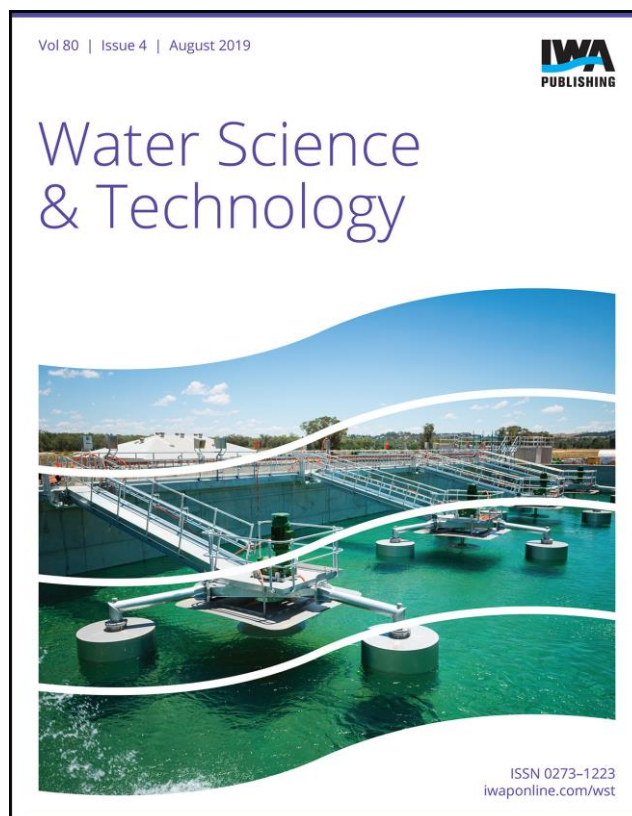


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A rapid and efficient removal approach for degradation of metformin in pharmaceutical wastewater using electro-Fenton process; optimization by response surface methodology

Maryam Dolatabadi and Saeid Ahmadzadeh

ABSTRACT

Presence of emerging contaminants such as pharmaceutical products in aquatic environments has received high concern due to their undesirable effect on wildlife and human health. Current work deals with developing a treatment model based on the electro-Fenton (EF) process for efficient removal of metformin (MET) from an aqueous medium. The obtained experimental results revealed that over the reaction time of 10 min and solution pH of 3, the maximum removal efficiency of 98.57% is achieved where the value of MET initial concentration, current density, and H_2O_2 dosage is set at 10 mg.L^{-1} , 6 mA.cm^{-2} , and $250 \text{ }\mu\text{L.L}^{-1}$, respectively, which is in satisfactory agreement with the predicted removal efficiency of 98.6% with the desirability of 0.99. The presence of radical scavengers throughout the mineralization of MET under the EF process revealed that the generation of $\cdot\text{OH}$ radicals, as the main oxidative species, controlled the degradation mechanism. The obtained kinetics data best fitted to the first order kinetic model with the rate constant of 0.4224 min^{-1} ($R^2 = 0.9940$). The developed treatment process under response surface methodology (RSM) was employed for modeling the obtained experimental data and successfully applied for efficient removal of the MET contaminant from pharmaceutical wastewater as an adequate and cost-effective approach.

Key words | degradation, electro-Fenton, metformin, pharmaceutical wastewater, response surface methodology

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INTRODUCTION

Emerging pollutants such as polycyclic aromatic hydrocarbons (PAHs), pharmaceuticals and personal care products (PPCPs), and heavy metals are a global concern and found extensively in the aquatic medium and water sources, threatening wildlife and human health to a great extent (Deblonde *et al.* 2011; Abdullah *et al.* 2016; Rocha *et al.* 2018). Non-methodical mass prescribing of PPCPs in human and veterinary medicine as well as sunscreens, fragrances and detergents that disrupt the endocrine system have caused great concern for health officials all over the world (Lin *et al.* 2010; Fakhri *et al.* 2018; Jamali-Behnam *et al.* 2018).

Among the most widely used pharmaceuticals, metformin (MET), which is applied as an anti-diabetic medicine for the treatment of type-2 diabetes, is extensively used in every country. MET is also applied for treatment of certain

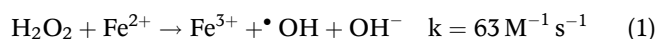
endocrine disorders by modulating the hormone metabolism, and for cancer treatment (Khajuria *et al.* 2018; Niemuth & Klaper 2018). According to the reports, only the absorbed fraction of 10% of this compound is metabolized in the human body and the rest of the MET is excreted unchanged in urine and feces. The statistics show that more than 360 million people all over the world suffer from diabetes and in the last 10 years the prescription rates for metformin in countries such as Germany almost tripled. Moreover, MET has antiobesity, antimicrobial, and antitumor activity and since more than 90% of MET is not metabolized and is excreted from the human body, it is not unexpected that the amount of reported MET in wastewater is about $3.5\text{--}88 \text{ }\mu\text{g.L}^{-1}$ (Trautwein & Kümmerer 2011; Scheurer *et al.* 2012). Therefore, in the current work, the removal of metformin (MET) as one of the

highest prescribed pharmaceuticals by mass, is desired from pharmaceutical wastewater.

To eliminate the propagation of environmental contaminants, several treatment techniques for their efficient degradation have been developed; among them, advanced oxidation processes (AOPs) based on the generation of reactive radicals such as hydroxyl radicals ($\cdot\text{OH}$) have received extraordinary attention recently. Throughout the electro-Fenton (EF) process, hydroxyl radicals, as a non-selective oxidizing agent, are mainly applied for degradation of organic compounds via electrophilic addition and hydrogen atom abstraction reactions during the wastewater treatment process (Chmayssem *et al.* 2017; Lanzalaco *et al.* 2017).

Four modified operating arrangements were developed for the EF process; in the first approach, H_2O_2 and Fe^{2+} as the Fenton reagents were directly added into the reactor. However, in the second approach due to the presence of a sacrificial anode, the ferrous ions were electrochemically generated *in situ* while the H_2O_2 was directly added into the reactor. The third approach deals with *in situ* generation of H_2O_2 in the cathode while the iron catalyst was directly added into the reactor. Finally, in the last approach, both of the Fenton reagents were generated through *in situ* mechanisms in the reactor (Sillanpää *et al.* 2018).

The EF process, as a promising environmentally friendly approach for effective removal of organic emerging contaminants, is considered to have a non-toxic effect which degrades persistent organic pollutants into CO_2 , H_2O , and inorganic ions, expressed by the Fenton reaction as follows (Gu *et al.* 2017):



Throughout the EF process, as a cost-effective wastewater treatment, the ferrous ions which are generated electrochemically from the iron electrode react with hydrogen peroxide (H_2O_2) to produce the hydroxyl radicals ($\cdot\text{OH}$) as the oxidative agents for the degradation of MET in the current work without generating treatment sludge and disposal issues (Liu *et al.* 2017).

The EF process provides a higher rate of contaminant oxidation in concentrated wastewater compared to the other AOPs; thus, in the current study it was employed for MET removal from pharmaceutical wastewater using iron electrodes and the applied procedure in comparison to some other reported investigations provided higher efficiency with lower cost over a satisfactory reaction time (Chmayssem *et al.* 2017; Cotillas *et al.* 2018; Queiroz *et al.* 2019).

The current study aims to evaluate the main effects of operating parameters including initial MET concentration, pH, current density, H_2O_2 dosage, and reaction time, their simultaneous interactions and quadratic effects on the removal efficiency of MET to achieve the optimum treatment condition as well as modeling the proposed EF treatment model. To the best of our knowledge, there are no reports on MET removal from pharmaceutical wastewater using the EF technique with iron electrodes. Moreover, to understand the mechanism of the treatment process, the kinetics of the removal and the effect of radical scavengers was investigated. Finally, the developed treatment model, using central composite design (CCD) under the response surface methodology (RSM), was employed for efficient removal of the MET contaminant from pharmaceutical wastewater.

MATERIALS AND METHODS

Chemicals

Metformin hydrochloride was obtained from Sigma-Aldrich. Analytical grade sulfuric acid, hydrochloric acid, formic acid, sodium hydroxide, acetic acid, n-hexane, 1-butanol, hydrogen peroxide 30%, ethylenediaminetetraacetic acid (EDTA), sodium carbonate, sodium sulfate, sodium chloride, tert-butyl alcohol, and chloroform were purchased from Merck. High-performance liquid chromatography (HPLC) analysis and HPLC grade methanol were purchased from Merck. All solutions were prepared by distilled water using chemicals of at least analytical grade.

Procedure

Cylindrical Plexiglas with a useful volume of 250 mL and two iron plates with immersed dimensions of 30 mm height and 10 mm width were employed for the EF treatment process in batch mode using a magnetic stirrer for continuous stirring. The desired current density was adjusted using a direct current power supply (Megatek 30D5 (0–30 V $\pm$ 0.1 V, 0–5 A $\pm$ 0.1 A)). The inter-electrode distance was kept constant at 3 cm and the pH of the treated solution ranged from 3 to 12, adjusted using a dilute solution of NaOH or H_2SO_4 . The surface of the electrodes was refreshed immediately by immersing them for 5 min in a solution of 15% W/V HCl after each run and afterward was washed and dried for further studies.

The removal efficiency of the EF process was evaluated by a Knauer Smartline HPLC system equipped with an ODS

analytical column (250 mm length, 4.6 mm i.d., and 5 μm particle size) employing isocratic elution of methanol and water (65:35) with a flow rate of 1 mL.min⁻¹, and temperature kept at 25 °C. The wavelength of the UV detector was set at 235 nm (Tache *et al.* 2001). To calculate the removal efficiency of the EF process, the following equation was employed:

$$\% \text{Removal MET} = \frac{C_0 - C_t}{C_0} \times 100 \quad (2)$$

C_0 and C_t (mg.L⁻¹) denote the concentration of MET before the EF process and at time t , respectively.

Central composite design approach

To optimize the value of the operating parameters that affect the degradation of MET under the EF process by the minimum number of experimental runs, CCD under the RSM category was employed using Design Expert 7[®]. Moreover, it provides useful information on the effect of each independent process parameter by itself as well as the interactions between these parameters. In the current work, CCD deals with optimizing the variables including the initial MET concentration (10–50 mg.L⁻¹), current density (2–10 mA.cm⁻²) and H₂O₂ dosage (100–400 $\mu\text{L.L}^{-1}$) for modeling of the applied EF process and statistical analysis of its removal efficiency. The actual value of the three mentioned independent variables with five levels of CCD approach ($-\alpha$, -1 , 0 , $+1$, $+\alpha$) are listed in Table 1.

To obtain an appropriate approximation for the dependence between the removal efficiency, as the model response, and the main parameters, the following second-order polynomial equation was employed (Najafpoor *et al.*

2016; Ghaedi *et al.* 2018).

$$Y = \beta_0 + \sum_{i=1}^n \beta_i X_i + \sum_{i=1}^n \beta_{ii} X_i^2 + \sum_{i=1}^{n-1} \sum_{j=i+1}^n \beta_{ij} X_i X_j \quad (3)$$

Y denotes the removal efficiency as the response of the model, β_i denotes the linear coefficient, β_{ii} denotes the quadratic coefficient, and β_{ij} denotes the interaction coefficient. X_i and X_j denote the independent coded variables. The 3-D plot was employed for depicting the interaction effect of the main variables on the removal efficiency of MET throughout the EF process. The adequacy and accuracy of the developed model was assessed by the regression coefficient (R^2) and the other factors attained from analysis of variance (ANOVA) such as F -value, P -value ($P < 0.05$) and lack-of-fit of the model. Moreover, Pareto analyses were employed to assess the effect of the main variables on the removal efficiency of the developed model.

RESULTS AND DISCUSSION

Effect of initial solution pH and reaction time

The effect of initial solution pH on the removal efficiency of MET was investigated. It provided valuable information on the mechanism of contaminant degradation throughout the EF process. Therefore, initial MET concentration, current density, and H₂O₂ dosage were kept constant at 30 mg.L⁻¹, 5 mA.cm⁻², and 200 $\mu\text{L.L}^{-1}$, respectively, while the initial solution pH was varied from 2 to 11. According to Figure 1, which demonstrates the relationship between

Table 1 | Codes and levels of experimental parameters applied for developing of MET degradation process

Coded variables (X_i)	Factors (U_i)	Experimental field				
		$-\alpha$	-1 level	0	$+1$ level	$+\alpha$
X_1	A: initial MET concentration (mg.L ⁻¹)	10	18	30	41	50
X_2	B: Current density (mA.cm ⁻²)	2	3.6	6	8.3	10
X_3	C: H ₂ O ₂ dosage ($\mu\text{L.L}^{-1}$)	100	160	250	340	400

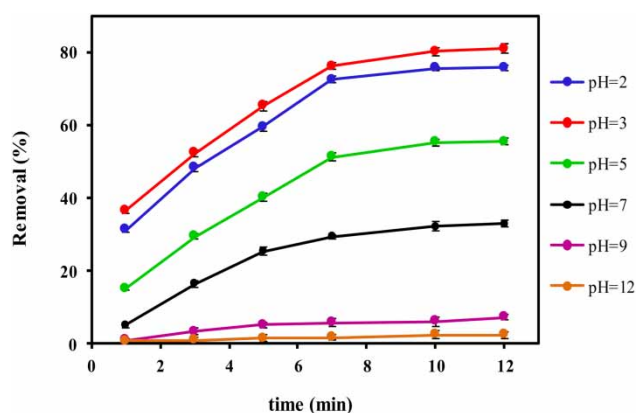


Figure 1 | The effect of pH solution on the degradation of MET throughout EF process.

the pH and removal efficiency, it is concluded that the highest removal efficiency of 81.4% achieved at the initial solution pH of 3 within the reaction time of 10 min, which is in accordance with the optimal pH of 2.5–3.5 for Fenton processes (Nidheesh & Gandhimathi 2012; Ahmadzadeh *et al.* 2015b).

As seen from Figure 1, the removal efficiency of the EF process within the reaction time of 10 min at solution pH of 2, 3, 5, 7, 9 and 11 was 75.7%, 81.4%, 55.4%, 33.8%, 7.4%, and 2.1%, respectively. The superior MET degradation at a solution pH of 3 could be attributed to the efficient decomposition of H_2O_2 that generated the desired active $\cdot\text{OH}$ radicals. However, the observed decrease in removal efficiency for solution pH higher than 3 is ascribed to hydroxyl radicals quenching by the peroxide molecules as expressed by the following equations:



As seen from Equation (4), the hydroperoxyl radicals, $\text{HO}_2\cdot$ with lower oxidation potential ($E_0 = 1.7 \text{ V}$) compared to hydroxyl radicals, $\cdot\text{OH}$ ($E_0 = 2.8 \text{ V}$) are generated. Moreover, it would be worthwhile adding that the acidic condition resulted in loss of both H_2O_2 and $\cdot\text{OH}$ radicals due to the scavenging process, as expressed below:



As seen from Equation (7), in the acidic condition some of the generated $\cdot\text{OH}$ radicals were scavenged by the H^+ , which resulted in reduction of the available hydroxyl radicals for the degradation of MET. Moreover, the electrophilic species of H_3O_2^+ deter the H_2O_2 activity to react with ferrous ions to generate hydroxyl radicals (Asadollahzadeh *et al.* 2014; He *et al.* 2018). Therefore, the solution pH of 3 and a reaction time of 10 min were chosen as the optimum acidic condition for further studies.

RSM developed treatment model

According to the suggested runs by the developed experimental design model, the treatment process was conducted and the removal efficiency for all experiments is summarized in Table 2 where it ranged between 50.3–98.5% at the stated conditions.

The regression relationship between the parameters of the developed quadratic model is expressed as below:

$$\begin{aligned} \text{Removal MET (\%)} = & 88.02 - 7.46X_1 + 6.18X_2 \\ & + 9.05X_3 + 4.95X_2X_3 - 8.82X_2^2 \\ & - 8.51X_3^2 \end{aligned} \quad (8)$$

X_1 , X_2 , and X_3 denote the initial MET concentration, current density, and H_2O_2 dosage, respectively. The removal efficiency of 88.02%, as the intercept of the developed regression equation, denotes the average value of MET removal while all the mentioned parameters are kept constant at their center points.

As seen from Equation (8), the current density (X_2) and the H_2O_2 dosage (X_3) with the higher positive coefficients revealed a synergistic effect on the removal efficiency as the response of the model (Y). This means that by increasing the value of the mentioned variables, the response value is increased. In contrast, the negative sign of the other terms revealed their antagonistic effects; this means that by increasing their value, the response value decreased. On the other hand, graphical Pareto analysis was plotted to demonstrate the contribution effect of each operating parameter on the removal efficiency of MET as the response of the developed model according to the following equation (see Figure 2) (Ranjbar *et al.* 2016; Ahmadzadeh *et al.* 2017):

$$P_i = \frac{b_i^2}{\sum b_i^2} \times 100 \quad (i \neq 0) \quad (9)$$

From the obtained Pareto chart it was concluded that X_3 (H_2O_2 dosage) revealed the highest impact on the MET removal progress with a contribution of 23.37%. However, X_1 and X_2 revealed lower contributions of 15.88% and 10.9, respectively (see Figure 4). Additionally, the contributions of quadratic effects of main operating parameters (X_2^2 and X_3^2) on the MET removal efficiency was found to be 22.20% and 20.66%, respectively. However, the interaction effect of X_2X_3 only revealed a low contribution of 6.99% on MET removal.

ANOVA analysis of the developed treatment model is summarized in Table 3. As can be seen, the value of lack of fit for the model was found to be non-significant. However, the significant values of other relevant parameters confirmed the validity of the developed quadratic model in the current work. Moreover, the adequate amount of 176.13 for F-value and the low P -value of less than 0.0001 indicated that the developed RSM model was highly

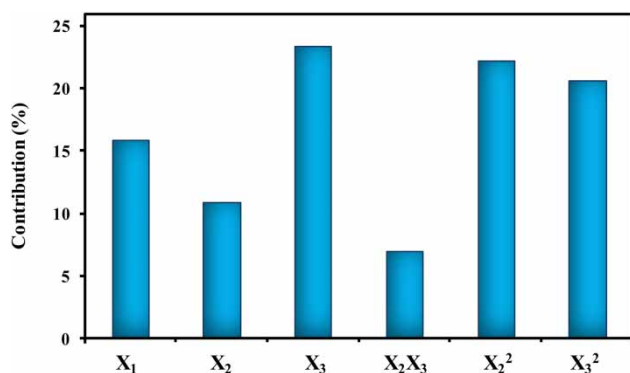
Table 2 | CCD experimental conditions and the obtained values for response

Run order	Actual values			Coded values			MET removal (%)
	A (mg.L ⁻¹)	B (mA.cm ⁻²)	C (μL.L ⁻¹)	X ₁	X ₂	X ₃	
1	18	3.6	339	-1	-1	1	78.24
2	10	6.0	250	-1.68	0	0	98.57
3	18	3.6	161	-1	-1	-1	68.35
4	18	8.4	161	-1	1	-1	70.27
5	30	6.0	250	0	0	0	88.54
6	42	8.4	339	1	1	1	86.15
7	30	10.0	250	0	1.68	0	74.26
8	42	3.6	339	1	-1	1	62.04
9	30	6.0	250	0	0	0	89.35
10	30	6.0	400	0	0	1.68	76.87
11	42	3.6	161	1	-1	-1	52.85
12	30	6.0	100	0	0	-1.68	50.24
13	30	2.0	250	0	-1.68	0	51.12
14	42	8.4	161	1	1	-1	53.04
15	30	6.0	250	0	0	0	88.54
16	30	6.0	250	0	0	0	87.00
17	30	6.0	250	0	0	0	88.30
18	30	6.0	250	0	0	0	90.72
19	50	6.0	250	1.68	0	0	72.95
20	18	8.4	339	-1	1	1	96.25

significant. As can be seen, the parameters of X_1 , X_2 , X_3 , X_2^2 , X_3^2 , and X_2X_3 with P -values of less than 0.05 are significant. The R^2 value for the model was found to be 0.9878, which is satisfactorily close to the ideal model value of 1.

To verify the normality of the data, the predicted values for the removal efficiency according to the developed model were plotted versus the actual obtained values of removal

efficiency (see Figure 3). This revealed great satisfaction, implying that the established model provided accurate and satisfactory results. Moreover, the distribution of the residuals versus probability for the removal efficiency of MET, which is demonstrated in Figure 4, confirmed the normality assumptions and proved that the developed second-order polynomial model with the calculated quadratic and interaction coefficients could be employed for fitting the coded values of the experimental data.

**Figure 2** | Pareto diagram of the main operating parameter effects on the removal efficiency of MET.

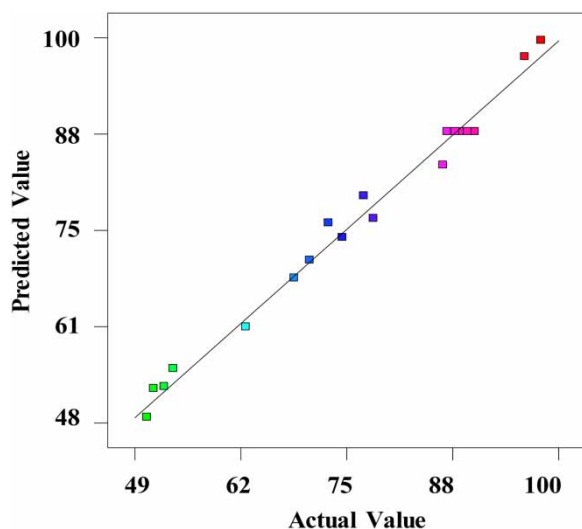
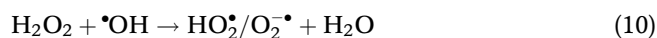
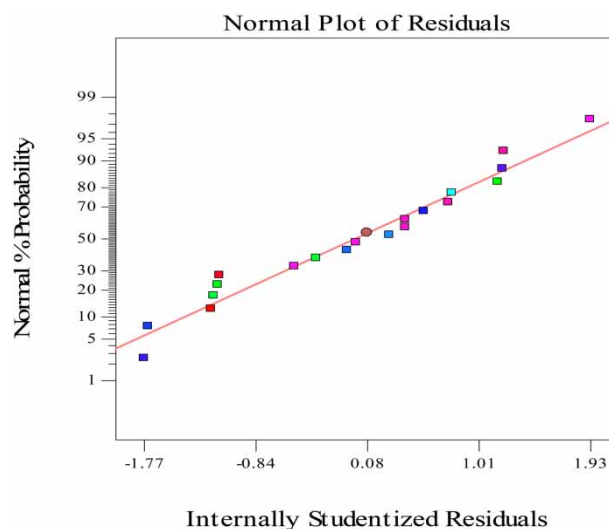
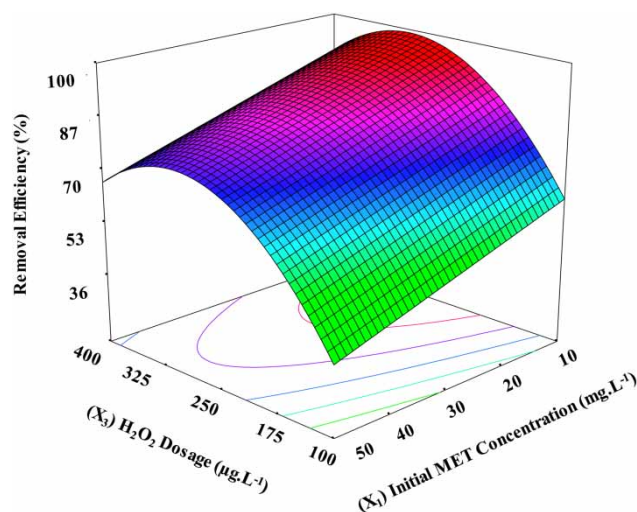
Congruent effect of operating parameters

According to the obtained 3-D surface plot in Figure 5, the congruent effect of H_2O_2 dosage and initial concentration of MET revealed that increasing the H_2O_2 dosage up to 300 $\mu\text{L.L}^{-1}$ resulted in enhancement of removal efficiency of the treatment process; however, at the higher H_2O_2 dosage the removal efficiency diminished, which could be attributed to consumption of the significant fraction of the generated $\cdot\text{OH}$ by the excessive H_2O_2 molecules. Hence, the optimal H_2O_2 dosage of 300 $\mu\text{L.L}^{-1}$ was applied for

Table 3 | ANOVA of the developed MET degradation model

Source	Sum of squares	Degree of freedom (df)	Mean square	F-value	Probability P-value > F
Model	4,602.5	6	767.1	176.1	<0.0001
X_1	760.7	1	760.7	174.7	<0.0001
X_2	521.8	1	521.8	119.8	<0.0001
X_3	1,118.0	1	1,118.0	256.7	<0.0001
X_2X_3	196.0	1	196.0	45.0	<0.0001
X_2^2	1,133.2	1	1,133.2	260.2	<0.0001
X_3^2	1,053.8	1	1,053.8	242.0	<0.0001
Residual	56.6	13	4.4	–	–
Lack of fit	49.7	8	6.2	4.5	0.0574
Pure error	6.9	5	1.4	–	–
Cor total	4,659.1	19	–	–	–
Model summary statistics					
R-Squared (R^2)	0.9878	Adeq precision (AP)		41.98	
Adj R-Squared (Adj. R^2)	0.9822	Coefficient of variance (CV) (%)		2.74	
Pred R-Squared (Pred. R^2)	0.9633	Press		170	

further studies. The observed scavenging effect resulted in the generation of other radicals such as $\text{HO}_2^\bullet$, $\text{O}_2^{\bullet-}$ and $\text{O}_2^\bullet$ with lower activation, as expressed below:

**Figure 3** | The relation between the experimental and the predicted removal efficiency as the response values of MET degradation.**Figure 4** | The normal probability plot of studentized residuals for the developed treatment model.**Figure 5** | The 3-D surface plot of the combined effect of H_2O_2 dosage and initial MET concentration on MET removal efficiency.

Moreover, from Figure 5, it can be concluded that increasing the initial concentration of MET from 18 to 42 mg.L^{-1} revealed a negative effect on the removal efficiency from 95.5% to 80.6% while the current density of 6 mA.cm^{-2} , H_2O_2 dosage of $250 \mu\text{L.L}^{-1}$, and reaction time of 10 min were kept constant at their central point values. This means the number of generated $\bullet\text{OH}$ was not efficient for effective degradation of such a high concentration of MET. Moreover, the observed behavior probably attributed to the formation of some intermediates that are tougher to oxidize compared to MET and required a higher amount of hydroxyl radicals for degradation (Abdallah *et al.* 2017).

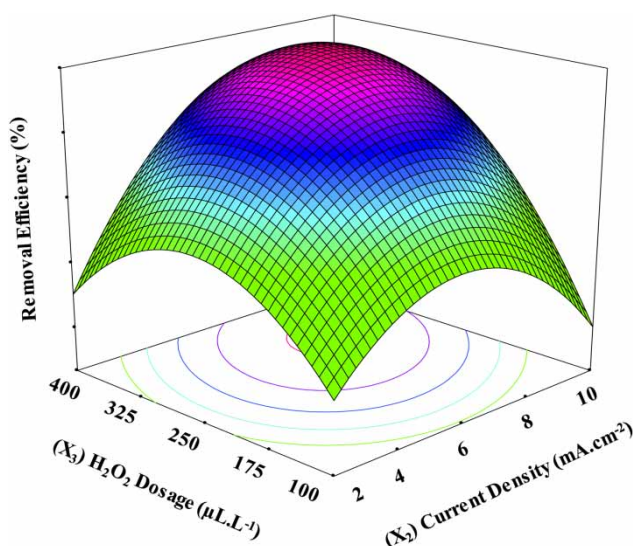


Figure 6 | The 3-D surface plot for the combined effect of H_2O_2 dosage and current density on the MET removal efficiency.

The effect of H_2O_2 dosage and current density (CD) on the removal efficiency are illustrated by the 3-D surface plot (see Figure 6). Increasing the value of current density from 2 to 6.8 mA.cm^{-2} as the key parameter controlling the EF reaction rate resulted in improving the MET degradation efficiency from 56.2% to 91.2%. However, by increasing CD from 6.8 to 10 mA.cm^{-2} , the removal efficiency of MET diminished from 91.2% to 77.6%.

As seen from Equation (12), increasing the current density resulted in an enhancement of metal ion generation on the surface of the sacrificial anode. The extra amount of Fe^{2+} resulted in consuming the hydroxyl radicals as expressed below:



Furthermore, by enhancing the current density, there was an increased chance of some side reactions occurring, such as oxidation of water and generation of some inorganic oxidants, which indirectly affected the MET degradation and reduced the removal efficiency of the treatment process (Cotillas *et al.* 2018).

Optimization of MET degradation process

The optimization criteria in the software were set on 'maximize' for removal efficiency as the response of the developed model and set on 'in range' for MET initial concentration; current density and H_2O_2 dosage were set to achieve the optimal condition throughout the EF process.

According to the obtained results, shown in Table 2, over the reaction time of 10 min and solution pH of 3, the maximum experimental removal efficiency of 98.57% was achieved where the MET initial concentration of 10 mg.L^{-1} , the current density of 6 mA.cm^{-2} , and H_2O_2 dosage of $250 \mu\text{L.L}^{-1}$ were kept constant. On the other hand, the predicted maximum removal efficiency for MET was found to be 98.6% with the desirability of 0.99 theoretically under the following condition: initial concentration of 19.8 mg.L^{-1} , current density of 7 mA.cm^{-2} , and H_2O_2 dosage of $313 \mu\text{L.L}^{-1}$.

Kinetics models of MET degradation

To understand the mechanisms involved throughout the EF process, the kinetics of MET degradation were studied. This provided useful information for designing the forthcoming large-scale treatment equipment. To fit the obtained experimental kinetics data, several models were employed including a first-order and second-order model which defines the kinetics of the degradation process based on the expressed equation as follows (Vatanparast *et al.* 2014; Ahmadzadeh *et al.* 2015a):

$$\ln\left(\frac{C_0}{C_t}\right) = +k_{\text{app}}t \quad (13)$$

$$\frac{1}{C_t} = k_{\text{app}}t + \left(\frac{1}{C_0}\right) \quad (14)$$

C_0 and C_t denote the initial concentration and concentrations at time t of MET. k_{app} denotes the first-order constant of MET degradation throughout the EF process. The kinetic experiment was carried out in the optimum condition of pH 3, initial concentration of 19.8 mg.L^{-1} , current density of 7 mA.cm^{-2} , and H_2O_2 dosage of $313 \mu\text{L.L}^{-1}$ during a reaction time 10 min. The value of k_{app} for the first-order and second-order model were found to be 0.4224 and 0.5904, with correlation coefficients (R^2) of 0.9940 and 0.8412, respectively. It was concluded that the obtained kinetic data were best fitted to the first-order model.

Effect of radical scavengers on MET removal efficiency

Radical trapping experiments were conducted to describe the role of $\bullet\text{OH}$ radicals as the main active oxidant species in the EF treatment mechanism, using two categories of scavengers including inorganic (Na_2CO_3 , Na_2SO_4 , and NaCl) and organic (tert-butanol (TB), EDTA, and chloroform)

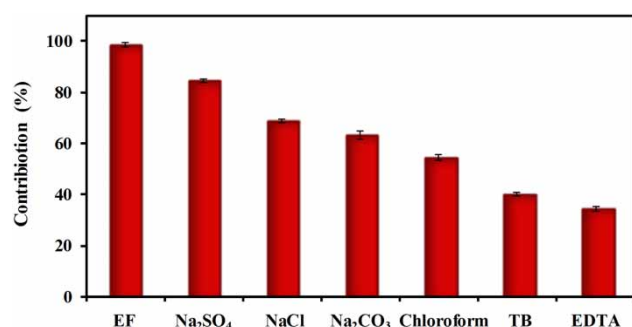
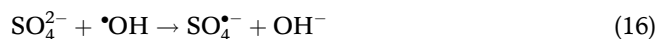
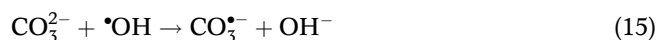


Figure 7 | The effect of different radical scavengers on the MET degradation efficiency.

scavengers with the same concentration of 0.5 M under the optimum treatment condition. As seen in Figure 7, by adding inorganic radical scavengers, including Na₂SO₄, Na₂CO₃, and NaCl, the removal efficiency of the process decreased to 84.5%, 63.2%, and 68.8%, respectively. This could be attributed to the formation of weaker radical species with lower oxidation activity compared to the inhibited $\cdot\text{OH}$ radicals as expressed below:



Moreover, the addition of TB and EDTA resulted in significant diminishing in MET removal efficiency to 40.2% and 34.4%, respectively. This means $\cdot\text{OH}$ radicals, as the main oxidative species, controlled the EF process and revealed higher oxidation activity compared to the other, existing $\cdot\text{OH}$, $\text{O}_2\cdot$, and $\text{HO}_2\cdot$ radicals that were generated after adding the mentioned organic compounds.

Pharmaceutical wastewater treatment

The HPLC technique was employed according to the suggested protocol by Amini et al. for evaluating MET removal efficiency through the pharmaceutical wastewater treatment process. Firstly, the extraction process was conducted using 100 μL wastewater, which was transferred into the microcentrifuge tube. The volume of 1.3 mL binary solution of 1-butanol/n-hexane (50:50, v/v) and 100 μL of NaOH, 8M added and the mixture shook for 2 min. And afterward, the content of the microcentrifuge tube was centrifuged for 2 min at 11,300 g. The separated organic phase was transferred into another microcentrifuge tube and the volume of 100 μL of 1% acetic acid was added and then the obtained solution was mixed using a

vortex-mixer and finally centrifuged for 2 min. The volume of 50 μL of the obtained aqueous phase was injected into the HPLC (Amini et al. 2005). The obtained results revealed that the initial concentration of $1.15 \pm 0.21 \text{ mg.L}^{-1}$ MET in the examined pharmaceutical wastewater samples reached to $0.22 \pm 0.21 \text{ mg.L}^{-1}$ after implementing the EF treatment process under the optimum condition.

CONCLUSION

The presented findings in the current work established that the EF process as a cost-effective and green approach for the treatment of pharmaceutical wastewater provided satisfactory efficiency employing response surface methodology to achieve the optimum condition. The effects of the main operating parameters such as initial solution pH, reaction time, the initial MET concentration, the current density, and H_2O_2 dosage on the MET removal efficiency were investigated. A quadratic polynomial model for efficient removal of MET from pharmaceutical wastewater was developed. The exact mechanism of the treatment process was investigated and the presence of radical scavengers confirmed that the $\cdot\text{OH}$ radicals, as the main oxidative species, controlled the removal process. The obtained kinetics data were best fitted to the first-order kinetic model with the rate constant (K_{app}) of 0.4224 min^{-1} ($R^2 = 0.9940$). The satisfactory proximity of the predicted and the obtained experimental removal efficiency indicated that the developed treatment model was a promising approach for real pharmaceutical wastewater treatment. The obtained results of the present study can be used by the environmental protection agencies and other relevant organizations as well as wastewater treatment units in pharmaceutical manufacturing industries, hospitals, and medical centers.

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DISCLOSURE STATEMENT

All authors declare that they have no competing or no conflict of interests.

COMPLIANCE WITH ETHICS REQUIREMENTS

This article does not contain any studies with human or animal subjects.

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