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Oxidative degradation of acetaminophen by continuous flow classical Fenton process

Mehwish Anis*, Sajjad Haydar

Institute of Environmental Engineering & Research (IEER), University of Engineering & Technology (UET), Lahore, Pakistan, Tel. +923214101534, email: mehwish@uet.edu.pk (M. Anis), sajjad@uet.edu.pk (S. Haydar)

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ABSTRACT

Contaminants of emerging concern (CECs) are mainly composed of products used in large quantities in everyday life such as pharmaceuticals, personal care products, surfactants, plasticizers, and different industrial additives. Some of the emerging contaminants are persistent and their complete removal is hard to achieve using conventional wastewater treatment processes. The current study focused on the application of classical Fenton process for the removal of selected pharmaceutical compounds (a sub-category of CECs). Acetaminophen was selected to represent this class of compounds and Fenton oxidation was carried out in a column packed with synthetic Zeolites analcime. Face-centered central composite design strategy was adopted to design and perform the experimentation. Three factors, pH, Fe^{2+}:H_2O_2, and empty bed contact time, were used with three levels of each for experimental design. Quadratic model (with reduced terms) was observed to best fit the experimental data. Experimental results supported with ANOVA indicated that pH and Fe^{2+}:H_2O_2 ratio had significant effect on removal of acetaminophen whereas empty bed contact time did not. pH (3–6) and Fe^{2+}:H_2O_2 ratio (1.5–3) is available to achieve complete removal of acetaminophen. Acidic pH of 3, a limitation of homogeneous Fenton process, could be subdued by increasing the Fe^{2+}:H_2O_2 ratio. The mechanism of removal of acetaminophen were observed to be Fenton oxidation as well as the adsorption on zeolites packed in column.

Keywords: Emerging contaminants; Fenton process; Acetaminophen removal; Response surface; ANOVA; Packed column

1. Introduction

The presence of contaminants of emerging concern (CECs) in municipal wastewater and receiving water has been a growing area of interest for environmental research for the last decade. This is because of their potential impacts on human health and the environment [1,2]. These emerging contaminants mainly consist of products used in large quantities in everyday life, such as human and veterinary pharmaceuticals, personal care products, surfactants, plasticizers, and different industrial additives [3,4].

Although CECs are not new in environment, their detection and analysis was not possible in the past. This is due to their low concentrations and chemical diversity, requiring extremely sensitive and sophisticated analytical equipment for their detection. However, advancement in technology has made this possible now [5].

Emerging contaminants ends up in wastewater through several pathways including the disposal and use of consumer products, toxic spills, and excretion via the urine and feces of those who consume the pharmaceuticals [6]. The human body metabolizes a percentage of each drug taken and expels the rest into urine and feces which finally ends up in the municipal wastewater system [4].

Another source of emerging contaminants is from consumer products such as shampoo, soap, disinfectant washes, and toothpaste which contain biologically active compounds that, after their use, are being released into the municipal wastewater system and ultimately transported to the receiving waters [3,4,6].

*Corresponding author.

Pharmaceuticals and personal care products (PPCPs) are one of the most frequently occurring groups of compounds among thousands of CECs. PPCPs include pharmaceutically active compounds and drugs, and personal care products used in variety of different consumer products and their metabolites [7]. Although most of the pharmaceuticals are easily biodegradable in the environment, some of these drugs and their metabolites are found to be persistent in wastewater treatment plants and the aquatic environment [8]. If these PPCPs are not sufficiently removed in wastewater treatment plant (WWTP), they may enter into drinking water supplies. If an antibiotic enters the drinking water supply, humans can continuously and unknowingly ingest small amounts of the drug. One of the concerns of continuous exposure to an antibiotic is bacterial resistance, which counterattacks the effectiveness of an antibiotic. Strains of resistant bacteria have been found in surface and ground waters around the globe possessing several harmful characteristics [9]. PPCPs have also been found active in the disruption of endocrine systems and thus are included in a group of endocrine disrupting chemicals [7]. Antibiotics, anti-inflammatory drugs, analgesics, contraceptives, antiseptics, fragrances, beta blockers, sunscreen agents etc. are some of the examples of the PPCPs [10–12].

Municipal wastewater treatment plants are not specifically designed to deal with the trace levels of emerging contaminants found in municipal wastewater. Thus, many compounds and contaminants pass through conventional treatment systems without removal [13]. Persistent nature of CEC and inability of conventional wastewater treatment plants for their complete removal has led to use of advanced treatment technologies for their removal [14]. Membrane filtration, nanofiltration, reverse osmosis, membrane bioreactor, activated carbon adsorption, and advanced oxidation processes (AOPs) such as ozonation, Fenton and Fenton-like oxidation, and photo-Fenton process are some of the emerging technologies for the treatment of CEC. Each of them has its own merits and demerits [6,15–17].

Advanced oxidation processes (AOPs) have recently been recognized as one of the successful methods for the destruction of CEC. AOPs rely on the non-selective strong $^{\bullet}OH$ radical for the oxidation and fragmentation of these compounds into simpler molecules. Oxidation through ozone O_3, Fenton reagents i.e. H_2O_2/Fe^{2+}, UV-radiations and various combinations of these three oxidants comprise the AOPs. Ozone, and UV based processes have been known for their efficacy for the removal of many of the pharmaceutical and personal care products (PPCPs), a prominent class of CEC [8,18].

Classical Fenton oxidation is a famous technique used for the degradation of variety of organic contaminants such as phenols, formaldehyde, pesticides, rubber chemicals etc. present in wastewaters. Fenton oxidation depends on the catalytic activity of iron Fe^{2+} to generate hydroxyl radical from hydrogen peroxide [19]. Although numerous studies have been conducted for the removal of several organic contaminants in water and wastewater by classical Fenton oxidation [20–22], little research can be found in literature regarding its utilization for PPCPs removal.

Various modifications have been tested in the Fenton oxidation to improve the removal of PPCPs, however, classical Fenton is not much investigated for the removal of these calcitrant compounds. Electro-Fenton process was used to degrade 17 beta-estradiol from aqueous acetonitrile mixture [23]. Complete degradation of diclofenac was observed in a pilot scale study of photo-Fenton oxidation [24].

A variety of advanced oxidation processes (i.e., O_3/OH^-, Fe^{3+}/H_2O_2, H_2O_2/UV, Fe^{2+}/H_2O_2, Fe^{2+}/H_2O_2/UV and Fe^{3+}/H_2O_2/UV) have been investigated for the oxidative removal of penicillin formulation effluent. Alkaline ozonation and the photo-Fenton's reagents both appeared to be the most promising AOPs in terms of COD (49–66%) and TOC (42–52%) abatement rates [25].

Fenton oxidation was found useful in improving the biodegradability of pharmaceutical wastewater [26]. Furthermore, Fenton oxidation of amoxicillin [27], photo-Fenton oxidation of caffeine [28], bezafibrate, amoxicillin and paracetamol [29], UV-C Fenton and classical Fenton oxidation of paracetamol [30] have been investigated.

Extensive literature review revealed that despite its numerous advantages, classical Fenton oxidation has not been explored fully for its application in PPCPs removal. These include: rapid reaction rates; reduction in toxicity; small foot prints; and complete mineralization of several toxic compounds. This has led to a renewed interest of researchers in the process for PPCPs removal [31].

Furthermore, the classical approach of taking one factor at a time (OFAT) for process optimization usually results in incomplete set of information and hence questions the reliability of the results. With this background, this study was undertaken to explore the potential of classical Fenton oxidation for the degradation of most commonly available over the counter drug, acetaminophen which is used as a pain reliever.

Continuous mode Fenton studies were carried out in glass columns packed with synthetic zeolites. The process conditions were numerically optimized employing face-centered central composite design (FCCCD).

2. Materials and methods

2.1. Preparation of standard and stock solutions

Standard solution of Acetaminophen (100 ppm) was prepared in deionized water. Stock solution of H_2O_2 (1000 mg/L) was prepared using 35% H_2O_2 solution. The working concentrations for further experimentation were obtained by diluting this stock solution to appropriate levels with deionized water. Desired concentrations of $FeSO_4$ solution were also obtained by diluting 1000 mg/L of stock solution of $FeSO_4 \cdot 7H_2O$ with deionized.

2.2. Packed column setup for fenton oxidation studies

The Fenton oxidation was carried out in a glass column having internal diameter of 2.5 cm and a total length of 60 cm. The total volumetric capacity of the column was 19 cm^3. The glass column was packed with synthetic zeolite, analcime, to provide contact time to the reactants for degradation of acetaminophen. The glass column had two inlets, one for mixture of acetaminophen and H_2O_2 and second for iron sulphate solution. The outlet at the bottom of the

column was fitted with a quick fit valve to control outflow. Acetaminophen and the Fenton reagents were pumped to the column using Master Flex peristaltic pumps. The schematic diagram of the setup is shown in Fig. 1.

2.3. Design of experiments and process description

Design Expert 11.0 software employing face-centered central composite design (FCCCD) of Response Surface Methodology was used for design of experiments (DOE). Three variables with three levels of each i.e. pH (3,5,7), contact time (30, 45, 60 min), and Fe^{2+}:H_2O_2 (1:1,1:2,1:3) were selected for DOE which resulted in 20 combinations for experimental runs. The flow rates of mixture of acetaminophen and H_2O_2 and iron sulphate solution were maintained according to Fe^{2+}:H_2O_2 ratio suggested for each combination. The pH was adjusted using 0.1 M H_2SO_4 and 0.1 M NaOH. After each contact time as per the combination, the sample was collected at the outlet of the column. The reaction was immediately stopped by raising the pH of the solution to 10 by adding 1 M NaOH in the sampling vials to cease the H_2O_2 activity.

2.4. Analytical methods

High performance liquid chromatography (HPLC) technique was employed to determine the residual concentration of acetaminophen after each run. Hitachi Elite gradient HPLC system equipped with UV detector L-2420 was used for this analysis. The column used was inertsilODS-3 having dimensions of ID of 4.6 mm × 250 mm. The flowrate was set at 1 ml/min. The temperature of the column was set at 25°C. The mobile phase used for the elution of acetaminophen was methanol/water in 1:3 v/v ratio. The wavelength of 243 nm was used for acetaminophen detection. For this purpose, calibration curve was initially constructed by analyzing the standard solutions of 10, 20, 30, 40, and 50 ppm concentrations of acetaminophen and detecting its absorbance. The residual concentrations of acetaminophen after each run were estimated from the calibration curve.

2.5. Model fitting and analysis of variance

Sequential model fitting was done by Design Expert software to determine the most feasible and the best fit model based on sequential p-value that indicated the significance of sequential addition of terms in the previous model. Analysis of variance (ANOVA) was carried out to determine the statistical significance of suggested model. For ANOVA, the null hypothesis tested was that "all of the regression coefficients are equal to zero". This implied that the suggested model has no predictive capability. The non-zero coefficients indicated that the variable of that coefficient has an impact on the removal efficiency of the acetaminophen.

The objective of ANOVA was to accept or reject the null hypothesis with certain level of confidence i.e. alpha (α) which was set at 0.05. The acceptance and rejection of null hypothesis was based on the comparison of this α value with the p-value obtained through ANOVA. Comparison of F-value and F-critical values also aided in the approval or denial of the null hypothesis. If F-value > F-critical value, null hypothesis can be rejected with at least 95% confidence level.

3. Results and discussion

The removals of acetaminophen for each of the 20 experimental runs at various combinations of pH, contact time and Fe^{2+}:H_2O_2 are presented in Table 1.

It can be deduced from Table 1 that Fenton process is very effective in removal of acetaminophen. In most

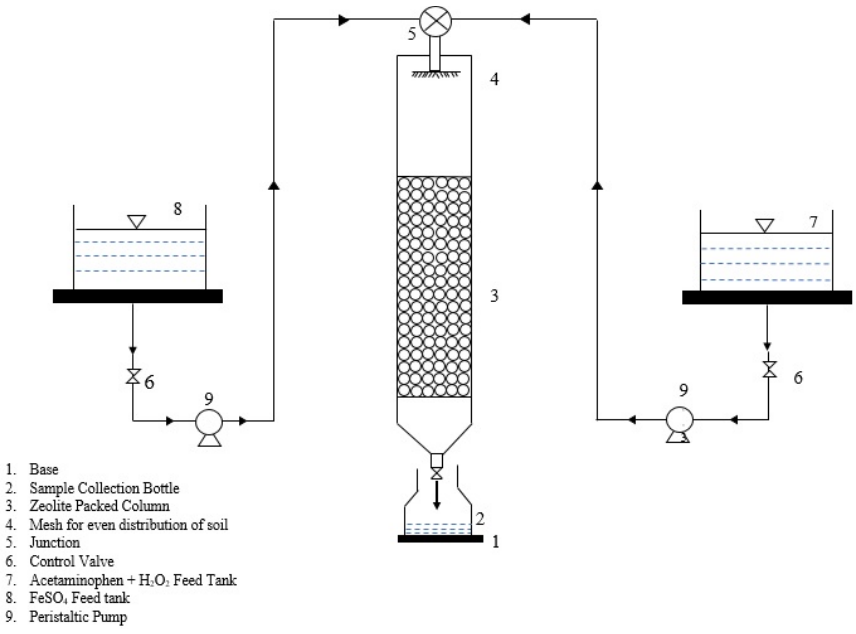

Fig. 1. Schematic diagram of packed column setup for Fenton oxidation.

Table 1
Factor combinations and removal efficiency of acetaminophen

Run	A: pH	B: Empty bed contact time, min	C: Fe^{2+}:H_2O_2	Removal efficiency, %
1	5	60	1:2	97.85
2	5	45	1:2	100
3	3	30	1:1	91.526
4	7	45	1:2	81.44
5	5	30	1:2	100
6	5	45	1:2	100
7	3	60	1:3	100
8	7	30	1:1	68.93
9	5	45	1:2	100
10	5	45	1:2	100
11	5	45	1:1	96.86
12	7	60	1:1	71.24
13	7	60	1:3	83.43
14	5	45	1:2	100
15	5	45	1:2	100
16	3	60	1:1	89.31
17	3	30	1:3	100
18	3	45	1:2	100
19	5	45	1:3	100
20	7	30	1:3	93.64

of experimental runs, removal efficiency of >80% was achieved. It can also be seen that pH and Fe^{2+}:H_2O_2 affected the removal efficiency more as compared to contact time. The most significant factor seems to be Fe^{2+}:H_2O_2.

3.1. Model fitting and analysis of variance

The data obtained of acetaminophen removal were then progressively fitted to various models (i.e. linear, 2FI, quadratic, cubic) to identify the best fit model. The results showed that data were most suitably described by quadratic model. However, model terms were reduced to obtain better statistical results. The equation of the quadratic model in terms of coded factors can be useful for the identification of the relative impact of the factors. This is done by the comparison of the coefficients of each factor. The reduced quadratic model for the removal of acetaminophen in terms of coded factors is given in Eq. (1).

$$R.E = 99.47 - 8.22A - 1.23B + 5.92C + 2.22AC - 11.52A^2 \quad (1)$$

where *A*, *B*, and *C* are pH, empty bed contact time (EBCT) in min, and Fe:H_2O_2 ratio respectively. It is evident from Eq. (1) that Fe:H_2O_2 ratio significantly influences the removal of the acetaminophen (coefficient of +5.92). Furthermore, the pH and higher order pH term i.e. A^2 has a significant negative effect on the removal of the acetaminophen (coefficients of –8.22 and –11.52 respectively).

The reduced quadratic model in terms of actual factors is utilized for the prediction of removal of acetaminophen as is given in Eq. (2).

$$R.E = 50.94 + 22.47pH - .08EBCT + 0.38Fe:H_2O_2 + 1.11pH:Fe:H_2O_2 - 2.88pH^2 \quad (2)$$

ANOVA was performed to ascertain the adequacy of the selected model, ensure the model sufficiency, and identify the significant terms of the model. Results of ANOVA for the removal efficiency data are presented in Table 2.

The F value of the model (41.28) is greater than $F_{critical}$ (2.47) which implied that model is statistically significant to predict removal of acetaminophen. Further, p-value of <0.001 for model suggested that there is only 0.01% chance that such large F value could occur due to noise. Model terms with p-value < 0.05 are considered significant. In this case, model terms A (pH), C (Fe:H_2O_2), AC and A^2 are significant. The maximum allowable difference between the predicted R^2 and adjusted R^2 is 0.2 for the model to be capable of prediction of the response. For the reduced quadratic model, predicted R^2 (0.8111) and adjusted R^2 (0.9138) have a difference of 0.1027.

3.2. Perturbation plot

Perturbation plots indicate the relative significance of each factor. It is plotted by varying one factor over its entire range and removal is plotted while all other factors remain constant at their reference value (coded 0 in Design Expert 11.0). The perturbation plot of three factors is presented in Fig. 2.

The steep slope for A and C indicates that the removal of acetaminophen is more sensitive to the changes in factor A i.e. pH and C the Fe^{2+}:H_2O_2 ratio. pH regulates the generation of hydroxyl radicals through catalytic activity of Fe^{2+} on H_2O_2. Factor B, i.e. empty bed contact time, has relatively flat line indicating insensitivity of the response towards empty bed contact time. The results are similar as shown by statistical analysis. Fenton process takes place quickly. Therefore, the contact time may not be a significant factor in improving removal of acetaminophen. It was confirmed when contact time was increased from 30 to 60 min with no associated increase in the removal of acetaminophen. Hence, perturbation plot is a useful aid in identifying the axis and constants for the contour and 3D surface plots. Consequently A (pH) and C (Fe^{2+}:H_2O_2) were selected as the axes of the contour and 3D plots while the EBCT (due to its insignificant effect on removal) was kept constant.

3.3. Contour and 3-D surface plots

Contour plot was developed, to explain the relationship of removal of acetaminophen with pH and Fe^{2+}:H_2O_2 ratio at empty bed contact time of 30 min and is shown in Fig. 3.

The curvature of contour lines indicated the existence of interaction between pH and Fe^{2+}:H_2O_2. The region of maximum removal (i.e. 100%) extended over pH range of 3–6 and Fe^{2+}:H_2O_2 ratio 1:1.5–3. The contour showing maximum removal started with a combination of Fe^{2+}:H_2O_2 ratio of 2.6 and pH 3 (shown flagged in Fig. 2), resulting in 100% elimination of acetaminophen. The contour then followed a decline in Fe^{2+}:H_2O_2 ratio and minima of Fe^{2+}:H_2O_2 ratio (1:1.6) was observed at a pH of 4.1 to achieve complete removal. The requirement of lowest Fe^{2+}:H_2O_2 ratio

Table 2
ANOVA for reduced quadratic model

Source	Sum of squares	Degree of freedom (df)	Mean square	F-value	p-value	
Model	1743.32	5	348.66	41.28	< 0.0001	Significant
A-pH	674.96	1	674.96	79.9	< 0.0001	
B-Empty bed contact time	15.05	1	15.05	1.78	0.2033	
C-Fe:H_2O_2	350.51	1	350.51	41.49	< 0.0001	
AC	39.32	1	39.32	4.65	0.0488	
A^2	663.48	1	663.48	78.54	< 0.0001	
Residual	118.26	14	8.45			
Lack of fit	118.26	9	13.14			
Pure error	0	5	0			
Cor Total	1861.58	19				

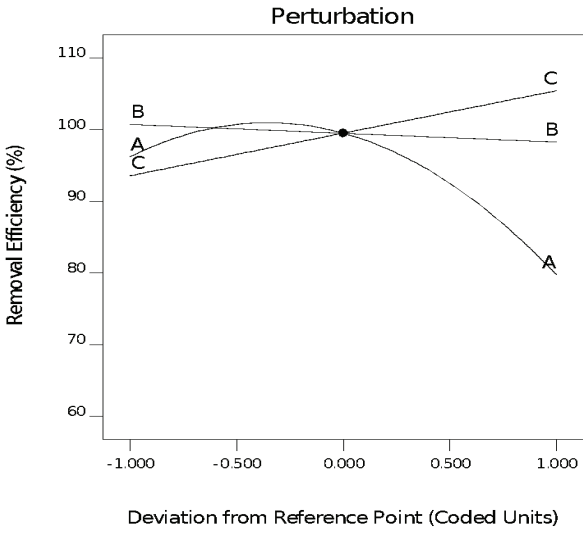

Fig. 2. Perturbation plot.

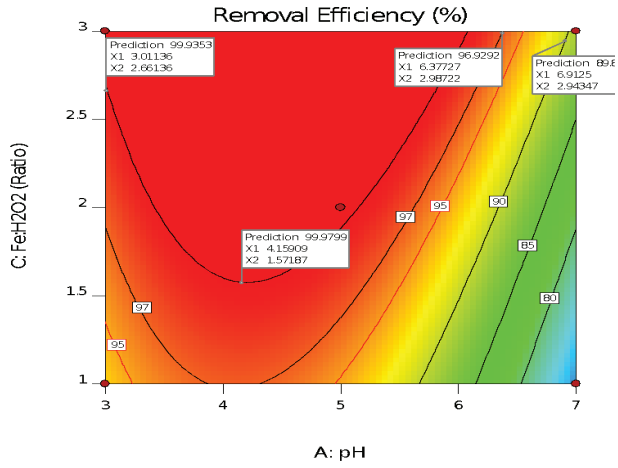

Fig. 3. Contour plot of response surface for acetaminophen removal.

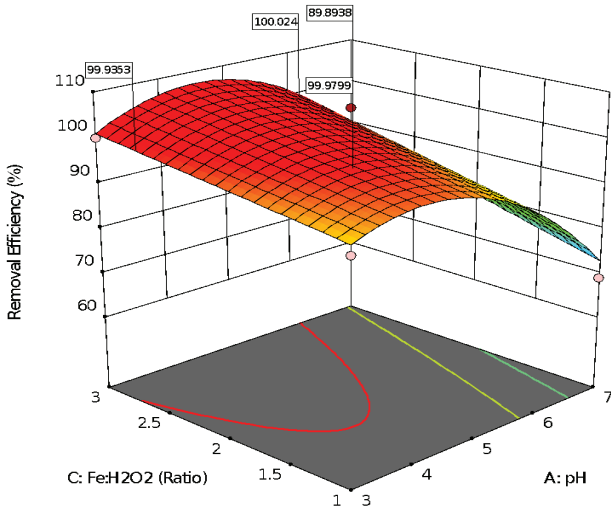

Fig. 4. 3D plot of the response surface of acetaminophen removal.

for a given range could be attributed to the fact that Fenton process is more efficient in the acidic pH range of 3–4. The generation of hydroxyl radicals increases at acidic pH range. Hence, small quantity of Fe^{2+}:H_2O_2 ratio is sufficient for the acceleration of reaction. It was observed that when the pH was increased beyond the minimum pH of 4.1, the Fe^{2+}:H_2O_2 ratio increased. Hence, the same maximum removal resulted at pH 6 and Fe^{2+}:H_2O_2 ratio of 3. Higher amounts of oxidant are therefore required to overcome the decreased oxidation potential of hydroxyl radicals at higher pH. Moreover, at higher pH iron precipitates as $Fe(OH)_3$ and is no more available in free form thereby reducing its catalytic activity. Furthermore, the results emphasized that there existed an interaction between pH and Fe^{2+}:H_2O_2 ratio and their influence on the removal of the acetaminophen which was previously not explored. Fig. 4 presented 3D representation of the design space and response surface of the design.

Fig. 4 indicates the same trend as depicted by contour plot. The two factors i.e. pH and Fe^{2+}:H_2O_2 ratio interacted with each other to influence the removal of acetaminophen.

At lower pH (considered favorable for Fenton oxidation), lower amount of catalyst to oxidant ratio was required. However, to overcome the limitation of acidic pH, it was observed that the requirement of catalyst to oxidant ratio was doubled (from 1.5 to 3) to achieve almost 90% removal at a neutral pH due to the reasons mentioned earlier in section 3.3.

3.4. Numerical optimization

Numerical optimization (NO) of response surface methodology (RSM) provides powerful insight to the most desirable operating conditions within the specified range to achieve the desired removal. Numerical optimization uses the model to explore the factor space for the best trade-offs to achieve multiple goals. The criteria for individual factors (in range) and the response (target 100% removal) were set using the desirability function. RSM identified various combinations of operating factors that satisfied the criteria set for each factor and the response. The targeted removal of 100% (with maximum desirability of 1) was achieved at pH 6, empty bed contact time of 30 minutes, and Fe^{2+}:H_2O_2 ratio of around 3 as shown by the optimization ramps in Fig. 5.

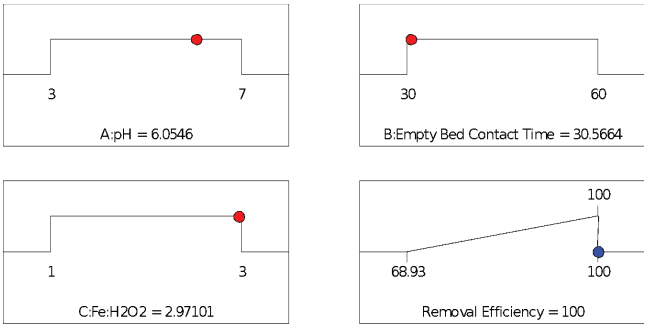

Fig. 5. Optimized combination of factors.

Fig. 6a indicates the contour plot of "desirability" while 6b shows the 3-D surface plot of desirability of the proposed optimum combination of the operating factors. The flagged point described the optimum point signaling the maximum desirability of 1.

3.5. Validation of model result

The confirmatory tests were then performed under optimum operating conditions suggested by numerical optimization to validate the model. Experiments were carried out in triplicate. The model is confirmed, according to Design Expert 11.0, when the average removal of the confirmatory tests lies within the 95% prediction interval (PI). In this study, as the average removal of the confirmatory tests (88.66%) was within the low PI (84.34%) and high PI (95.65%), hence the suggested model was substantiated.

3.6. Adsorptive removal of acetaminophen

The contribution of adsorptive removal of acetaminophen through continuous mode column packed with synthetic zeolite, analcime was also determined. The numerically optimized conditions were set, and 100 ppm solution of acetaminophen was passed through the column. The only difference in the adsorptive removal studies was the absence of Fenton's reagent to observe the acetaminophen removal through adsorption only.

The adsorption of acetaminophen gradually decreased from 30% to 20% over a period of 30 min with an average of 26% as shown in Fig. 7.

Hence, the possible removal mechanisms for acetaminophen in packed column can be the homogeneous Fenton oxidation as well as the adsorption on the synthetic zeolite. The continuous mode operation of Fenton oxidation through packed bed of zeolites, therefore, resulted in enhanced removal of acetaminophen (88.6%) at numerically optimized conditions than Fenton oxidation or adsorption alone.

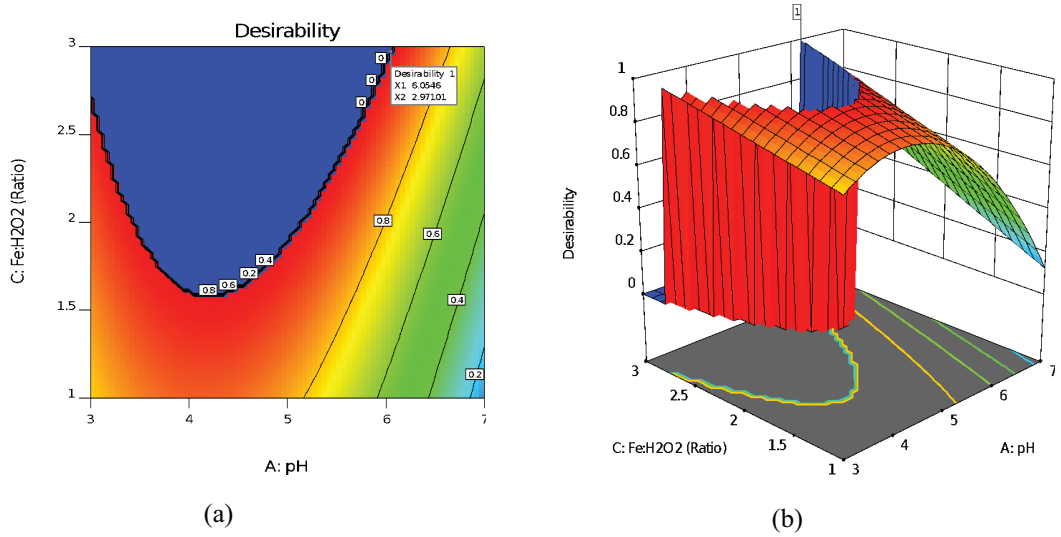

Fig. 6. Contour and surface plots of desirability.

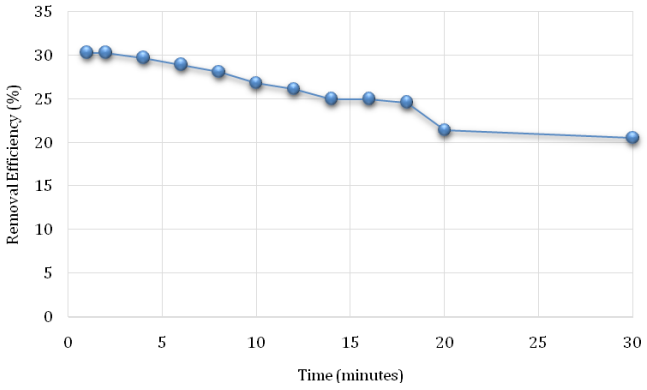

Fig. 7. Adsorptive removal of acetaminophen.

4. Conclusions

Continuous mode homogeneous Fenton process was found successful in efficient removal of acetaminophen with an average removal of 93% and maximum removal of 100%. Face-centered central composite design of experiments (FCCCD) indicated that reduced quadratic model was found to best fit the data. ANOVA explained that the model was significant with model F-value of 41.28 and $p < 0.0001$. pH, Fe^{2+}:H_2O_2 ratio, interaction of pH and Fe^{2+}:H_2O_2 ratio and higher order pH were identified as significant terms affecting the removal of acetaminophen. However, empty bed contact time was not observed to be a significant factor. Contour and 3D surface plots indicated that the extended design space i.e. pH (3–6) and Fe^{2+}:H_2O_2 ratio (1.5–3) is available to achieve complete removal of acetaminophen. Acidic pH of 3, a limitation of homogeneous Fenton process, could be subdued by increasing the Fe^{2+}:H_2O_2 ratio. Moreover, the mechanism for the removal of acetaminophen appeared to be the combination of homogenous Fenton oxidation and adsorption onto synthetic zeolites packed in the column.

Conflict of interest statement

On behalf of all the authors, the corresponding author states that there is no conflict of interest.

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References

[1] S.T. Glassmeyer, The cycle of emerging contaminants, Wat. Res. Impact, 9 (2007) 5–7.
[2] D.E. Vidal-Dorsch, S.M. Bay, K. Maruya, S.A. Snyder, R.A. Trenholm, B.J. Vanderford, Contaminants of emerging concern in municipal wastewater effluents and marine receiving water, Environ. Toxicol. Chem., 31 (2012) 2674–2682.
[3] G. Birch, D. Drage, K. Thompson, G. Eaglesham, J. Mueller, Emerging contaminants (pharmaceuticals, personal care products, a food additive and pesticides) in waters of Sydney estuary, Australia, Mar. Pollut. Bull., 97 (2015) 56–66.
[4] M. Petrović, S. Gonzalez, D. Barceló, Analysis and removal of emerging contaminants in wastewater and drinking water, TrAC, Trends Anal. Chem., 22 (2003) 685–696.
[5] D. Shaver, Sources and fate of emerging contaminants in municipal wastewater, Thesis, Univ. of Guelph, Canada, 2011.
[6] T.A. Ternes, A. Joss, H. Siegrist, Scrutinizing pharmaceuticals and personal care products in wastewater treatment, Environ. Sci. Technol., 38 (2004) 392A–399A.
[7] S. Esplugas, D.M. Bila, L.G.T. Krause, M. Dezotti, Ozonation and advanced oxidation technologies to remove endocrine disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs) in water effluents, J. Hazard. Mater., 149 (2007) 631–642.
[8] K. Ikehata, M. Gamal El-Din, S.A. Snyder, Ozonation and advanced oxidation treatment of emerging organic pollutants in water and wastewater, Ozone Sci. Eng., 30 (2008) 21–26.
[9] L. Hannmann, Removal of ciprofloxacin from water with chemical oxidation, Thesis, Worcester Polytechnic Institute, 2012.
[10] R.L. Oulton, T. Kohn, D.M. Cwiertny, Pharmaceuticals and personal care products in effluent matrices: a survey of transformation and removal during wastewater treatment and implications for wastewater management, J. Environ. Monit., 12 (2010) 1956–1978.
[11] X. Li, W. Zheng, W.R. Kelly, Occurrence and removal of pharmaceutical and hormone contaminants in rural wastewater treatment lagoons, Sci. Total Environ., 445 (2013) 22–28.
[12] J.-L. Liu, M.-H. Wong, Pharmaceuticals and personal care products (PPCPs): a review on environmental contamination in China, Environ. Int., 59 (2013) 208–224.
[13] R. Hirsch, T.A. Ternes, K. Haberer, A. Mehlich, F. Ballwanz, K.-L. Kratz, Determination of antibiotics in different water compartments via liquid chromatography–electrospray tandem mass spectrometry, J. Chromatogr. A, 815 (1998) 213–223.
[14] U.S. EPA, Treating Contaminants of Emerging Concern: A Literature Review Data Base, US Environmental Protection Agency, August 2010, pp. 100.
[15] M. Klavarioti, D. Mantzavinos, D. Kassinos, Removal of residual pharmaceuticals from aqueous systems by advanced oxidation processes, Environ. Int., 35 (2009) 402–417.
[16] S. Mondal, A. Sinha, Treatment of pharmaceutical waste with special emphasis to treatment processes-A review, Int. J. Environ. Res. Develop., 4 (2014) 171–176.
[17] X. Yang, R.C. Flowers, H.S. Weinberg, P.C. Singer, Occurrence and removal of pharmaceuticals and personal care products (PPCPs) in an advanced wastewater reclamation plant, Water Res., 45 (2011) 5218–5228.
[18] T.A. Ternes, J. Stüber, N. Herrmann, D. McDowell, A. Ried, M. Kampmann, B. Teiser, Ozonation: a tool for removal of pharmaceuticals, contrast media and musk fragrances from wastewater, Water Res., 37 (2003) 1976–1982.
[19] D. Bishop, G. Stern, M. Fleischman, L. Marshall, Hydrogen peroxide catalytic oxidation of refractory organics in municipal waste waters, Ind. Eng. Chem. Process Design Develop., 7 (1968) 110–117.
[20] J. Bergendahl, S. Hubbard, D. Grasso, Pilot-scale Fenton's oxidation of organic contaminants in groundwater using autochthonous iron, J. Hazard. Mater., 99 (2003) 43–56.
[21] J.A. Bergendahl, T.P. Thies, Fenton's oxidation of MTBE with zero-valent iron, Water Res., 38 (2004) 327–334.
[22] S.A. Hubbard, Pilot-scale study of Fenton's reagent for the oxidation of organic contaminants in groundwater, 2001.
[23] I. Naimi, N. Bellakhal, Removal of 17β-estradiol by electro-fenton process, Mat. Sci. Applic., 3 (2012) 880–886.
[24] L.A. Pérez-Estrada, S. Malato, W. Gernjak, A. Agüera, E.M. Thurman, I. Ferrer, A.R. Fernández-Alba, Photo-Fenton degradation of diclofenac: identification of main intermediates and degradation pathway, Environ. Sci. Technol., 39 (2005) 8300–8306.
[25] I. Arslan-Alaton, S. Dogruel, Pre-treatment of penicillin formulation effluent by advanced oxidation processes, J. Hazard. Mater., 112 (2004) 105–113.

[26] H. Tekin, O. Bilkay, S.S. Ataberk, T.H. Balta, I.H. Ceribasi, F.D. Sanin, F.B. Dilek, U. Yetis, Use of Fenton oxidation to improve the biodegradability of a pharmaceutical wastewater, J. Hazard. Mater., 136 (2006) 258–265.
[27] F. Ay, F. Kargi, Advanced oxidation of amoxicillin by Fenton's reagent treatment, J. Hazard. Mater., 179 (2010) 622–627.
[28] A.G. Trovó, T.F. Silva, O. Gomes, A.E. Machado, W.B. Neto, P.S. Muller, D. Daniel, Degradation of caffeine by photo-Fenton process: Optimization of treatment conditions using experimental design, Chemosphere, 90 (2013) 170–175.
[29] A.G. Trovó, S.A.S. Melo, R.F.P. Nogueira, Photodegradation of the pharmaceuticals amoxicillin, bezafibrate and paracetamol by the photo-Fenton process—application to sewage treatment plant effluent, J. Photochem, Photobiol., A, 198 (2008) 215–220.
[30] B. Manu, S. Mahamood, Enhanced degradation of paracetamol by UV-C supported photo-Fenton process over Fenton oxidation, Water Sci. Technol., 64 (2011) 2433–2438.
[31] S. Sharma, J. Ruparelia, M.L. Patel, A general review on Advanced Oxidation Processes for waste water treatment, in: Nirma University International Conference, Ahmedabad, Gujarat, 2011.