RAPID DESTRUCTION OF THE NON-STERoidal ANTI-INFLAMMATORY DRUG DICLOFENAC USING ADVANCED NANO-FENTON PROCESS IN AQUEOUS SOLUTION

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ABSTRACT

Introduction: Pharmaceuticals have been attracting the attention of many researchers and are considered as a xenobiotic and emerging pollutant in the environment. Diclofenac (DCF) as a non-steroidal pharmaceutical has been detected in water and wastewater samples more than other compounds due to high consumption and limited biodegradability. The disastrous event of a reduction in the number of vultures due to kidney damage following feeding on the corpse of domestic animals contaminated with DCF and the high bioaccumulation capacity of this drug in the tissue of organisms indicate the significance of this compound as a potential contaminant.

Materials and methods: In this study, advanced Nano-Fenton process (ANF) was applied to remove DCF from aqueous solutions. The full factorial design was applied using R software (3.1.0) to optimize variables. DCF residual concentration was determined by high-pressure liquid chromatography device and the degree of mineralization was determined through TOC analysis.

Results: The mean DCF removal efficiency under different operational conditions and at the time of 1-10 min was obtained to be about 83%. With the increase in the time and H/F along with the reduction in initial concentration of the drug, the response variable (DCF removal) increased.

Conclusion: Our research showed that ANF can be considered as a quick and efficient process for the removal of DCF from wastewater with a significant amount of mineralization.

Keywords: Diclofenac, Pollutant, Advanced Nano-Fenton, water.

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Introduction

In the past two decades, researchers have focused on Pharmaceuticals as a xenobiotic due to their continuous entrance into the environment(1). Although Pharmaceuticals are found in very low concentrations, most of them have caused environmental and health concerns(2). Diclofenac (DCF) with a chemical formula of $C_{14}H_{11}C_{12}NO_2$ is a non-steroidal, analgesic and anti-inflammatory drug, which has been detected in water and wastewater samples more than other compounds due to high consumption) (around 1000 tons/year(3)) and limited biodegradability in wastewater treatment plant(4).

According to the statistics provided by food and drug organization of Iranian health ministry, in 2015 about 37 tons of DCF was produced, imported, and distributed in different ways in the country(5). Due to its complex chemical structure and aromatic rings along with double bonds, the effi-
ciency of wastewater treatment plants in the removal of DCF from wastewater is limited and has been reported to be about 21-69%\(^\text{[6,7]}\). The disastrous event of a reduction in the number of vultures due to kidney damage following feeding on the corpse of domestic animals contaminated with DCF in Pakistan and India\(^\text{[8,9]}\) and the high bioaccumulation capacity of this drug in the tissue of organisms (\(\text{Log } K_{\text{ow}} > 3\)) indicate the significance of this compound as a potential contaminant\(^\text{[10]}\).

As pharmaceuticals show a great resistance to biodegradation, recent research has been focusing on the application of nonbiological methods for their degradation in water and with an emphasis on advanced oxidation processes (AOPs)\(^\text{[11]}\). Among them\(^\text{[12,13,14]}\), use of Fenton process (stage-like addition of \(\text{H}_2\text{O}_2\) and Iron (II) salt to aqueous solutions) has been taken into account thanks to its simple operation, short reaction time, benefiting from flocculation and coagulation process, non-toxicity of its compounds, the possibility to use it across various scales, and economic considerations\(^\text{[15,16,17]}\).

In Fenton process, to produce enough OH free radical, large amounts of catalyst (i.e. \(\text{Fe}^{2+}\)) are required and this is due to the excessive \(\text{Fe}^{2+}\) consumption rate when compared with its production in Fenton reaction series. On the other hand, it has been found that zero-valent iron (ZVI) has a great efficiency in Fenton process when compared with bivalent iron and thus the removal efficiency of contaminants will be higher. This heterogeneous Fenton process was called advanced Fenton (AF), as it is a fast reaction with high efficiency\(^\text{[18]}\). The surface of ZVI particles becomes oxidized when they enter the water, thereby generating bivalent iron, which induces Fenton reaction indirectly. On the other hand, in the case of presence of dissolved oxygen together with the production of bivalent iron ion, hydrogen peroxide is also produced, which can contribute to decreasing hydrogen peroxide consumption\(^\text{[19]}\).

In this study, the efficiency of nanoparticle zero-valent iron as Fenton catalyst was examined. So, the process was named advanced Nano-Fenton process (ANF). By considering operating variables (initial concentration, pH, the molar ratio of hydrogen peroxide to iron, and reaction time) and testing their different values, the optimal conditions were determined by specifying the DCF removal efficiency.

### Materials and methods

#### Materials

Sodium diclofenac with a high purity and zerovalent iron nanoparticle (35-45 nm, 99.5%) were purchased from Sigma-Aldrich. Hydrogen peroxide (30%), tert-butanol (99.5%) as radical scavenging and quenching agent of the reaction, methanol with a high purity and ultrafiltrated water specific for HPLC, and acetic acid to be used as the mobile phase of HPLC and phosphoric acid and NaOH for pH adjustment, sodium carbonate and sodium chloride with analytical purity for the mobile phase and preparation of standard solutions of ion chromatography and MQuant strips for measuring the residual values of hydrogen peroxide were purchased from Merck Millipore. Distilled water (\(\text{EC} \sim 1.2\pm0.2\)) produced by Ultrapure filtration device (Human) was used.

#### Experiments procedures

Following addition of certain amounts of the drug and ZVI nanoparticles (NZVI) to distilled water and preparing of the intended solutions, the reaction of ANF was initiated by adding hydrogen peroxide to the samples. All of the experiments were performed in a 100-mL Erlenmeyer flask. As the use of diffuser aeration is more feasible in large-scale wastewater treatment in comparison with magnetic stirrers and considering the role of soluble oxygen in the preservation of hydroxyl radicals produced in Fenton process, for mixing the contents of the reactor, mild aeration was used by a microporous air diffuser\(^\text{[20]}\). During experiments, the temperature was controlled at 25±2 °C. Within certain time intervals, 100 µL of the sample was withdrawn and after adding 100 µL tert-butanol 2 M (for quenching the reaction), the samples were injected into HPLC for measuring the drug level. Thereafter, factors influencing DCF removal efficiency were investigated.

#### Experimental Design

In order to determine the major effects of different parameters that influence the drug removal efficiency in ANF process, a full factorial design was applied using R software (3.1.0). In the study reaction time (\(\text{rTime}\)), the initial concentration of DCF (Conc), and the molar ratio of hydrogen peroxide to iron (\(\text{H/F}\)) were studied as more effective factors. Table 1 indicated the parameters along with their high and low levels.
Analytical methods

DCF residual concentration was determined by high-pressure liquid chromatography (HPLC) device, KNAUER Model, with a C18 column, the diameter of 5 µ, and dimensions of 250×4.6 mm at the wavelength of 278 nm. A mixture of methanol and water solution with 60:40 ratio) containing 0.1% acetic acid) with a flow rate of 1 ml/min along the analysis was used as the mobile phase. The drug measurement was conducted under working conditions at 30°C and column pressure of about 18 MPa. The degree of mineralization was determined through TOC analysis and with TOC-CSH device, Schimadzu. The extent of hydrogen peroxide consumption across different reactions was determined using calorimetry strips (MQuant) and through dilution. The colorimetric method of 1,10-phenanthroline was used to determine Ferrous iron in solutions\(^{(21)}\).

Results and discussion

In the preliminary design of ANF study, the time variable was chosen to be 10-60 min based on the reaction time of classic Fenton process. After performing the preliminary experiments and having observed the insignificance of some variables, it was found that ANF can remove the target contaminant far more quickly so that, the greater amount of DCF was converted in the first 10 minutes. Therefore, the reaction time period in ANF process was determined within shorter times (1-10 min).

In ANF process, the mean removal efficiency within the studied time was over 83%. With the increase in the time and H/F along with the reduction in initial concentration, the response variable (DCF removal) rose (Fig. 1).

The mechanism of the effect of ANF process is generation of free radicals and reaction with the target analyte. At acidic pH, the catalytic role of Fe\(^{2+}\) ions is bolder in bulk environment, on the one hand, and due to presence of molecular state of DCF at this pH, the possibility of development of Fenton process grows at the surface of (NZVI) where the surface of particles becomes oxidized and bivalent iron is produced), on the other. Therefore, as an influential parameter, pH was removed from the full factorial study and all of the experiments were conducted at pH=3. Results of full factorial design showed that only H/F variable became significant at the level of 0.1, while the concentration and time became significant at the level of 0.05 \(^{(2)}\).

<table>
<thead>
<tr>
<th>Factors</th>
<th>Low level</th>
<th>High level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time(min)</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Conc(mgL(^{-1}))</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>(H/F)</td>
<td>5</td>
<td>15</td>
</tr>
</tbody>
</table>

\textbf{Table 1:} Levels and factors of factorial designs for ANF processes.

\textbf{Table 2:} Estimated coefficients and other results of the fitted models for DCF removal using ANF processes (Full factorial design).

<table>
<thead>
<tr>
<th>Model Terms</th>
<th>Estimated Coefficient</th>
<th>t-value</th>
<th>p-value</th>
<th>Other Model Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>84.83125</td>
<td>127.6066</td>
<td>2.26×10^{-08}</td>
<td>Multiple R(^2): 0.9894 Adjusted R(^2): 0.9814 F-statistic: 124.5 on 3 and 4 DF p-value: 0.000001 Std. Error: 0.664</td>
</tr>
<tr>
<td>X1=Time</td>
<td>12.42875</td>
<td>18.6958</td>
<td>4.82×10^{-05}</td>
<td></td>
</tr>
<tr>
<td>X2=(H/F)</td>
<td>1.88125</td>
<td>2.8299</td>
<td>0.05235</td>
<td></td>
</tr>
<tr>
<td>X3=Conc</td>
<td>-2.64375</td>
<td>-5.9768</td>
<td>0.01644</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Main Effect of individual factors for DCF removal efficiency in ANF process.

The reason for the minor changes in the drug removal efficiency in comparison with variations in different ratios of H/F may be attributed to bilateral effects of the concentration of hydrogen peroxide. Although when the concentration of hydrogen peroxide exceeds more free radicals generally are developed and subsequently DCF removal efficiency increases, the radical scavenging effect of the high amount of hydrogen peroxide causes conversion of radicals to molecular genera in the reaction and results in diminishing efficiency of DCF removal to some extent\(^{(22)}\).
The reactions of radical scavenging effect are as follows\(^{19}\):

\[
\begin{align*}
\text{OH}^+ + \text{H}_2\text{O}_2 &\rightarrow \text{H}_2\text{O} + \text{HO}_2^- \\
\text{H}^+ + \text{H}_2\text{O}_2 &\rightarrow \text{HO}_2^- + \text{H}_2 \\
\text{HO}_2^- + \text{OH}^+ &\rightarrow \text{O}_2 + \text{H}_2\text{O}
\end{align*}
\]

Finally, Optimum values of variables affecting on ANF process were determined using fitted model for DCF removal (Table 3). In the optimum conditions, the DCF removal efficiency was achieved to be around 97%.

<table>
<thead>
<tr>
<th>Time(min)</th>
<th>H/F</th>
<th>DCF Conc(mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>13.5</td>
<td>6.62</td>
</tr>
</tbody>
</table>

Table 3: Optimal value for independent variables of ANF model.

**TOC abatement**

The mineralization of DCF in terms of TOC removal was investigated. Fig. 2 indicates the extent of TOC abatement in ANF. At the optimal variables, initial TOC (3.7 mg/L) decreased to 1.7 mg/L after 10 min representing that 54% of DCF was mineralized to HCl or CO\(_2\) in the ANF process. ANF process used to degrade 4-chloro-3-methyl phenol in a study indicated TOC removal of 63% after 60 min in optimum condition\(^{25}\). Furthermore, a Fenton-like process using pyrite as catalyst applied to eliminate DCF could achieve to 81% TOC removal after 5 minutes\(^{24}\). The difference between TOC abatement rate and drug removal efficiency is probably owing to the presence of stable organic intermediates and formation of recalcitrant by-products\(^{11}\).

**Conclusion**

ANF process showed a suitable efficiency in a short period of time. Unlike initial concentration of DCF and reaction time, H/F was not significant in full factorial design of ANF. It may be attributed to bilateral effects of H\(_2\)O\(_2\) concentration. Although when the H\(_2\)O\(_2\) concentration exceeds more free radicals generally are developed and subsequently DCF removal efficiency increases, the radical scavenging effect of the high amount of hydrogen peroxide causes conversion of radicals to molecular genera in the reaction and results in diminishing efficiency of DCF removal. Our research showed that ANF can be considered as a quick and efficient process for the removal of DCF from wastewater with a significant amount of mineralization.

**References**


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