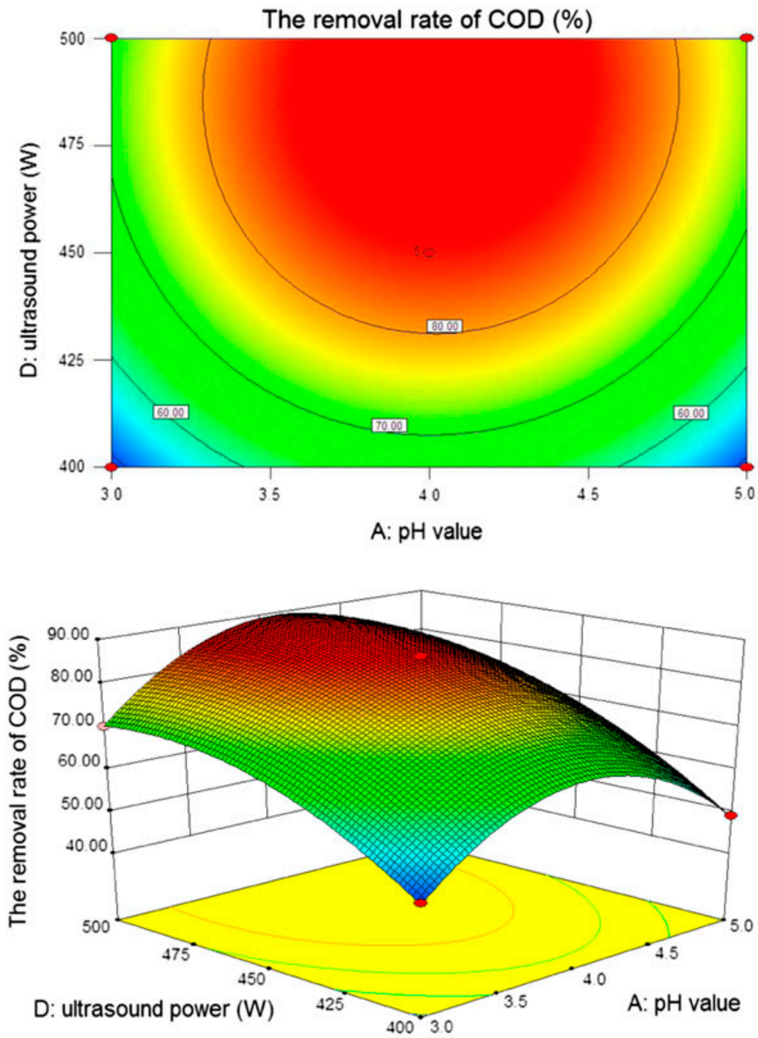

Fig. 3. Contour and response surface plots for initial pH and ultrasound power on the COD removal rate.

Initial pH (3, 4, 5), Fe^{2+} concentration (0.006, 0.008, 0.010 mol/L), mole ratio of H_2O_2 to Fe^{2+} (1:1, 2:1, 3:1), and ultrasound power (400, 450, 500 W) were chosen as the critical variables which were designated as X_1, X_2, X_3, and X_4 and prescribed into three levels, coded +1, 0, and −1 for high, intermediate, and low values, respectively, as shown in Table 1. The actual design of the array of 29 experiments and responses for the treatments of cephems pharmaceutical wastewater by ultrasound/Fenton process are given in Table 2. For statistical calculations, the variables were coded according to the following equation [26]:

$$X_i = (x_i - x_0)/(\Delta x) \quad (5)$$

where X_i is a coded value of the variable; x_i represents the actual value of variable; x_0 denotes the actual value of the x_i at the center point; and Δx stands for the step change of variable. A second-order polynomial model corresponding to BBD was fitted to correlate the relationship between the independent variables and the response to predict the optimized conditions. The four significant variables can be approximated by the quadratic model equation as follows:

$$\eta = B_0 + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_4 + B_{12}X_1X_2 + B_{13}X_1X_3 + B_{14}X_1X_4 + B_{23}X_2X_3 + B_{24}X_2X_4 + B_{34}X_3X_4 + B_{11}X_1^2 + B_{22}X_2^2 + B_{33}X_3^2 + B_{44}X_4^2 \quad (6)$$

where η is the measured response associated with each factor-level combination; B_0 is an intercept; $B_{1\text{–}4}$ are the linear regression coefficients computed from the observed experimental values of η; B_{12}, B_{13}, B_{23}, B_{14}, B_{23}, B_{24}, and B_{34} are the interaction coefficients; B_{11}, B_{22}, B_{33}, and B_{44} are the quadratic coefficients.

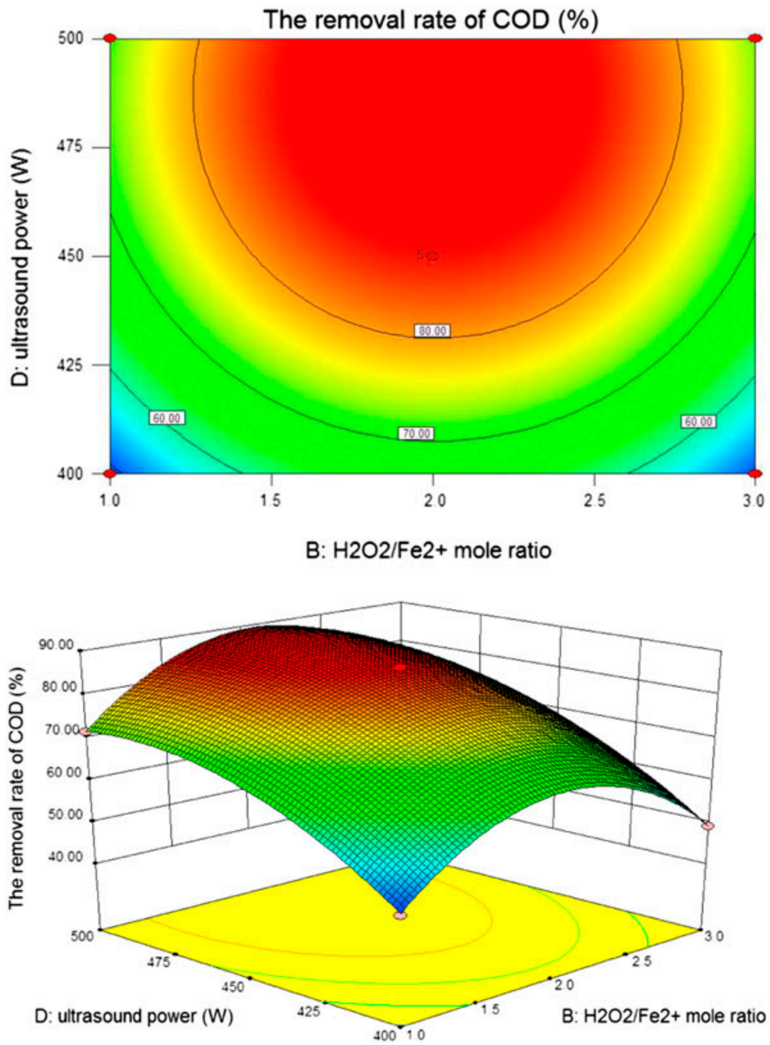

Fig. 4. Contour and response surface plots for H_2O_2/Fe^{2+} molar ratio and ultrasound power on the COD removal rate.

Design Expert software (version 8.0, Stat-Ease, Inc., Minneapolis, USA) was used to analyze the experimental design data and calculate the predicted values.

3. Results and discussion

3.1. Analysis of variance and regression coefficients

US/Fenton is an effective hybrid process to treat industrial wastewater. However, due to presence of multiple competing variables, reaction condition must be thoroughly examined to the optimal treatment conditions.

The results of analysis of variance (ANOVA) are shown in Table 3 and the regression coefficients and their confident levels are summarized in Table 4. As can be seen, the results of the model are statistically significant ($p_{\text{model}} < 0.0001$) and the predictability of the model is within 95% confidence interval. The model also revealed statistically insignificant lack of fit, as is evident from the relative higher p value and the smaller F value (Table 3), which indicate the standard errors of each experiment are insignificant and thus can be ignored. In essence, the equation is highly reliable and this model can be used to optimize the experiment conditions of US/Fenton process and to predict the experiment results for the purpose of actual pharmaceutical wastewater treatment.

The 8 of the 14 factors, X_1, X_3, X_4, X_3X_4, X_1^2, X_2^2, X_3^2, and X_4^2, were found to be significant for the US/Fenton process ($p < 0.0001$, Table 3). Among the variables and their relative levels that were investigated, ultrasound power showed strongest effect on the COD removal efficiency in the ultrasound/Fenton process, followed by Fe^{2+} concentration, initial pH, and mole ratio of H_2O_2 to Fe^{2+}.

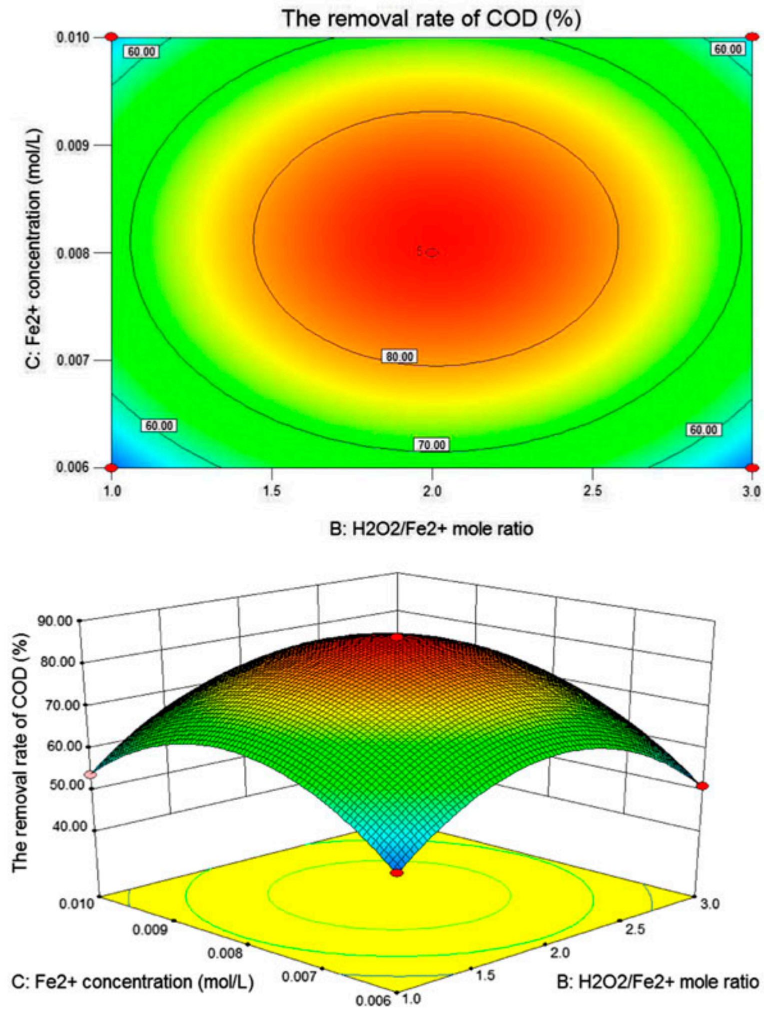

Fig. 5. Contour and response surface plots for H_2O_2/Fe^{2+} molar ratio and Fe^{2+} concentration on the COD removal rate.

By performing multiple regression analysis on the experimental data, the response variable and the test variables were related by the following second-order polynomial equation:

COD removal efficiency:

$$\eta = 85.47 + 0.82X_1 + 0.43X_2 + 2.09X_3 + 11.62X_4 - 0.96X_1X_2 + 0.93X_1X_3 + 0.66X_1X_4 + 0.13X_2X_3 + 0.16X_2X_4 - 1.41X_3X_4 - 17.56X_1^2 - 17.09X_2^2 - 15.86X_3^2 - 7.75X_4^2 \quad (7)$$

3.2. Effects of the four variables on COD removal efficiency and response surface analysis

Using RSM, the combined effect of four variables can be predicted which is difficult to observe in conventional techniques. The interactive influences of these variables on COD removal during ultrasound/Fenton treatment of cephems pharmaceutical wastewater are shown in response surface plots and isotherms obtained by holding the other two variables constant (Figs. 1–6).

Fig. 1 shows the 3D response surface plot of correlations between varying pH and H_2O_2/Fe^{2+} on COD removal efficiency at standardized values of 0.008 mol/L Fe^{2+} and 450 W ultrasound power. This surface plot indicates that the increase in COD removal efficiency with the increase in pH concentration at pH <4; while the COD removal efficiency decreases with pH increase when pH is greater than 4. For different catalyst concentration ratios, the reaction system needs certain pH values for optimal treatment. Varying pH values has a significant influence on COD removal efficiency, which is consistent with the regression ANOVA results. The

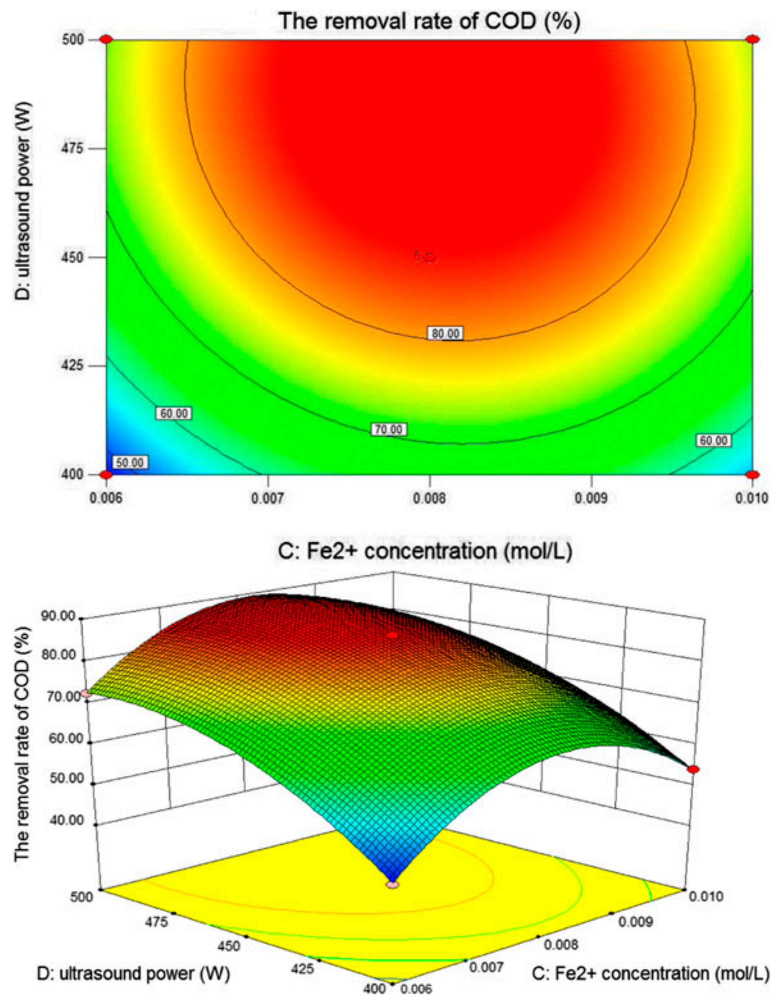

Fig. 6. Contour and response surface plots for Fe^{2+} concentration and ultrasound power on the COD removal rate.

COD removal efficiency exceeded 80.0% at the range 1.41–2.64 mol L^{-1} of the mole ratio of H_2O_2/Fe^{2+} (when pH was from 3.46 to 4.58).

Fig. 2 shows the correlations between Fe^{2+} concentration and pH on COD removal efficiency at the mole ratio of H_2O_2/Fe^{2+} = 2:1 and 450 W ultrasound. As can be seen, the COD removal efficiency increases with the increase of Fe^{2+} concentration at [Fe^{2+}] < 0.008 mol/L; while COD removal efficiency decreases with the increase in Fe^{2+} concentration when Fe^{2+} concentrations are greater than 0.008 mol/L. The COD removal efficiency exceeded 80.0% at the range 0.0071–0.0097 mol/L of Fe^{2+} concentration (when pH was from 3.46 to 4.60).

Fig. 3 depicts the correlations between pH and ultrasound power on COD removal efficiency at the mole ratio of H_2O_2/Fe^{2+} = 2:1 and 0.008 mol/L Fe^{2+}. The 3D surface plot and contour indicate that the COD removal efficiency increases with the increase in ultrasound power when the power is between 400 and 487 W and decreases when the power is between 487 and 500 W. The COD removal efficiency was 80.0% when the ultrasound power was 431 W (pH between 3.23 and 4.82). The system needs an optimum pH value to effectively make use of the catalysts.

Fig. 4 shows the correlations between ultrasound power and H_2O_2/Fe^{2+} at pH of 4.0 and 0.008 mol/L Fe^{2+}. As can be seen, the COD removal efficiency increased when the mole ratio of H_2O_2/Fe^{2+} rose; however, the trend reverses after the H_2O_2/Fe^{2+} passed an optimized value. The COD removal efficiency reached 80.0% when the ultrasound power was 432 W (the mole ratio of H_2O_2/Fe^{2+} between 1.24 and 2.76).

The correlations between Fe^{2+} and H_2O_2/Fe^{2+} at pH of 4.0 and 450 W ultrasound power are illustrated in Fig. 5. COD removal efficiency was found to rise with the mole ratio of H_2O_2/Fe^{2+} at low range

Table 5
Comparison of experimentally obtained and theoretically predicted values for COD removal efficiency

Exp. #	Coded variables X_1	X_2	X_3	X_4	Response: COD removal efficiency (%) Experiment value	Prediction value	Residue
1	−1	−1	0	0	48.85	48.61	−0.24
2	1	−1	0	0	52.4	52.17	−0.23
3	−1	1	0	0	51.16	51.39	0.23
4	1	1	0	0	50.89	51.11	0.22
5	0	0	−1	−1	46.34	46.74	0.4
6	0	0	1	−1	54.06	53.74	−0.32
7	0	0	−1	1	72.49	72.8	0.31
8	0	0	1	1	74.56	74.16	−0.4
9	−1	0	0	−1	48.78	48.38	−0.4
10	1	0	0	−1	49.02	48.7	−0.32
11	−1	0	0	1	70.23	70.3	0.07
12	1	0	0	1	73.12	73.26	0.14
13	0	−1	−1	0	50.44	50.13	−0.31
14	0	1	−1	0	51.13	50.73	−0.4
15	0	−1	1	0	53.89	54.05	0.16
16	0	1	1	0	55.1	55.17	0.07
17	−1	0	−1	0	50.02	50.07	0.05
18	1	0	−1	0	49.87	49.85	−0.02
19	−1	0	1	0	52.11	52.39	0.28
20	1	0	1	0	55.66	55.89	0.23
21	0	−1	0	−1	48.23	48.74	0.51
22	0	1	0	−1	49.12	49.28	0.16
23	0	−1	0	1	71.56	71.66	0.1
24	0	1	0	1	73.08	72.84	−0.24
25	0	0	0	0	85.04	85.47	0.43
26	0	0	0	0	85.23	85.47	0.24
27	0	0	0	0	86.24	85.47	−0.77
28	0	0	0	0	85.46	85.47	0.01
29	0	0	0	0	85.36	85.47	0.11
Optimum condition	0.04	0	0	0.74	87.5	87.9	0.40

(H_2O_2/Fe^{2+} < 2:1), while it decreases when the ratio of these two components exceeds 2:1. The COD removal efficiency reached 80.0% when Fe^{2+} was 0.0071 mol/L (the mole ratio of H_2O_2/Fe^{2+} was between 1.44 and 2.58). Therefore, there is an optimum mole ratio of H_2O_2/Fe^{2+} for COD treatment.

The correlations between Fe^{2+} and ultrasound power on COD removal efficiency are provided in Fig. 6. In this graph, COD removal efficiency is shown to directly correlate with Fe^{2+} concentration at low concentration range ([Fe^{2+}] < 0.008 mol/L), but above this level, the treatment performance decreases. The COD removal efficiency exceeded 80.0% at the range 0.0066–0.0096 mol L^{-1} of Fe^{2+} concentration (when the ultrasound power was 432 W).

In addition, ultrasound power showed a strong positive effect on COD removal efficiency, which is consistent with the regression ANOVA results.

3.3. Optimum conditions and model verification

From the experimental responses, we have calculated the optimum experiment conditions for maximum COD removal using ultrasound/Fenton treatment of cephems pharmaceutical wastewater by performing the stationary point analysis on the 3D surface using partial differential calculus. The optimum conditions of initial pH, Fe^{2+} concentration, mole ratio of H_2O_2 to Fe^{2+}, and ultrasound power were found to be 4.04, 0.008 mol/L, 2:1, and 487 W, respectively, and together they achieved a maximum COD removal efficiency of 87.9% for the test solution. Among all the variables and the ranges that were investigated, ultrasound power showed strongest effect on the COD removal efficiency in the ultrasound/Fenton process, followed by Fe^{2+} concentration, initial pH, and mole ratio of H_2O_2 to Fe^{2+}.

In order to verify the model, the quadratic equation was used to predict the COD removal efficiency using the actual experiment conditions and a comparison between the experimentally obtained and theoretically predicted values was summarized in Table 5. As can be seen, the model can accurately predict the COD removal efficiency, as evidenced by the small residues in Table 5. In addition, an actual cephems pharmaceutical wastewater was treated using ultrasound/Fenton process under above optimum condition to verify the accuracy of the model. As can be seen from Table 5, the actual COD removal efficiency in the verification experiment was 87.5%, which is very close to the prediction value (87.9%). These indicate that the predicted data of the response from the empirical model is in good agreement with the experimentally obtained data.

4. Conclusions

The purpose of this study was to optimize the experiment conditions by using RSM for the treatment of cephems pharmaceutical wastewater by ultrasound/Fenton process. The key findings of this study can be summarized as follows:

(1) Box–Behnken model was used to obtain a quadratic relationship between the response, COD removal efficiency, and four variables (initial pH, Fe^{2+} concentration, mole ratio of H_2O_2 to Fe^{2+}, and ultrasound power). The quadratic model was highly significant ($p < 0.0001$) and showed good regression ($R^2 = 0.9995$ and $R^2_{adj} = 0.9991$). The model also revealed statistically insignificant lack of fit and the experimental values were in good agreement with predicted values.

(2) The effects of four investigated factors including initial pH, Fe^{2+} concentration, mole ratio of H_2O_2 to Fe^{2+}, and ultrasound power on the response, COD removal efficiency did not showed simply linear regression, interactions between variables were also found. Among all the variables and ranges investigated, ultrasound power showed strongest effect on the COD removal efficiency in the ultrasound/Fenton process, followed by Fe^{2+} concentration, initial pH, and mole ratio of H_2O_2 to Fe^{2+}.

(3) Using the actual cephems pharmaceutical wastewater (initial COD of 460.5 mg/L, pH 3.6), the ultrasound/Fenton process was conducted under the optimum condition (initial pH, Fe^{2+} concentration, mole ratio of H_2O_2 to Fe^{2+}, and ultrasound power were 4.04, 0.008 mol/L, 2:1, and 487 W, respectively) to verify the model. The actual COD removal efficiency in the verification experiment was 87.5%, which is very close to the prediction value (87.9%). This indicates that the predicted data of the response from the empirical model is in good agreement with the experimentally obtained data.

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