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**Optimization of ciprofloxacin degradation in wastewater by homogeneous sono-Fenton  
process at high frequency**

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**Abstract**

Emerging pollutants such as pharmaceuticals have been focusing international attention for a  
few decades. Ciprofloxacin (CIP) is a common drug that is widely found in hospital and  
wastewater treatment plants effluents, as well as in rivers. In this work, the feasibility of CIP  
degradation by ultrasound process at high frequency is discussed and sonolysis, sonolysis  
with hydrogen peroxide and sono-Fenton are evaluated. The amounts of hydrogen peroxide

and ferrous ions ( $\text{Fe}^{2+}$ ) needed were optimized using response surface methodology. Best results were obtained with the sono-Fenton process resulting in a total pharmaceutical degradation within 15 minutes and a mineralization greater than 60% after one hour. Optimal conditions were tested on a real matrix from a municipal wastewater treatment plant. Even if the degradation of the pollutants by sono-Fenton was hampered, the removal efficiency of both CIP and total organic carbon (TOC) is interesting as an increase in the biodegradability of the wastewater is found. These results show that sono-Fenton oxidation can be a promising pre-treatment process for pharmaceutical-containing wastewaters.

**KEYWORDS:** Advanced oxidation processes, pharmaceuticals, optimization, sono-Fenton, ultrasound, wastewater treatment

## Introduction

The use of thousands of tons of pharmaceuticals to treat human and animal illnesses, but also in farming and aquaculture has become a serious problem for environment and human health. <sup>[1-4]</sup> They could be toxic to aquatic life when released in the environment <sup>[5-9]</sup>, even at very low concentrations (parts-per-trillion to parts-per-billion) in aquatic systems. <sup>[10, 11]</sup> Depending on the drugs, up to 95% of the administered dose can be excreted unchanged or as active metabolites and enter the environment altering rivers, lakes and groundwater. <sup>[1-4,12]</sup> Most drugs are designed so that they keep their chemical structure long enough to exert their therapeutic effect. This property, combined with their continuous input into the ecosystem, may enable them to persist for an extended period of time. <sup>[13]</sup> Antibiotics are of particular concern because their presence in natural waters could contribute to the rise of antibiotic resistance in microorganisms. <sup>[14-19]</sup> Fluoroquinolones are a group of antibiotics widely used in human and animal therapy. Among them, ciprofloxacin (1-cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-ylquinoline-3-carboxylic

acid, CIP) is a non-biodegradable antibiotic that has been detected in wastewater treatment plant effluents in concentrations from  $5.6 \mu\text{g L}^{-1}$  to  $6.5 \text{ mg L}^{-1}$ .<sup>[21, 22]</sup> The molecular structure of CIP is shown in figure 1.

Conventional wastewater treatment processes such as biological degradation or adsorption have been verified to be ineffective for the removal of most antibiotics.<sup>[17, 20]</sup> In recent years, a considerable interest has been shown in the development and application of Advanced Oxidation Processes (AOPs) for the treatment of pharmaceutical contaminants in water.<sup>[7, 23]</sup> Several techniques such as ozonation, photocatalysis or UV/H<sub>2</sub>O<sub>2</sub> have been the focus of a great deal of research. More recently, ultrasonic irradiation has received significant attention thanks to its ability to promote the fast degradation of environmental pollutants in water.<sup>[24, 25]</sup> The mechanism of sonolysis is based on cavitation, which is the formation, growth, and sudden collapse of bubbles in liquids. The collapse of these bubbles leads to extremely high local temperatures and pressures. These localized hot spots were estimated to have temperatures of roughly 5200 K, pressures of about 500 atm and lifetimes of a few microseconds.<sup>[26-28]</sup> Two possible degradation routes are usually proposed. First, the contaminant can undergo thermal degradation inside the cavity and in the interfacial region (cavity-liquid). Second, formed free radicals (mainly OH<sup>\*</sup>), can react with the contaminant in the interfacial region or in the bulk solution.<sup>[29]</sup> This route allows sonolysis to be considered as an AOP. High frequency ultrasound (US) generally raises the amounts of free radicals because there are more cavitation events which subsequently lead to an increase in contaminant degradation. However, an optimum frequency maximizes the degradation rate of pollutant. The same phenomenon occurs with the ultrasound power. An increase of ultrasound power could improve the degradation of pollutants; the rates of degradation may decrease with further increase in power that is beyond its optimum value due to bubble cloud formation on the ultrasonic probe surface.<sup>[30]</sup> The addition of strong oxidants such as hydrogen peroxide

or Fenton reagent to sonolysis can be used to improve the biodegradability of a real pharmaceutical wastewater. [23, 31, 32]

There are not many previous studies concerning the sonolysis of CIP and its combination with H<sub>2</sub>O<sub>2</sub> and the Fenton reagent. The influence of operational parameters in the sonolysis on CIP degradation and CIP initial concentration was studied by De Bel and collaborators. [33] Xiao et al. [11] studied the role of matrix organic compounds on the sonolysis of CIP in aqueous solutions. The effective destruction of CIP at the frequencies of 20 and 620 kHz has been proven. It was also demonstrated that a larger size and lower concentration of matrix organics in water have a smaller impact on the CIP degradation as compared to a smaller size and higher concentration of matrix organics. [11] A report on ultrasound assisted Laccase catalysed degradation of CIP at low frequency, 22 kHz, showed a maximum degradation of 51% at 0.02% (wt v<sup>-1</sup>) enzyme loading. As compared to conventional method, this technique not only increases CIP degradation rate but also reduces degradation time. [34] Moreover, it was observed that pH affected the ultrasonic degradation rate of aqueous CIP solution. [35]

In previous studies, Quesada et al. [30] showed that the integration of AOPs with the use of oxidants such as hydrogen peroxide and Fenton's reagent improved the degradability of pharmaceutical pollutants in water. They reported the use of H<sub>2</sub>O<sub>2</sub> as a radical promoter to the sono-degradation of paracetamol and levodopa. It has been also reported that the Fenton chemistry combined with ultrasound treatment remarkably enhanced the sulfadiazine [36] and paracetamol [32] degradation when concentrations of H<sub>2</sub>O<sub>2</sub> and Fe<sup>2+</sup> are optimized.

In this study, the application of sonolysis for the degradation of CIP in water is examined. The intensification of the oxidation with H<sub>2</sub>O<sub>2</sub> and the Fenton reagent under acidic conditions on the CIP degradation rate is studied. Moreover, the hydrogen peroxide concentration and relation between c(H<sub>2</sub>O<sub>2</sub>)/c(Fe<sup>2+</sup>) in the sono-Fenton process are optimized using surface response methodology (SRM). In addition, the best sono-Fenton conditions were evaluated on a real matrix from a municipal wastewater treatment plant (WWTP).

## Materials and Methods

### *Reagents*

All solutions were prepared by dissolving CIP (Sigma-Aldrich, 99%) in distilled water. The pH adjustment was carried out using 1 M solution of H<sub>2</sub>SO<sub>4</sub>, which was prepared with concentrated sulfuric acid (95–97% purity) from Sigma-Aldrich. For high-performance liquid chromatography (HPLC) analysis, acetonitrile (HPLC quality) and o-phosphoric acid (85%) from Merck and Fisher, respectively, were used. The other chemicals employed were FeSO<sub>4</sub>·7H<sub>2</sub>O (99.5%), potassium iodide (99.5%), sodium hydroxide (99%) and sodium sulfite (98%) obtained from Sigma-Aldrich, and hydrogen peroxide (30% wt v<sup>-1</sup>), from Fluka.

### *Sonication experiments*

An US multifrequency generator (Meinhardt Ultraschall technik) operating in continuous mode at frequencies of 580 and 862 kHz and variable electric power output was connected to a stainless steel transducer (E 805/T/M, Ø 40 mm) for the sonication experiments. Actual power dissipated into the liquid was measured by the standard calorimetric method according to procedures detailed in other studies.<sup>[26, 27]</sup> Reactions were performed in a 0.5 L cylindrical glass reaction vessel (internal Ø 75 mm) with the transducer placed at the bottom of the vessel in direct contact with the solution, at a depth of 57 mm from the liquid surface. Cooling of the reaction mixture was achieved by circulating water through the vessel jacket, to maintain an average temperature of 30±1°C, monitored by a thermometer immersed in the solution. The experimental set-up is shown in figure 2. Solution pH was adjusted to the initial value (pH 3), but not controlled over reaction time due to the particularities of the reactor. All US experiments were performed with 250 mL of aqueous solutions containing CIP at 100 mg L<sup>-1</sup>. Sono-Fenton experiments were carried out with a relation of concentrations of H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup> between 2-6.

The best conditions obtained for the sono-Fenton experiment were tested in a real matrix. Influent samples were collected from WWTP “María del Carmen”, in Boyeros, Havana City, Cuba, (W 82.40; N 23.04). Samples were collected in 2.5 L amber glass bottles and transferred from the WWTP to our laboratory in cooled box and then kept refrigerated (+4 °C). Wastewater samples were filtered after reaching room temperature using medium density cellulose filter. The samples were then acidified to pH 3 by adding H<sub>2</sub>SO<sub>4</sub>. The wastewater was characterized by Standard Method for the examination of water and wastewater.<sup>[37]</sup> In all experiments, liquid samples periodically were drawn from the reaction vessel for chemical analyses; the total volume withdrawn during a single experiment was less than 6% of the total reacting volume. A solution containing KI, Na<sub>2</sub>SO<sub>3</sub>, and NaOH (each 0.1 M) was used to quench the reaction in the samples when H<sub>2</sub>O<sub>2</sub> and the Fenton reagent were used. The obtained precipitate was removed on a 0.45 µm RC syringe filter prior to chemical analyses.

### ***Chemical analysis***

An HPLC system (SHIMADZU Prominence High Pressure model), involving a two solvent delivery pump, UV/VIS diode array detector (SHIMADZU SPD-M20A model) and an autosampler was used to follow the concentration-time profiles of CIP. The antibiotic was analyzed at 40°C using a RP18 column (Super Sphere 100 model, 250 mm×4.6 mm; 5 µm) with acetonitrile/ acidified water 13/87% (v/v) at 1.5 mL min<sup>-1</sup> as the mobile phase. The injection volume was 20 µL, and detection was set at 278 nm. The CIP retention time was about 9 min. The calibration curve ( $R^2=0.999$ ) was obtained from external standards prepared with known concentrations of the target compound.

A total organic carbon (TOC) analysis was performed using a TOC-LCPN Shimadzu analyzer equipped with a non-dispersive infrared detector. The injection volume was 50 µL. The



150 combustion reaction was achieved in a quartz pipe at 680 °C with a regular platinum catalyst.  
 151 The carried flow was oxygen at 150 mL min<sup>-1</sup>.  
 152 Degradation experiments were performed at an initial CIP concentration of 100 mg L<sup>-1</sup>, 30°C,  
 153 pH 3, and frequencies of 580 and 862 kHz and at three different ultrasonic powers. The  
 154 degradation of CIP by the US-process, D, is defined by Equation 1.

$$D(\%) = \frac{C_0 - C}{C_0} * 100 \quad (1)$$

155 where C<sub>0</sub> represents the initial concentration of CIP and C is the concentration of CIP at time  
 156 t. The mineralization (M) of CIP in the US-process, based on TOC concentration, was  
 157 calculated by Equation 2.

$$M(\%) = \frac{TOC_0 - TOC}{TOC_0} * 100 \quad (2)$$

158 where TOC<sub>0</sub> represents the initial concentration of the total organic carbon and TOC is the  
 159 concentration of total organic carbon at time t.

160 For checking the reproducibility of the evaluated processes, some experiments were  
 161 triplicated. The observed relative error was less than 5% for CIP concentration and TOC.

162

## 163 **Results and discussion**

### 164 *Influence of ultrasonic frequency and power*

165 The most important parameters in the sonolysis process are ultrasound power and frequency.

166 The sonochemical degradation of CIP at different powers was investigated using a 2x3

experimental design (Table 1), for two ultrasonic frequencies: 580 and 862 kHz. Figure 3 shows the influence of ultrasonic frequency and power on CIP degradation and mineralization at 100 mg L<sup>-1</sup> initial concentration, 30°C and pH 3. The best mineralization and degradation correspond to the highest power for both values of frequency studied. Figure 3 shows that the highest efficiency on CIP degradation after 120 min was obtained at 580 kHz.

US power affects cavitation activity and has a significant influence on TOC removal (22%) mainly at the lowest frequency. In these experimental conditions, the initial removal rates increased with the power. Similar results were obtained for US degradation of levodopa and paracetamol at 574 and 860 kHz, but significantly lower removals were reported, 66 and 67% respectively, at the highest frequency 1,134 kHz. <sup>[30]</sup> De Bel et al. <sup>[33]</sup> found that the lowest frequency, 544 kHz, proved to be the most favorable on CIP degradation. The ultrasonic frequency significantly affects sonolysis due to both the critical size and lifetime of cavitation bubbles, which consequently affects the number of cavitation bubbles, the violence of the bubble collapse and the OH• radical production. <sup>[11, 38, 39]</sup> Higher ultrasound frequencies are more effective for generating hydroxyl radicals owing to the rapid microbubble collapse. However, a maximum frequency should not be exceeded to avoid affecting degradation rates and cavitation effects. Actually, the rarefaction cycle of the sound wave produces a negative pressure and the compression cycle occurs faster than the time needed for the microbubble to collapse. Therefore, fewer HO• radicals are released. <sup>[39]</sup> Other authors have reported faster degradation of organic compounds at 200-600 kHz frequencies. <sup>[11, 39-42]</sup> In any case, the operating frequency must be optimized for the particular US-driven treatment process. However, due to the formation of highly hydrophilic by-products during the process, poor mineralization is usually observed using this process alone. <sup>[43]</sup>

Table 2 shows the pseudo first-order rate constant as a function of US frequency and power. The degradation of CIP by the US–Sy the ada consistent with pseudo-first-order kinetics, as follows:

$$\frac{-dc}{dt} = kc; \ln \frac{c_0}{c} = kt \quad (3)$$

De Bel et al. [33] found comparable results for CIP sono-degradation at 25°C as the production of HO• radicals was the highest at 544 kHz ( $k_1$  equal to 0.0067 min<sup>-1</sup>), in comparison with 801 kHz ( $k_1$  = 0.0055 min<sup>-1</sup>) and 1081 kHz ( $k_1$  = 0.0018 min<sup>-1</sup>).

Sonochemical reactions would be favored by an increase in US power at a fixed frequency. It is widely accepted that higher ultrasonic power input increases the frequency of cavitation, the number of active cavitation bubbles, the size of individual bubbles, as well as the rate of generation and concentration of hydroxyl radicals. [44] During ultrasonic irradiation, two main reactions occur: (1) pyrolysis due to the high temperature and pressure in the gas phase, and (2) hydroxyl radical attack in the bubble-liquid interface and/or in the bulk liquid. Gas phase pyrolytic reactions are considered to play a minor role in the case of non-volatile solutes. According to its low volatility (Henry's law constant = -18.3 atm.m<sup>3</sup> mol<sup>-1</sup> at 25°C [11]) and low water solubility (Log K<sub>ow</sub> = 0.28 [45]), it has been demonstrated that the attack of hydroxyl radicals on CIP molecules is the dominant reaction. [33, 35] Recent studies revealed the intensification of the sonochemical degradation of levofloxacin at 20 kHz using carbon tetrachloride as a rate enhancer. [44] The formation of °Cl radicals will lead to a series of recombination reactions conducting to the formation of additional active species, such as HClO, Cl<sub>2</sub> and chlorine-containing radicals (Cl•, CCl<sub>3</sub>• and :CCl<sub>2</sub>), having strong oxidizing property, which will markedly accelerate the degradation of levofloxacin in aqueous solution.

[44] It was reported<sup>[46]</sup> that the improvement of US power had a positive effect on the degradation rate of the antibiotic, until an optimal power dissipation. Beyond this value, cavitation activity and pollutant degradation, are either slightly affected or decreases. This optimal power is dependent on the reactor configuration and on the particular system/pollutant.

The values obtained for pseudo first-order rate constant (Table 3) are in the range which have been previously reported by other authors for CIP degradation by several AOPs<sup>[33, 35, 47-49]</sup>. The highest pseudo first-order rate constant obtained in this work is comparable with the reported value by De Bell and collaborators.<sup>[33]</sup>

Two regression models were adjusted to evaluate the influence of both the frequency and ultrasonic power on the degradation and mineralization of CIP according to Equations 4 and 5. The regression and variance analysis for both models are shown in Tables 1S and 2S (supporting information). Figure 4 shows the response surface models of degradation (a) and mineralization (b) for 2x3 experimental design. It is observed that increasing power is favorable, in both cases. Both lineal models confirm that ultrasonic power is the most influent variable for both the degradation and mineralization rate (Eq. 4 and 5).

$$\text{deg} = -6.032 + 0.021 F - 0.004 F * P + 2.612 P + 0.039 P * P \quad R^2 = 99.73\% \quad (4)$$

$$\text{min} = -3.249 + 0.007 F - 0.002 F * P + 1.949 * P + 0.017 P * P \quad R^2 = 99.49 \% \quad (5)$$

### ***Intensification of CIP sono-degradation with the oxidant H<sub>2</sub>O<sub>2</sub> as a radical promoter***

Few reports about the combination of ultrasound with H<sub>2</sub>O<sub>2</sub> on the fluoroquinolones degradation have been found.<sup>[48]</sup> It is well documented in the literature that during aqueous sonolysis, hydroxyl radicals are produced and recombined into H<sub>2</sub>O<sub>2</sub> at the bubble-liquid interface and/or in the bulk liquid.<sup>[50, 51]</sup> In general, H<sub>2</sub>O<sub>2</sub> is expected to promote degradation

234 since it may be decomposed by US and/or react with  $H^\bullet$  generated by water sonolysis thus  
 235 generating additional  $HO^\bullet$  according to Equations 6 and 7. [7, 52] For this reason, the degradation  
 236 of organic compounds maybe augmented by an increase in the  $H_2O_2$  dose. [53]

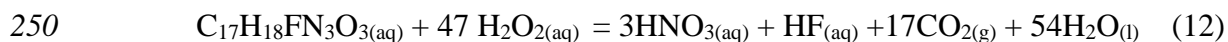


239 where US refers to the ultrasonic irradiation.

240 Hydroxyl radicals can (i) degrade organic compounds, (ii) react with  $H_2O_2$  (especially when  
 241 they are in large excess) forming less active species according to Equation 8 [36, 54, 55] (iii) or  
 242 recombine with different radicals according to Equations 9-11. [56-58]



247 Then, another set of experiments was carried out in order to study the effect of  $H_2O_2$  addition  
 248 on CIP sonolysis. The stoichiometric amount of the required  $H_2O_2$  for the complete oxidation  
 249 of CIP in aqueous solution was calculated according to Equation 12:



251 After one hour of reaction under stoichiometric conditions, a low CIP degradation was found:  
 252 5.9% under silent conditions . The influence of the oxidant concentration on CIP degradation  
 253 and mineralization was studied to understand the phenomena better. Experimental runs were  
 254 conducted with different concentrations of  $H_2O_2$  corresponding to 0.5, 1, 5, 10, and 15 times  
 255 the stoichiometric amount (Figure 5). No increase in the CIP degradation was observed with  
 256 the addition of  $H_2O_2$ . This was verified by comparing the means of CIP degradation by

Student test (for  $\alpha=0.05$ ). When ultrasound is applied without  $\text{H}_2\text{O}_2$  the degradation and mineralization (35.8% and 22.6% respectively) were similar to the results obtained for one time the stoichiometric amount of  $\text{H}_2\text{O}_2$  (36.5% and 24.4% respectively), the highest values obtained when hydrogen peroxide was added. In some of the experiments, the addition of  $\text{H}_2\text{O}_2$  showed a detrimental effect on US-driven CIP degradation in comparison to the performance of the ultrasound-driven process alone.

As previously stated here, despite the generation of hydroxyl radicals by its own sonolysis, the hydrogen peroxide can act as a hydroxyl radical scavenger, producing the much less reactive hydroperoxyl radicals (Eq. 8). The hydroxyl radicals in excess will be recombined forming water or hydrogen peroxide (Eqs. 9-11). At pH 3, the addition of different stoichiometric amounts of  $\text{H}_2\text{O}_2$  does not improve the CIP sonolysis process. Several authors reported this negative influence of  $\text{H}_2\text{O}_2$  in organic pollutant sonodegradation. [36, 52] Manousaki et al. [52] studied the degradation of sodium dodecyl benzene sulfonate in water by ultrasonic irradiation at 20 and 80 kHz and found a detrimental effect of hydrogen peroxide on the substrate degradation, besides the above-mentioned scavenging effect: the pollutant removal occurred mainly in the interfacial region, and thus the beneficial effect of extra hydroxyl radicals (Eq. 7) would be of marginal importance, even close to the cavitation bubbles, due to the thermal decomposition of hydrogen peroxide molecules to oxygen and water. Nevertheless, other authors claim that the addition of  $\text{H}_2\text{O}_2$  has a positive effect on the degradation of various organic compounds. [30, 32, 48, 59-61] The presence of an optimal amount of  $\text{H}_2\text{O}_2$  for the sonochemical degradation of the target compounds can occur, but it is difficult to determine the optimal concentration for each compound. [59, 60, 62] It is because the experimental conditions varied widely and a very limited range of  $\text{H}_2\text{O}_2$  concentrations was used in most previous studies. [61] Under our experimental conditions, this optimum amount of  $\text{H}_2\text{O}_2$  was not found.

## *Optimization of the sono-Fenton degradation of CIP*

The combination of ultrasound with Fenton reagent is an alternative way to increase the generation of free radicals in the ultrasonic system. As previously said,  $\text{H}_2\text{O}_2$  can be generated during ultrasonic treatment thanks to the recombination of hydroxyl radicals. Therefore, the addition of an iron salt can initiate the Fenton reaction during the sonolysis under acidic conditions. This coupling of ultrasonic irradiation and Fenton oxidation (i) promotes faster pollutant conversion/mineralization due to a higher generation of hydroxyl radicals according to Equations 6 and 13 <sup>[63]</sup>; (ii) improve mixing and contact between hydroxyl radicals and pollutant <sup>[46, 64]</sup>, (iii) and enhanced regeneration of ferrous ions according to Equation 14 <sup>[65]</sup>, in comparison with an uneasy regeneration of  $\text{Fe}^{2+}$  by conventional homogeneous Fenton reaction according to Equations 15 and 16.



Table 3 shows the results of ultrasonic degradation of CIP (initial concentration  $100 \text{ mg L}^{-1}$ ,  $F=580 \text{ kHz}$ ,  $P = 30.6 \text{ W}$ ,  $T = 30^\circ\text{C}$ ,  $\text{pH}= 3$ ) at different concentrations of  $\text{H}_2\text{O}_2$  and  $\text{Fe}^{2+}$  corresponding to a  $\text{H}_2\text{O}_2/\text{Fe}^{2+}$  ratio between 2 and 10, following a  $3^2$  factorial experimental design (rows 3-11). Sono-Fenton resulted, in all cases, in high CIP degradation (ten times more) within the first 15 min of treatment (higher than 89%) compared to the results obtained during sonolysis alone (row 1, 9.3% of degradation at 15 minutes and 17.4% of mineralization in one hour) and those obtained with the addition of hydrogen peroxide without  $\text{Fe}^{2+}$  (row 2, 9.5% of degradation at 15 minutes and 24.4% of mineralization in one hour).

An additional ultrasonic experiment was carried out, to evaluate the effect of adding only iron, using 2.37 mM of  $\text{Fe}^{2+}$  without additional amount of hydrogen peroxide. In this condition the CIP degradation at 15 minutes was 18.5%, higher than the value obtained in single sonication experiment but much lower than in the case of hydrogen peroxide was also added together with ferrous salt (98.4%, row 7 table 3). This result can be explained by the formation of hydrogen peroxide during sonication in water. However, it is known that the amount of generated  $\text{H}_2\text{O}_2$  is not significant comparing with those added as Fenton reagent. [66, 67]

The mineralization for the sono-Fenton process was also higher than for ultrasonic oxidation alone (row 1 in Table 3) and for sonolysis with hydrogen peroxide (rows 2 in Table 3). The best mineralization was obtained when 14.2 mM of  $\text{H}_2\text{O}_2$  and  $\text{H}_2\text{O}_2/\text{Fe}^{2+}$  ratio 6 (row 7 in Table 3) were used. An additional experiment was carried out at the same conditions of row 7 (Table 3) without ultrasound (Fenton reaction). It can be seen, that at 15 min the degradation of the sono-Fenton process was practically the same for both processes. With regard to the mineralization, sono-Fenton gave better results than the Fenton process: for example at 60 min, the mineralization rate was 30 % higher for sono-Fenton than for Fenton alone (62 vs. 30.3). This result shows that ultrasonic radiation combined with Fenton reagent enhances the mineralization of aqueous solution.

A mathematical model describing the mineralization behavior at 60 min as a function of  $\text{H}_2\text{O}_2$  concentration and  $\text{H}_2\text{O}_2/\text{Fe}^{2+}$  concentration ratio is proposed as follows:

$$\begin{aligned} \text{min} = & -13.2 + 3.12c(\text{H}_2\text{O}_2) + 13.86 \frac{c(\text{H}_2\text{O}_2)}{c(\text{Fe}^{2+})} - +3c(\text{H}_2\text{O}_2)^2 \\ & + 0.007c(\text{H}_2\text{O}_2) * \frac{c(\text{H}_2\text{O}_2)}{c(\text{Fe}^{2+})} - +. \left[ \frac{c(\text{H}_2\text{O}_2)}{c(\text{Fe}^{2+})} \right]^2 \end{aligned} \quad (17)$$



The above model describes adequately the experiment with  $R^2 = 81.52\%$ , a standard error of estimation of 8.1 % and a mean absolute error of 3.9 %. The regression and variance analysis for the model are shown in Table 3S (supporting information). Figure 6 shows the response surface model of mineralization, where an optimum of mineralization of 56.78% is observed for hydrogen peroxide concentration of 18.5 mM (stoichiometry of 1.3) and  $H_2O_2/Fe^{2+}$  ratio of 6. This value of mineralization is higher than those obtained by several AOPs,  $O_3$  (30.5%), UV (18%), UV/ $H_2O_2$  (42%) and is of the same order of magnitude as UV/ $H_2O_2/Fe^{2+}$  (63.3%) reported by Bobu and collaborators. [68]

#### ***Influence of a real waste water matrix on CIP removal***

The water treatment by AOPs can be affected by the presence of inorganic and organic components in the water matrix, significantly slowing the degradation of the target pollutants. [70-71] Several authors have reported the role of organic components on the sonochemical degradation of persistent contaminants that appears to be a complex task which need to be experimentally verified for different systems. [7, 72-77] On the one hand, the presence of an organic matrix reduces the sonochemical degradation of target contaminants. [7, 72-74] On the other hand, the presence of organic matter did not affect the sonochemical degradation of methyl tert-butyl ether, [76] perfluorooctane sulfonate and perfluorooctanoate. [77] In order to investigate the efficiency of the sono-Fenton degradation of CIP in real application, some experiments with a real wastewater matrix (WW) were performed. In the case of Fenton chemistry, the presence of organic and inorganic compounds in WW may hamper this reaction by scavenging hydroxyl radicals and/or forming iron complex. [7, 78] A positive effect has also been reported, phenolic compounds that WW may contain could reduce ferric ion to ferrous ion and thus enhance Fenton reaction. [76]

Table 4 shows the physicochemical characteristics of the WW influent from the WWTP “María del Carmen” before (WW-01) and after addition of CIP at  $100\text{ mgL}^{-1}$  and pH

adjustment to 3 (WW-02). As CIP is the major organic compound in this matrix, biochemical oxygen demand (BOD<sub>5</sub>), chemical oxygen demand (COD) and TOC concentration increased when it was added. However, the BOD<sub>5</sub>/COD ratio decreased from 0.33 to 0.21 showing a decrease in the biodegradability of CIP-dopped matrix WW-02. De Bel et al. [35] experimentally demonstrated the low degradability of the 15 mgL<sup>-1</sup> CIP aqueous solution with BOD<sub>5</sub>/COD ratio of only 0.06. The suspended solid concentration in WW-02 also decreased, due to the solubility of some solids with pH decreasing. The real matrix was treated by the sono-Fenton process. Two different series of experiments were carried out: (i) under the best conditions obtained during CIP degradation in aqueous solution (14.2 mM H<sub>2</sub>O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup> ratio of 6), (ii) recalculating the amount of hydrogen peroxide to be added, taking into account the increase in COD to keep the same H<sub>2</sub>O<sub>2</sub>/COD ratio as in the study with the synthetic solution (31.8 mM H<sub>2</sub>O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup> ratio of 6).

Figure 7 shows the CIP degradation and mineralization ([CIP]<sub>0</sub>: 100 mg L<sup>-1</sup>, T: 30°C, pH<sub>0</sub>=3) by the sono-Fenton process in a real WW matrix for both series of experiments. The degradation and mineralization of CIP are higher when a higher concentration of hydrogen peroxide is used. Nevertheless, even under this condition in a real matrix WW-02, degradation of both CIP and TOC by sono-Fenton is significantly hampered in WW. The degradation of CIP at 15 min and mineralization at 60 min are less important in real conditions (13.6% and 18.9%), than for synthetic water. This result shows the inhibition of CIP degradation and mineralization in a real WW matrix, as reported before for the sonolysis of CIP and other persistent pollutants in different organic matrices. [7, 70-72]

Although the sonochemical degradation of CIP is less efficient for the real matrix, the pollutant degradation and mineralization is still quite adequate: 97.1% of CIP degradation is reached after 60 min (Fig. 7), which practically guarantees the complete elimination of the antibiotic from WW. This is an important environmental issue in the fight against antibiotic

resistance in natural systems. On the other hand, in the best cases, the BOD<sub>5</sub> removal was 14.2% (Table 4), the COD and TOC removal were higher than 50% and the BOD<sub>5</sub>/COD ratio increased from 0.21 to 0.36, showing an increase in biodegradability.<sup>[35]</sup> This result is very promising because it opens the perspective of using ultrasound and sono-Fenton as a pretreatment of biological process in a WWTP for eliminating persistent organic pollutants.

## **Conclusion**

High frequency ultrasound guarantees the degradation of the antibiotic CIP following pseudo first-order reaction kinetics. It was verified that the ultrasonic power had a greater influence on CIP degradation than the frequency, at the values studied, in this field of investigation. Higher CIP percent removals and removal rates were observed for the lowest operating frequency studied (580 kHz) and higher ultrasonic power. Practically the total degradation of pharmaceutical was obtained in 15 min for all concentrations of hydrogen peroxide and ferrum salt studied.

The addition of hydrogen peroxide, as a radical promoter, does not markedly improve the sonolysis process in the range of operating studied conditions. In contrast, CIP degradation and mineralization are highly improved in the case of the US/Fenton system. The optimal conditions of the sono-Fenton process are 14.2 mM H<sub>2</sub>O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup> ratio of 6, ensuring at least a 60% mineralization rate. The degradation of both CIP and TOC by sono-Fenton was significantly hampered in a real waste water matrix. However, the pollutant degradation, COD and TOC removals can be considered as efficient in the real matrix, with an increase in the biodegradability of the wastewater. These results show that sono-Fenton oxidation can be considered as a promising pretreatment process for wastewater containing pharmaceutical compounds.

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## List of Figure Captions

**Figure 1.** Molecular structure of CIP

**Figure 2.** Experimental set-up: 1 –ultrasonic generator, 2 – transducer, 3 – glass reactor, 4 – stirrer, 5 –thermostat, 6 – temperature measurement

**Figure 3.** Influence of ultrasonic frequency and actual ultrasonic power on CIP degradation and mineralization after 120 min. Open markers with solid line represent degradation and filled markers with dash line represent mineralization. Experimental conditions: ( $[CIP]_0$ : 100 mg L<sup>-1</sup>, T: 30 °C, pH<sub>0</sub>=3)

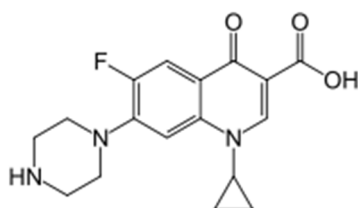
**Figure 4.** Response surface as a function of ultrasonic power. Degradation (a) and mineralization (b) of CIP

**Figure 5.** Degradation and mineralization trend in the US/H<sub>2</sub>O<sub>2</sub> process (F = 580 kHz y P = 21.7 W, pH = 3, t = 60 min)

**Figure 6.** Response surface as a function concentration of [H<sub>2</sub>O<sub>2</sub>] and the relation of  $c(H_2O_2)/c(Fe^{2+})$

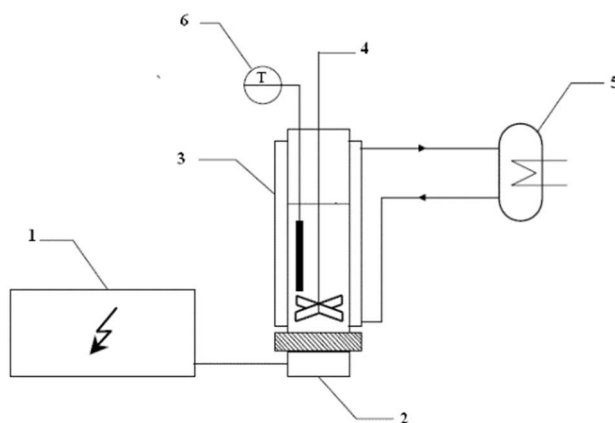
**Figure 7.** CIP degradation and mineralization by sono-Fenton process in a real WW matrix. Open markers with solid line represent degradation and filled markers with dash line mean mineralization for two different H<sub>2</sub>O<sub>2</sub> concentrations: 14.2 mM (○/●) and 31.8 mM (□/■). Experimental conditions: ( $[CIP]_0$ : 100 mg L<sup>-1</sup>, T: 30 °C, pH<sub>0</sub>=3)

642 **Figures**



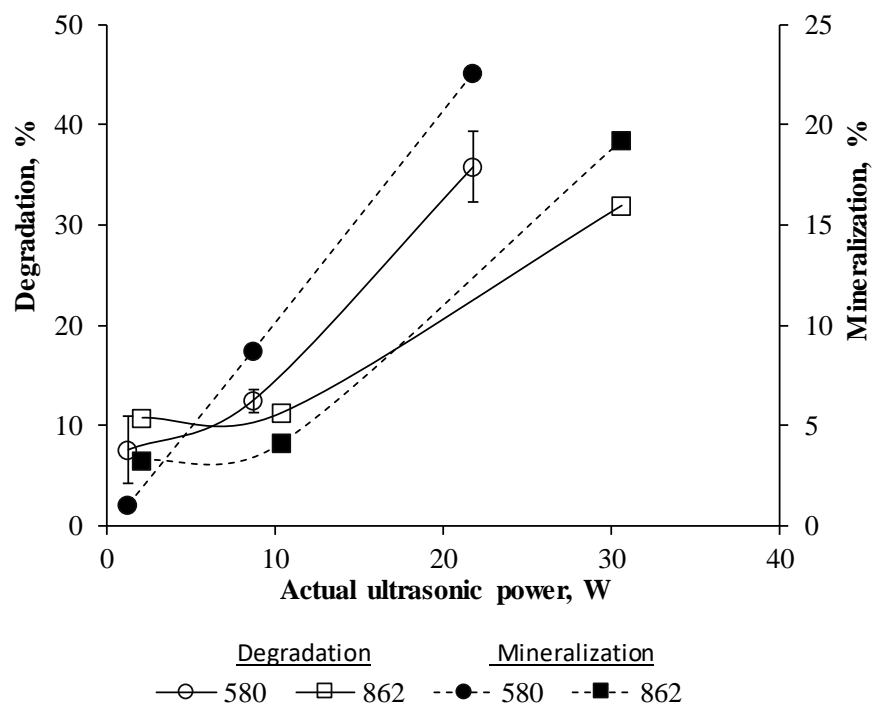
643

644 Fig 1.



645

646 Fig 2.



647

648 Fig. 3.

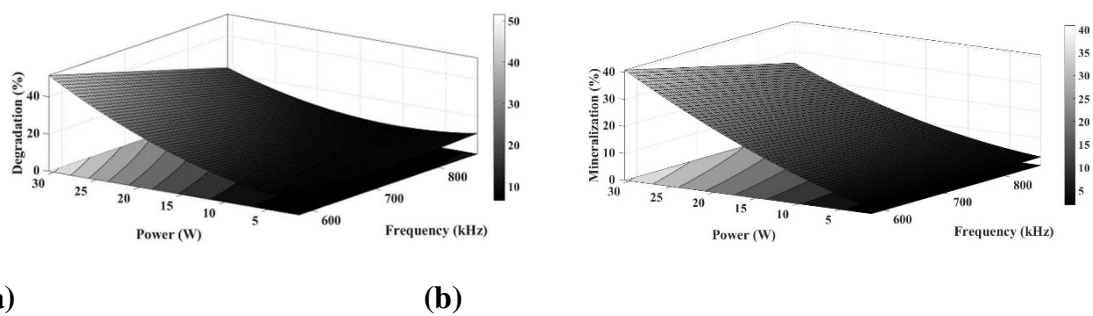


Fig. 4

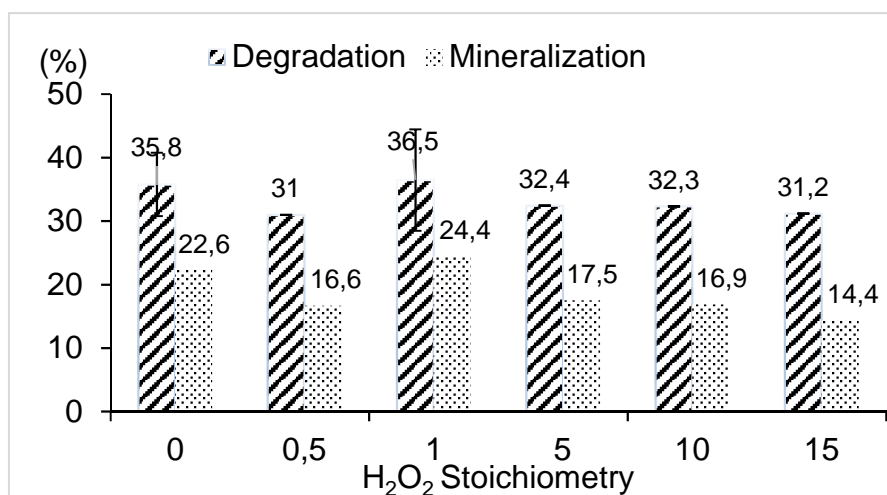
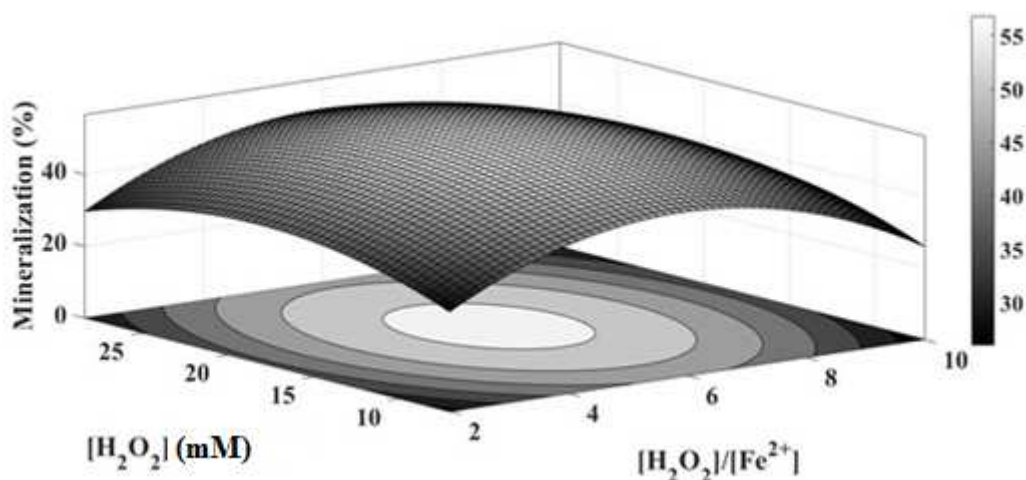
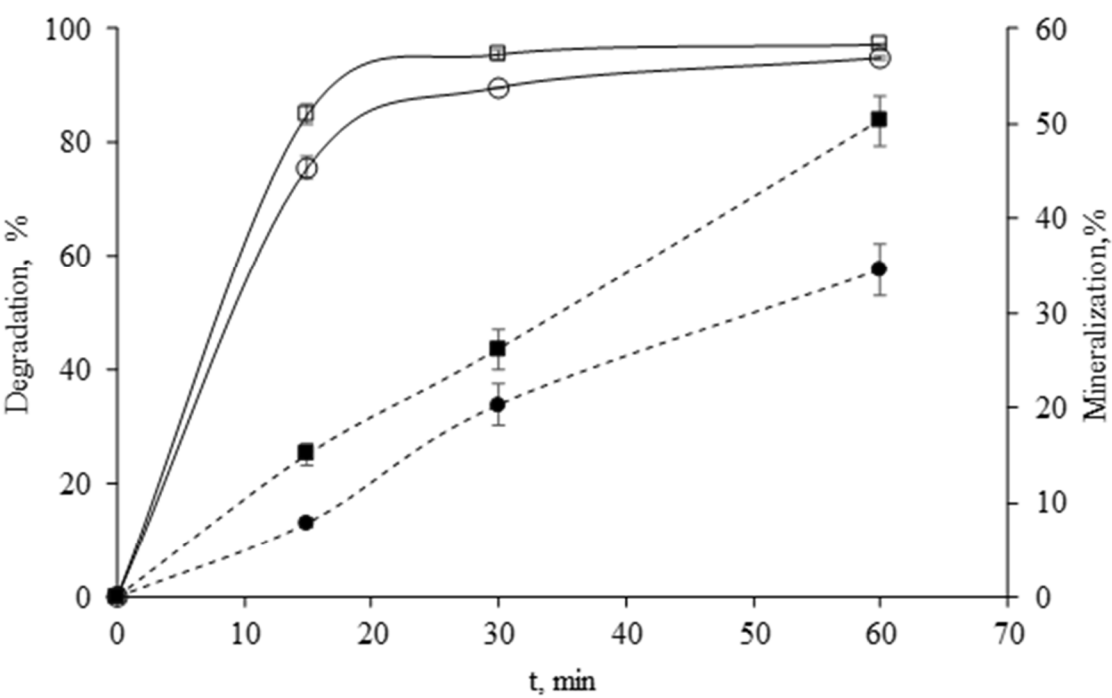


Fig 5.





657 Fig 6.



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659 Fig 7.

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## Tables

**Table 1.** Experimental design 2\*3 for the evaluation of ultrasonic frequency and power

No.	Frequency (kHz)	Actual
1	580	Min (1,35)
2	862	Min (2,07)
3	580	Med (8,74)
4	862	Med (10,37)
5	580	Max (21,77)
6	862	Max (30,57)
7	862	Max (30,57)

**Table 2.** Degradation pseudo first-order rate constant for three different ultrasonic power at frequency 580-862 kHz ( $[CIP]_0$ : 100 mg L<sup>-1</sup>, T: 30 °C, pH<sub>0</sub>=3)

Frequency (kHz)	P <sub>min</sub> (W) (value)	P <sub>med</sub> (W) (value)	P <sub>max</sub> (W) (value)
580	0.0039 (1.35)	0.0045 (8.74)	0.0066 (21.77)
862	0.0032 (2.07)	0.0040 (10.37)	0.0045 (30.57)

676 **Table 3.** Effect of  $\text{Fe}^{2+}/\text{H}_2\text{O}_2$  on CIP sonochemical degradation (t=15 min) and mineralization  
677 (t=60 min), (F=580 kHz, P = 30.6 W,  $[\text{CIP}]_0 = 100 \text{ mg L}^{-1}$ , T = 30°C, pH= 3). \*Fenton  
678 reaction without ultrasound

Row	c( $\text{H}_2\text{O}_2$ ) mM	c( $\text{H}_2\text{O}_2$ )/c( $\text{Fe}^{2+}$ )	Degradation (%), 15 min	Mineralization (%), 60 min
1	0	-	9.3	17.4
2	14.2	-	9.5	24.4
3	7.1	10	92.3	31.0
4	7.1	6	99.0	36.9
5	7.1	2	93.4	31.6
6	14.2	10	89.7	31.5
7	14.2	6	98.4±1.4 96.4*	62.0±2.3 30.3*
8	14.2	2	92.4	34.5
9	28.4	10	95.9	28.5
10	28.4	6	99.8	50.4
11	28.4	2	98.5	28.5

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**Table 4.** Physico-chemical characteristics of WW matrix before and after treatment by sono-Fenton process ([CIP]<sub>0</sub>: 100 mg L<sup>-1</sup>, T: 30 °C, pH<sub>0</sub>=3)

Parameter	Unit	WW-01 <sup>a</sup>	WW-02 <sup>a</sup>	After sono-Fenton <sup>b</sup>	
Temperature	°C	26	26	30	30
pH	-	6.7	3	3	3
H <sub>2</sub> O <sub>2</sub>	mM	-	-	14.2	31.8
H <sub>2</sub> O <sub>2</sub> /Fe <sup>2+</sup>	-	-	-	6	6
BOD <sub>5</sub>	mg O <sub>2</sub> L <sup>-1</sup>	66 ± 1	76 ± 5	72 ± 3	65 ± 4
COD	mg O <sub>2</sub> L <sup>-1</sup>	203 ± 43	368 ± 18	230 ± 21	180 ± 14
TOC	mg C L <sup>-1</sup>	74 ± 3	131 ± 1	85 ± 4	66 ± 4
SS	mL L <sup>-1</sup>	2.5 ± 0.1	2.3 ± 0.2	0	0
Conductivity	μS cm <sup>-1</sup>	1213	n.a.	n.a.	n.a.
Floating matter	-	present	present	non	non
BOD <sub>5</sub> /COD	-	0.33	0.21	0.31	0.36
BOD <sub>5</sub> removal	%	-	-	4.8*	14.2*
COD removal	%	-	-	37.4*	51.1*
TOC removal	%	-	-	34.6*	50.3*

<sup>a</sup>Average of three sampling results; <sup>b</sup>Average of two experiments; n.a: non available;

\*Referred to WW-02

## Supporting informat

**Table 1S.** Regression and variance analysis for equation 4 (Degradation as function of ultrasonic frequency and power).

Regression analysis				
Parameter	Estimate	Error	t-statistic	p-value
Constant	-6.032	4.82043	-1.251	0.429
F	0.021	0.007	3.08	0.2
F * P	-0.004	0.0005	-6.864	0.092
P	2.612	0.327	7.989	0.079
P * P	0.039	0.009	4.284	0.146
Analysis of variance				
Source	Sum of squares	Mean square	F-ratio	p-value
Model	744.985	186.246	93.91	0.076
Residual	1.98333	1.98333		
Total correlation	746.969			
R-squared = 99.73 %		Standard error of estimation = 1.408		
Mean absolute error = 0.515				

**Table 2S.** Regression and variance analysis for equation 5 (Mineralization as function of ultrasonic frequency and power).

Regression analysis				
Parameter	Estimate	Error	t-statistic	p-value
Constant	-3.249	4.91	-0.662	0.628
F	0.007	0.007	1.0	0.5
F * P	-0.002	0.0005	-4.137	0.151
P	1.949	0.333	5.852	0.108
P * P	0.017	0.009	1.831	0.318
Analysis of variance				
Source	Sum of squares	Mean square	F-ratio	p-value
Model	402.0	100.5	48.85	0.0105
Residual	2.06	2.06		
Total correlation	404.06			
R-squared = 99.49 %		Standard error of estimation = 1.434		
Mean absolute error = 0.524				

**Table 3S.** Regression and variance analysis for equation 17 (Mineralization as function of hydrogen peroxide concentration and  $\text{H}_2\text{O}_2/\text{Fe}^{2+}$  concentration ratio for sono-Fenton reaction).

Regression analysis				
Parameter	Estimate	Error	t-statistic	p-value
Constant	-13.2	20.8	-0.63	0.571
H <sub>2</sub> O <sub>2</sub>	3.12	2.19	1.42	0.25
H <sub>2</sub> O <sub>2</sub> /Fe <sup>+2</sup>	13.86	4.61	3.01	0.057
H <sub>2</sub> O <sub>2</sub> * H <sub>2</sub> O <sub>2</sub>	-0.09	0.06	-1.49	0.233
H <sub>2</sub> O <sub>2</sub> * H <sub>2</sub> O <sub>2</sub> /Fe <sup>+2</sup>	0.007	0.09	0.07	0.946
H <sub>2</sub> O <sub>2</sub> /Fe <sup>+2</sup> * H <sub>2</sub> O <sub>2</sub> /Fe <sup>+2</sup>	-1.18	0.35	-3.31	0.045
Analysis of variance				
Source	Sum of squares	Mean square	F-ratio	p-value
Model	856.2	171.2	12.65	0.102
Residual	194.1	64.7		
Total correlation	1050.3			
R-squared = 81.52 %		Standard error of estimation = 8.14		
Mean absolute error = 3.92				