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DEVELOPING MULTI-CRITERIA DECISION ANALYSIS AND TAGUCHI METHOD TO OPTIMIZE CIPROFLOXACIN REMOVAL FROM AQUEOUS PHASE

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Abstract

In this research, optimization of Homogeneous Fenton process was performed using Multi-Criteria Decision Analysis (MCDA) and Taguchi method to remove Ciprofloxacin (CIP) from an aqueous phase. Analytic Hierarchy Process (AHP) is one of the most comprehensive systems designed for multi-criteria decision making. In this study, paired comparisons based on the AHP method were performed for three criteria including (i) CIP removal, (ii) COD removal and (iii) Sludge to iron ratio (SIR) to select the best catalyst among $FeSO_4.7H_2O$ and $FeCl_2.4H_2O$. Taguchi method was used to optimize parameters and their levels via Minitab16® Software. Influence of different parameters including initial CIP concentration, Fe (II) concentration, H_2O_2 concentration, pH, and reaction time on CIP removal from the aqueous phase were investigated. Using Expert Choice® Software, and based on sensitivity analysis results, importance percentages for $FeCl_2.4H_2O$ and $FeSO_4.7H_2O$ were estimated as 63% and 37%, respectively. Taguchi optimal analysis indicated that a high S/N response ratio may be obtained with an initial CIP concentration of 10 mg/L, Fe^{2+} concentration of 50 mM, H_2O_2 concentration of 20 mM, pH of 3.5, and a reaction time of 20 min; making significance levels of the parameters as 81.63, 76.13, 75.13, 75 and 79.25, respectively. Analysis of variance (ANOVA) under Taguchi method showed that CIP concentration has the most impact on CIP removal with the highest sum of squares and lowest p-values (0.004). The maximum removal efficiency for two objectives, the antibiotic and COD, were 89.5% and 48%, respectively.

Key words: analytic hierarchy process, ciprofloxacin, homogeneous Fenton process, multi-criteria decision analysis, Taguchi method

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1. Introduction

The presence of various pollutants in the aquatic environment has caused the conventional water and wastewater treatment processes not to be able to remove these pollutants. Pharmaceutical compounds are present in water resources, even in small concentrations, their spread quickly and create higher environmental risks (Dirany et al., 2010; Gagnon et al., 2008). A family of antibiotics are Fluoroquinolones, which includes famous antibiotics such as Ciprofloxacin, Ofloxacin and Norfloxacin, broadly used in infection treatment. The presence of fluorine atoms in the structure of these antibiotics has caused them stability, and therefore, their are considered severe environment risks and serious contaminants (Capriotti et al., 2012; Yi et al., 2017).

Ciprofloxacin, known as CIP is a well-known pharmaceutical antibiotic used extensively for disease prevention, treatment of among the most important pollutants in water resources (Rakhshandehroo et al., 2018). Antibiotics have been particularly well considered for antibiotic resistance (Dimitrakopoulou et al., 2012).

Microbial infections, also this antibiotic can be absorbed into the sludge and, if used as a fertilizer, accumulated in the soil and enters the plants (Carabineiro et al., 2011; Hirsch et al., 1999; Hughes

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et al., 2012; Wang et al., 2018; Zhang et al., 2015). The main problem of CIP in the environment is its unsuccessful degredation by conventional water and wastewater treatment technologies and its bioaccumulation in humans. It has been broadly detected in environment such as surface water, groundwater, wastewater, and even plants (Han et al., 2015).

Recent studies show a rising consumption trend for antibiotics, and particularly CIP, hence, its complete degradation has become a important (Guo et al., 2013). Due to poor biodegradability of CIP, it seems essential to develop new time-saving and cost-effective methods to treat and manage pharmaceutical wastewaters in general and antibiotics in particular. Today, one of the best method have been widely utilized as efficient methods for treatment and management of toxic and resisting organic compounds are Advanced Oxidation Processes (AOPs) (Bobu et al., 2008; De Bel et al., 2009). AOPs are simple in principle, and work based on formation of hydroxyl radicals (Grcic et al., 2017; Jiang et al., 2015). As an AOP, Homogenous Fenton processes have been proven to be one of the best methods for control and reduction of organic pollutions, in which inexpensive and environmentally friendly reagents are employed (Biglarijoo et al., 2016). Several studies have been carried out on efficiency of homogenous Fenton process for a variety of pollutants, but one of the major problems of this method is the high amount of sludge production (Alver et al., 2015; Biglarijoo et al., 2016; Wang et al., 2017a, 2017b).

One of the goals of this study is to overcome some of the disadvantages of the Fenton classic method. Taguchi experimental design method often used as a statistical method that allows the optimization of various parameters in different levels with minimal number of experiments (Taheri et al., 2015). This method determines the impact of individual parameters on the contaminant removal, and investigates orthogonal arrays, Signal-to-Noise (S/N) ratio, and Analysis of Variance (ANOVA) (Taheri et al., 2015). One of the most important advantages of Taguchi method is that many factors can be optimized simultaneously and with fewer experimental trials can get good information (Pundir et al., 2016). A literature survey shows that AOPs and Taguchi method have both been used in various fields of wastewater treatment in different industries. For example, (Asghari et al., 2012; Dehghani et al., 2016; Khorsandi et al., 2016; Nandhini et al., 2014).

Researchers often employ Design of Experiment (DOE) to investigate the effect of parameters and their responses (Bhatia et al., 2007).

Although many studies have used AOPs for CIP removal, however, the novelty and main objectives of this study are (i) Evaluate a Multi-Criteria Decision Analysis (MCDA) for compare and contrast performance of a conventional catalyst compound ($FeSO_4.7H_2O$) with a other catalyst ($FeCl_2.4H_2O$) in removal of CIP from an aqueous phase with considered multiple-objective (ii) To evaluate practicability of COD removal when using Homogenous Fenton process, and (iii) To determine optimum values of parameters based on Taguchi method with the aim of improving degradation quality and reduce costs and experimental times.

2. Experimental

2.1. Chemical and reagents

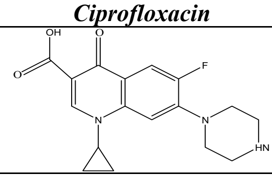
CIP (98%) was purchased from a local provider, Shiraz Serum Pharmaceutical Company, and distilled water was used as solvent to prepare all solutions. A standard CIP stock solution was prepared by dissolving appropriate quantities of CIP (500 mg/L) with a suitable dilution (of 2ml HCl) in distilled water. Ferrous sulfate ($FeSO_4.7H_2O$), Ferrous Chloride ($FeCl_2.4H_2O$), Sulfuric acid (H_2SO_4 (95–7%)), Sodium hydroxide (NaOH) and Hydrogen Peroxide H_2O_2 (30%) were all purchased from Merck (Germany). General characteristics of CIP are listed in (Table 1).

The flowchart for the methodology proposed in this paper is shown in (Fig. 1).

2.2. Antibiotic detection

In most analytical and research methods, HPLC is used to determine the concentration of CIP residues in solutions. There are also researchers who utilize UV or fluorescence for determination of CIP concentrations (Carlucci, 1998). Recently, some studies have reported employing UV-Visible detection for various contaminants (Ayoub et al., 2010). In the present study, concentration of CIP antibiotic was determined by UV-VIS device**.** Also, COD measurements for input and output were conducted with the spectrophotometer DR 5000 from HACH, by the Standard Method.

Table 1. General characteristics of CIP (Adopted from Xiong et al., 2017)

Properties	***Ciprofloxacin***
Structure	
Molecular structure	$C_{17}H_{18}FN_3O_3$
Molecular mass (g.mol^{-1})	331.35
λ_{max}	277

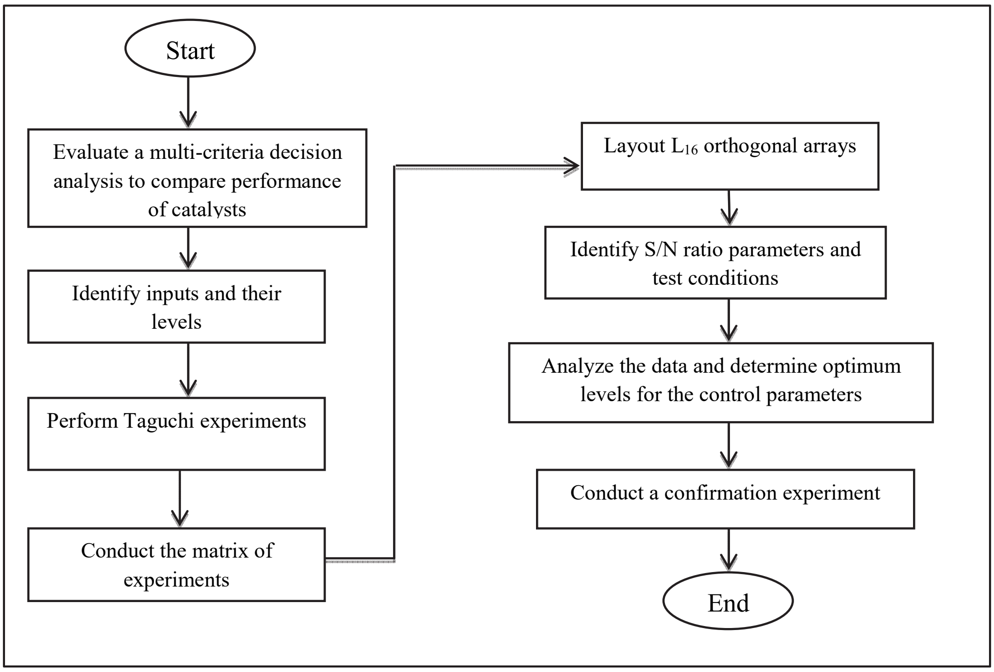


Fig. 1. Flowchart of the methodology utilized for CIP degradation

2.3. Homogeneous Fenton process

In recent years, AOPs have been used to reduce pollutions caused by the presence of pharmaceutical residues in water, without discharging any secondary toxic contaminants to the environment (Garoma et al., 2010). Fenton reaction initiates with addition of both iron and hydrogen peroxide to remove various contaminants (Wang et al., 2010). Significant advantages of Fenton method include high efficiency, biodegradability enhancement, simplicity in operation and flexibility. In conventional Fenton process, H_2O_2 as an oxidant and $FeSO_4.7H_2O$ as a catalyst are both employed, enabling it to treat refractory wastewaters to organic compound at room temperature (Alver et al., 2015). The reactions of Homogeneous Fenton Process are shown in (Eqs. 1-5):

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^- + OH^0 \quad (1)$$

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

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + O_2H^0 + H^+ \quad (3)$$

$$OH^- + H_2O_2 \rightarrow HO_2^0 + H^+ \quad (4)$$

$$H_2O_2 + OH \rightarrow H_2O + HO_2 \quad (5)$$

2.4. Analysis experiments

Solution of CIP showed a maximum absorption peak at 277 nm when scanning the wave length range of 190–600 nm using distilled water. Then, concentrations of CIP were determined using the spectrophotometer DR5000 at an absorbance level of 277 nm. Prior to the measurements, a calibration curve was obtained using the CIP standard with known concentrations. PH measurements from solutions were performed using a pH meter WTW (340i, WTW, Germany). Removal percentages (Re%) was determined using the following (Eq. 6):

$$\text{Re}\ (\%) = 1 - \frac{C_f}{C_0} \quad (6)$$

where: C_0 and C_f are initial and final concentrations of CIP in the solution at the corresponding wavelength λ_{max}, respectively.

COD measurements were performed according to the standard method (Eq. 7):

$$COD\ (\%) = 1 - \frac{COD_f}{COD_0} \quad (7)$$

where: COD_0 and COD_f are initial and final COD values of the solution, respectively (APHA, 1965).

2.5. Multi-criteria decision analysis and design of experiments based on Taguchi method

2.5.1. Analytic hierarchy process (AHP)

MCDA has been increasingly applied in different sciences (Diaby et al., 2013). One of the commonly applied MCDA techniques is Analytic Hierarchy Process (AHP) (Liberatore and Nydick, 2008). To accomplish the first objective, two catalysts ($FeSO_4.7H_2O$ and $FeCl_2.4H_2O$) were used for comparative experiments. In both cases Fe^{2+} concentrations varied at four levels (5, 10, 25 and 50 mM) while other conditions including the initial pH of 3.87, CIP concentration of 90 mg/L, H_2O_2 concentration of 45 mM and the reaction time of 18.5

min were all kept constant. COD and CIP removal rates as well as sludge to iron ratio (SIR) were determined for both catalysts. In this section, to choose between the two catalysts (literally $FeSO_4.7H_2O$ and $FeCl_2.4H_2O$) using AHP methods and considering their advantages and disadvantages Expert Choice® software was utilized. AHP distinguished five phases during the decision-making process; 1) Defining the decision problem to be solved and determining its goals, 2) Identifying and structuring the decision alternatives and criteria, 3) Judging the relative value of alternatives and criteria 4) Calculation of criteria weights and priority option, 5) Perform sensitivity analysis (Hummel et al., 2014; Ghinea et al., 2015). In order to identify and structure the decision hierarchy, goals, criteria and alternatives were chosen as presented in (Fig. 2).

In AHP method, the pairwise comparison is an import step to decide between three criteria and to determine weights of parameters. According to Table 2, higher CIP removal rates, lower SIR and higher COD removal rates were considered as targets. In this study, a new response called SIR is proposed due to its comprehensive concept as follow Eq. 8 (Amiri and Sabour, 2014).

$$Sludge\ to\ iron\ \ (SIR) = \frac{\Pr oduced\ \ sludge\ volume\ \ (gr)}{Added\ \ ferrous\ iron\ (mole)} \quad (8)$$

2.5.2. Design of experimental (DOE) based on Taguchi method

Taguchi method is a robust statistical tool that allows an independent evaluation of the responses, optimizes parameters, and employs orthogonal arrays for experimental design on a real time basis using Minitab or other Softwares (Mohan et al., 2005).

In this method, regarding the signal-to-noise ratio of parameters obtained from orthogonal arrays of the responses are optimized. "Signal" implies the mean value whereas "noise" shows the standard deviation term, and hence, a lowered variability is ensured in the process of maximizing S/N ratio (Ghanim, 2016).

The S/N ratio was used to measure the effect of the response parameters, and to determine the percent CIP removal. In this work, larger S/N ratio was the criteria for determining the optimal combination of parameter levels (according to (Eq. 9):

$$\frac{S}{N} = -10\log\frac{1}{n}\sum_{i=1}^{n}\frac{1}{y^2{}_i} \quad (9)$$

In Eq. (9) y_i and n are the measured response and the number of repetition (2 in this case) for each test, respectively. Taguchi design was adopted according to important three parts; a) planning of the experiments, b) implementing the experiments based on the design table, and c) analyzing and examining the results.

In the present study, studied levels for independent parameters are presented in Table 3. These levels were selected based on the results of the initial experiments and similar experiments in literature (Dehghani et al., 2016).

L_{16} orthogonal array design was required to study the five parameters with four different levels for each parameter. Table 4 shows the Taguchi design for the Homogeneous Fenton process employed to CIP.

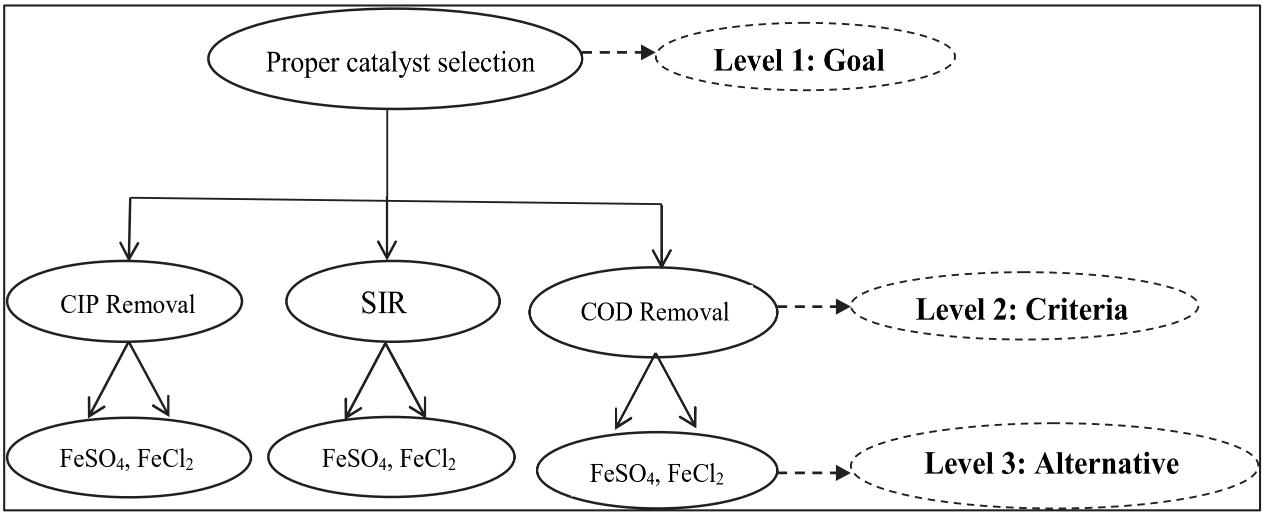


Fig. 2. The analytic hierarchichy process decision structure

Table 2. Summary of pairwise comparisons to decide among three criteria and to determine weights for parameters

Goal	*Criteria*	*Weight of Criteria*	*Alternatives*	*Weights of Alternatives*	*Objective*
Selection of the best Catalyst	CIP* removal SIR Value COD removal	0.769 0.147 0.084	$FeSO_4.7H_20$ $FeCl_2.4H_20$	0.37 0.63	Maximize Minimize Maximize

CIP = Ciprofloxacin

Table 3. Parameters and their levels in the Taguchi design with Homogenous Fenton process

Parameter	*Description*	*Coded Experimental Field*			
		1	*2*	*3*	*4*
A	Concentration of Ciprofloxacin (mg/L)	10	50	100	200
B	Concentration of ferrous ions (mM)	5	10	25	50
C	Concentration of hydrogen peroxide (mM)	10	20	50	100
D	Time (min)	10	15	20	30
E	pH	2	3.5	4.5	5.5

Table 4. Taguchi's L_{16} Orthogonal array and the values for response functions (Re%); CIP and COD removals and S/N ratio

RUN	*CIP (mg/L)*	*Fe^{2+} (mM)*	*H_2O_2 (mM)*	*Time (Min)*	*pH*	*First Run*	*Second Run*	*Average of the two Runs*	*COD removal*	*(S/N) for CIP*
1	1	1	1	1	1	80	76	78	23	37.84
2	1	2	2	2	2	91	88	89.5	36	39.04
3	1	3	3	3	3	89	81	85	45	38.59
4	1	4	4	4	4	78	70	74	27	37.38
5	2	1	2	3	4	68	73	70.5	31	36.96
6	2	2	1	4	3	73	76	74.5	35	37.44
7	2	3	4	1	2	78	84	81	34	38.17
8	2	4	3	2	1	68	74	71	42	37.03
9	3	1	3	4	2	72	83	77.5	48	37.79
10	3	2	4	3	1	77	74	75.5	38	37.56
11	3	3	1	2	4	68	73	70.5	46	36.96
12	3	4	2	1	3	76	69	72.5	44	37.21
13	4	1	4	2	3	65	58	61.5	43	35.78
14	4	2	3	1	4	58	62	58	24	35.27
15	4	3	2	4	1	67	69	68	45	36.65
16	4	4	1	3	2	66	72	69	44	36.78

3. Results and discussion

3.1. Developing a multi-criteria decision analysis to choose the best catalyst type

As shown in Fig. 1, the first stage to optimize the Fenton process was selecting the appropriate catalyst. The comparison between two considered catalyst with three criteria including COD and CIP removal rate, as well as SIR show that efficiency for COD removal rate was slightly higher for $FeSO_4.7H_2O$ whereas SIR production was slightly lower for $FeCl_2$. $4H_2O$.

These results are consistent to the findings of some researchers (Li et al., 2010; Biglarijoo et al., 2016). Based on the results of experiments performed, one may conclude that sludge production for $FeCl_2.4H_2O$ catalyst was lower, and hence, more favorable compared to $FeSO_4.7H_2O$ catalyst.

In Fenton classical process, due to the use of the catalyst of $FeSO_4.7H_2O$, a large amount of sulfate is introduced into the environment, where high sulfate concentrations may cause an unbalance of the natural sulfur cycle (Li et al., 2010; Biglarijoo et al., 2016; Salari et al., 2018a, b). Additionally, acid adjustment and generation of sulfuric acid would cause accumulation of sulfur in the environment and create odor, corrosion and health problems (Ghigliazza et al., 2000; Ghanim, 2016). From this perspective, regarding environmental conditions $FeCl_2$ is a more acceptable catalyst which has lower health risks. Based on these results, this study tried to consider $FeCl_2.4H_2O$ as an alternative catalyst instead of the conventional $FeSO_4.7H_2O$ catalyst. Fig. 3 indicates results achieved by sensitivity analysis for both catalysts using Expert choice software.

As shown, according to sensitivity analysis results, priority percentage for $FeCl_2.4H_2O$ was about 63% while for $FeSO_4$ it was about 37%. In other words, $FeCl_2.4H_2O$ was more acceptable than $FeSO_4.7H_2O$, with a less environmental stability and a lower SIR production.

3.2. Main effect plot

Table 5 shows mean CIP removal (%) for different parameters (A, B, C, D, and E) at different levels (1, 2, 3, and 4). Also, the plot for main effects of the independent parameters in CIP removal using Homogenous Fenton process and Taguchi is shown in Fig. 4. As shown, any increase in CIP concentration leads to an improvement in its removal efficiency. Based on the data obtained from experimental design, H_2O_2 concentration of 20 mM was considered as optimal for CIP degradation, although further increase in hydrogen peroxide concentration led to a slight increase in CIP degradation rate. It was concluded that CIP reduction rate increased with the increase in Fe (II) concentration up to a specific level (5-25 mM), and reduction of the CIP was basically attributed to formation of OH° (Gonzalias et al., 2007; Oliveira et al., 2006). On the other hand, antibiotic decrease was higher at 20 min when the concentrations of CIP and hydrogen peroxide were high probably due to destruction of hydroxyl radical over time. Fundamentally, an optimal reaction time is one of the most important parameters in any chemical reaction (Gonzalias et al., 2007). As shown in the plot and the table, pH = 3.5 is significant probably due to the fact that hydroxyl radical generation is high at acidic pH, resulting in an increase in CIP removal rate.

3.3. Analysis of S/N ratio

As mentioned earlier, the term ‘signal’ to ‘noise’ (S/N) ratio represents the ratio of a desirable to an undesirable value for the output response. The S/N ratios for CIP removal using Homogenous Fenton process are shown in Table 6 and Fig. 5. As shown in Table 6, highest S/N ratios are observed at level 1 for parameters ‘A’, at level 2 for parameter ‘C’ and ‘E’ at level 3 for parameter ‘B’ and ‘D’. Parameter 'A' has the highest and parameter 'C' the lowest rank. Obviously, experiments may optimally be performed at levels with highest S/N ratios.

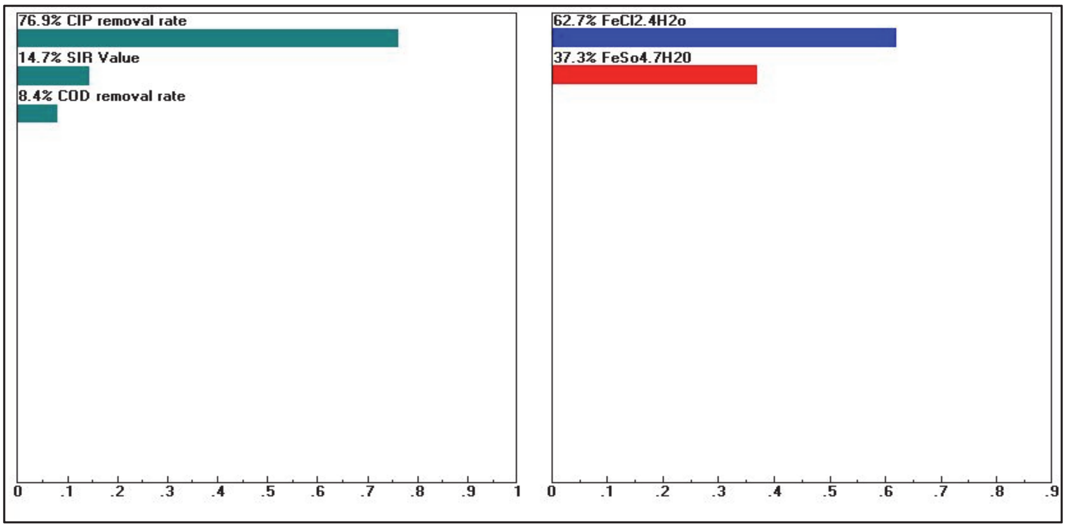


Fig. 3. Sensitivity analysis graph for $FeSO_4.7H_2O$ and $FeCl_2.4H_2O$

Table 5. Mean CIP removal (%) using Homogenous Fenton process

	Parameters				
Level	***A***	***B***	***C***	***D***	***E***
1	81.63	71.88	73.00	72.38	73.13
2	74.25	74.38	75.13	73.13	79.25
3	74.00	76.13	72.88	75.00	73.38
4	64.13	71.63	73.00	73.50	68.25
Delta	17.50	4.50	2.25	2.63	11
Rank	1	3	5	4	2

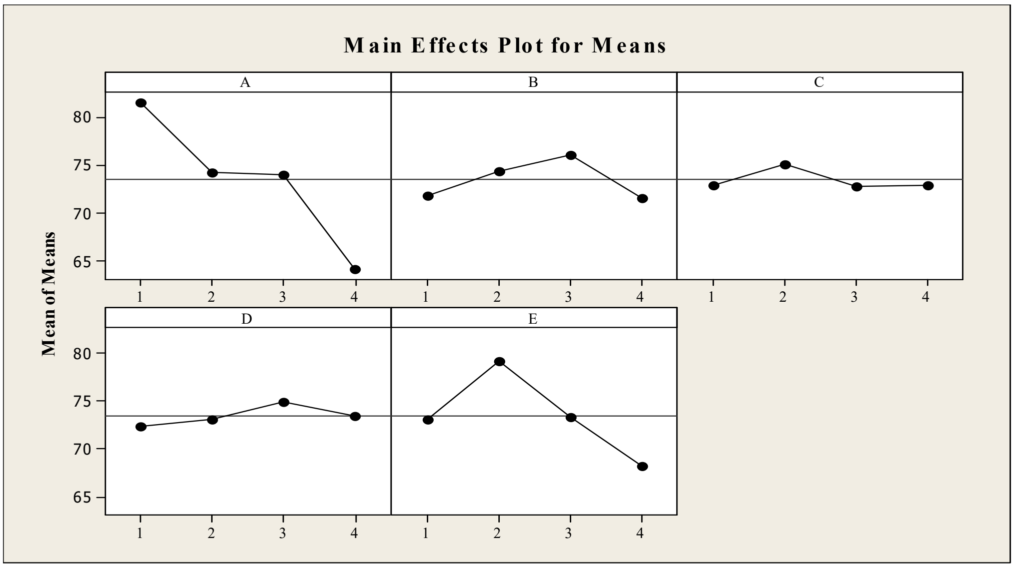


Fig. 4. Main affects plots for independent parameters in CIP removal ((A) CIP concentration; (B) Fe^{2+} concentration; (C) H_2O_2 concentration; (D) Time and (E) pH)

3.4. Analysis of Variance (ANOVA)

In order to study the importance of each parameter statistically analysis of variance (ANOVA) was performed (Zhao et al., 2017; Xu et al., 2017). ANOVA results for CIP removal is presented in Table 7. F-test, as a tool to check which process parameters have significant effects on the CIP removal, was utilized. According to the table, the main and interacting effects of each parameter having $p<0.05$ were considered as potentially notable. The most influential parameter was CIP concentration with a P-value of 0.004 that has the highest corresponding sum of squares compared to other parameters.

Among five considered parameters, CIP seems the most important one probably due to its hydroxyl radical generation and high oxidation capability.

Fig. 6 shows changes in UV-VIS absorbance for different wavelengths under optimal conditions. As it stands, the highest peak was observed for the CIP antibiotic sample at a wavelength of 277 nm, and the sample was left on the stirrer for different times. Peak reduction obviously represents a breakdown and removal of the antibiotic CIP. Therefore, it was concluded that most absorption reduction, and hence CIP removal, occurred 20 minutes after addition of the super acid.

Table 6. S/N ratio for CIP removal in the Homogeneous Fenton process

	Parameters				
Level	***A***	***B***	***C***	***D***	***E***
1	38.21	37.09	37.26	37.12	37.27
2	37.4	37.33	37.46	37.20	37.94
3	37.38	37.59	37.17	37.47	37.25
4	36.12	37.10	37.22	37.32	36.65
Delta	2.09	0.50	0.30	0.35	1.30
Rank	1	3	5	4	2

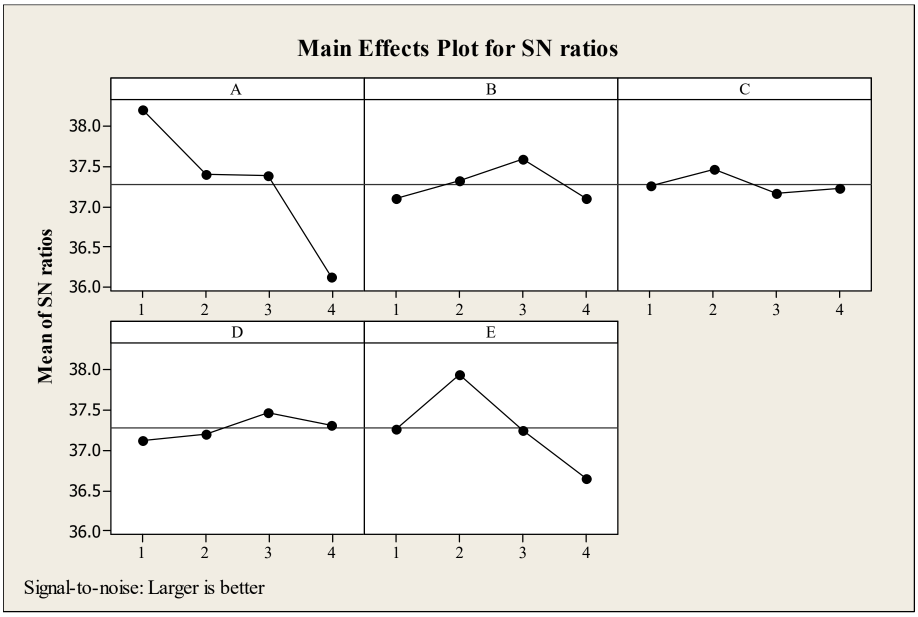


Fig. 5. S/N ratio plot for CIP removal based on the Homogenous Fenton process ((A) CIP concentration; (B) Fe^{2+} concentration; (C) H_2O_2 concentration; (D) Time and (E) pH)

Table 7. Analysis of Variance (ANOVA) results for CIP removal

Parameter	***Degree of freedom***	***Sum of the squares***	***Mean of squares***	***F- Value***	***P- Value***
A	**3**	**618.9**	**206.3**	**7.57**	**0.004**
B	3	55.3	18.4	0.25	0.681
C	3	14.1	4.7	0.06	0.980
D	3	14.6	4.9	0.06	0.978
E	3	243.1	81	1.38	0.295

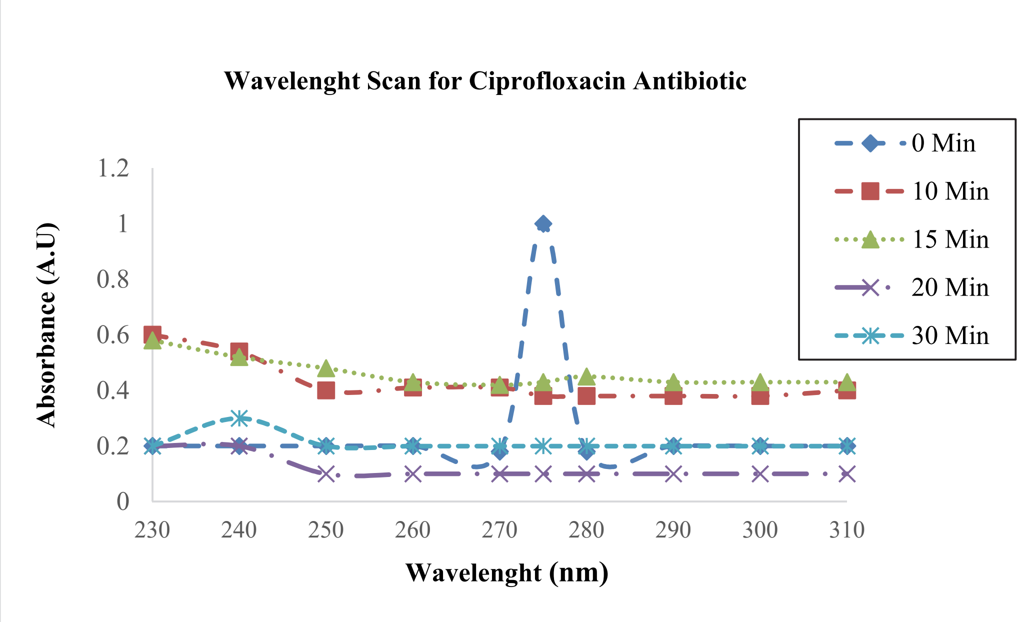


Fig. 6. Wavelengths scan for CIP antibiotic under optimal experimental conditions

4. Conclusions

The main objective of this study was to remove CIP antibiotics by optimizing the homogenous Fenton process using the MCDA and Taguchi method. Criteria considered for paired comparison included (i) CIP removal, (ii) COD removal and (iii) Sludge to iron ratio (SIR) were done to select the best catalyst from $FeSO_4.7H_2O$ and $FeCl_2.4H_2O$ based on an AHP method. Based on the sensitivity analysis results obtain by Expert Choice software, importance for $FeCl_2.4H_2O$ and $FeSO_4.7H_2O$ were 63% and 37%, respectively. $FeCl_2.4H_2O$ was identified as a new favorable catalyst compared to for Fenton process due to its higher removal rate, lower sludge generation, and less environmental risk.

The important advantage of Taguchi method was its time saving by minimization of the number of experimental runs. Taguchi analysis shows that the high S / N response ratio can be obtained with an initial CIP value of 10 mg/L, Fe^{2+} 50 mM concentration, 20 mM H_2O_2 concentration, pH 3.5, and a reaction time of 20 minutes. The significant level structure of the parameters was 81.63, 76.13, 75.13, 75 and 79.25, respectively. Analysis of variance (ANOVA) using Taguchi method showed that CIP concentration had the greatest effect on CIP removal with the highest square and lowest value of p (0.004). Maximum removal efficiency for two purposes, antibiotics and COD, were 89.5% and 48%, respectively.

ANOVA analysis result showed that the most significant parameter was CIP concentration as evidenced by its highest total sum of squares (618.9) and lowest p-value (0.004) compared to other parameter in the process. It may be concluded that Taguchi is a suitable method for experimental design and parameter optimization process for CIP removal. Finally, the results indicated that the proposed method and the use of the proposed catalyst for CIP degradation in pharmaceuticals wastewaters with adequate efficiency.

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