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

Katia González-Labrada, Diana Rosa Alcorta Cuello, Israel Saborit Sánchez, Marise García Batle, Marie-Hélène Manero, Laurie Barthe, Ulises Javier Jáuregui-Haza

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

3  
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20 **Abstract**

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

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

34

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

### 37 **Introduction**

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

49 Fluoroquinolones are a group of antibiotics widely used in human and animal therapy. Among  
50 them, ciprofloxacin (1-cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-ylquinoline-3-carboxylic

51 acid, CIP) is a non-biodegradable antibiotic that has been detected in wastewater treatment  
52 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  
53 of CIP is shown in figure 1.

54 Conventional wastewater treatment processes such as biological degradation or adsorption  
55 have been verified to be ineffective for the removal of most antibiotics.<sup>[17, 20]</sup> In recent years, a  
56 considerable interest has been shown in the development and application of Advanced  
57 Oxidation Processes (AOPs) for the treatment of pharmaceutical contaminants in water.<sup>[7, 23]</sup>

58 Several techniques such as ozonation, photocatalysis or UV/H<sub>2</sub>O<sub>2</sub> have been the focus of a  
59 great deal of research. More recently, ultrasonic irradiation has received significant attention  
60 thanks to its ability to promote the fast degradation of environmental pollutants in water.<sup>[24,</sup>

61 <sup>25]</sup> The mechanism of sonolysis is based on cavitation, which is the formation, growth, and  
62 sudden collapse of bubbles in liquids. The collapse of these bubbles leads to extremely high  
63 local temperatures and pressures. These localized hot spots were estimated to have  
64 temperatures of roughly 5200 K, pressures of about 500 atm and lifetimes of a few  
65 microseconds.<sup>[26-28]</sup> Two possible degradation routes are usually proposed. First, the

66 contaminant can undergo thermal degradation inside the cavity and in the interfacial region  
67 (cavity–liquid). Second, formed free radicals (mainly OH<sup>\*</sup>), can react with the contaminant in  
68 the interfacial region or in the bulk solution.<sup>[29]</sup> This route allows sonolysis to be considered

69 as an AOP. High frequency ultrasound (US) generally raises the amounts of free radicals  
70 because there are more cavitation events which subsequently lead to an increase in  
71 contaminant degradation. However, an optimum frequency maximizes the degradation rate of

72 pollutant. The same phenomenon occurs with the ultrasound power. An increase of ultrasound  
73 power could improve the degradation of pollutants; the rates of degradation may decrease  
74 with further increase in power that is beyond its optimum value due to bubble cloud formation

75 on the ultrasonic probe surface.<sup>[30]</sup> The addition of strong oxidants such as hydrogen peroxide

76 or Fenton reagent to sonolysis can be used to improve the biodegradability of a real  
77 pharmaceutical wastewater. <sup>[23, 31, 32]</sup>

78 There are not many previous studies concerning the sonolysis of CIP and its combination with  
79 H<sub>2</sub>O<sub>2</sub> and the Fenton reagent. The influence of operational parameters in the sonolysis on CIP  
80 degradation and CIP initial concentration was studied by De Bel and collaborators. <sup>[33]</sup> Xiao et  
81 al. <sup>[11]</sup> studied the role of matrix organic compounds on the sonolysis of CIP in aqueous  
82 solutions. The effective destruction of CIP at the frequencies of 20 and 620 kHz has been  
83 proven. It was also demonstrated that a larger size and lower concentration of matrix organics  
84 in water have a smaller impact on the CIP degradation as compared to a smaller size and  
85 higher concentration of matrix organics. <sup>[11]</sup> A report on ultrasound assisted Laccase catalysed  
86 degradation of CIP at low frequency, 22 kHz, showed a maximum degradation of 51% at  
87 0.02% (wt v<sup>-1</sup>) enzyme loading. As compared to conventional method, this technique not only  
88 increases CIP degradation rate but also reduces degradation time. <sup>[34]</sup> Moreover, it was  
89 observed that pH affected the ultrasonic degradation rate of aqueous CIP solution. <sup>[35]</sup>

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

96 In this study, the application of sonolysis for the degradation of CIP in water is examined.  
97 The intensification of the oxidation with H<sub>2</sub>O<sub>2</sub> and the Fenton reagent under acidic conditions  
98 on the CIP degradation rate is studied. Moreover, the hydrogen peroxide concentration and  
99 relation between  $c(\text{H}_2\text{O}_2)/c(\text{Fe}^{2+})$  in the sono-Fenton process are optimized using surface  
100 response methodology (SRM). In addition, the best sono-Fenton conditions were evaluated  
101 on a real matrix from a municipal wastewater treatment plant (WWTP).

102 **Materials and Methods**

103 ***Reagents***

104 All solutions were prepared by dissolving CIP (Sigma-Aldrich, 99%) in distilled water. The  
105 pH adjustment was carried out using 1 M solution of H<sub>2</sub>SO<sub>4</sub>, which was prepared with  
106 concentrated sulfuric acid (95–97% purity) from Sigma-Aldrich. For high-performance liquid  
107 chromatography (HPLC) analysis, acetonitrile (HPLC quality) and o-phosphoric acid (85%)  
108 from Merck and Fisher, respectively, were used. The other chemicals employed were  
109 FeSO<sub>4</sub>·7H<sub>2</sub>O (99.5%), potassium iodide (99.5%), sodium hydroxide (99%) and sodium sulfite  
110 (98%) obtained from Sigma-Aldrich, and hydrogen peroxide (30% wt v<sup>-1</sup>), from Fluka.

111 ***Sonication experiments***

112 An US multifrequency generator (Meinhardt Ultraschall technik) operating in continuous  
113 mode at frequencies of 580 and 862 kHz and variable electric power output was connected to  
114 a stainless steel transducer (E 805/T/M, Ø 40 mm) for the sonication experiments. Actual  
115 power dissipated into the liquid was measured by the standard calorimetric method according  
116 to procedures detailed in other studies. [26, 27] Reactions were performed in a 0.5 L cylindrical  
117 glass reaction vessel (internal Ø 75 mm) with the transducer placed at the bottom of the vessel  
118 in direct contact with the solution, at a depth of 57 mm from the liquid surface. Cooling of the  
119 reaction mixture was achieved by circulating water through the vessel jacket, to maintain an  
120 average temperature of 30±1°C, monitored by a thermometer immersed in the solution. The  
121 experimental set-up is shown in figure 2. Solution pH was adjusted to the initial value (pH 3),  
122 but not controlled over reaction time due to the particularities of the reactor. All US  
123 experiments were performed with 250 mL of aqueous solutions containing CIP at 100 mg L<sup>-0</sup>.  
124 Sono-Fenton experiments were carried out with a relation of concentrations of H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup>  
125 between 2-6.

126 The best conditions obtained for the sono-Fenton experiment were tested in a real matrix.  
127 Influent samples were collected from WWTP “María del Carmen”, in Boyeros, Havana City,  
128 Cuba, (W 82.40; N 23.04). Samples were collected in 2.5 L amber glass bottles and  
129 transferred from the WWTP to our laboratory in cooled box and then kept refrigerated (+4  
130 °C). Wastewater samples were filtered after reaching room temperature using medium density  
131 cellulose filter. The samples were then acidified to pH 3 by adding H<sub>2</sub>SO<sub>4</sub>. The wastewater  
132 was characterized by Standard Method for the examination of water and wastewater. <sup>[37]</sup> In  
133 all experiments, liquid samples periodically were drawn from the reaction vessel for chemical  
134 analyses; the total volume withdrawn during a single experiment was less than 6% of the total  
135 reacting volume. A solution containing KI, Na<sub>2</sub>SO<sub>3</sub>, and NaOH (each 0.1 M) was used to  
136 quench the reaction in the samples when H<sub>2</sub>O<sub>2</sub> and the Fenton reagent were used. The  
137 obtained precipitate was removed on a 0.45 µm RC syringe filter prior to chemical analyses.

138

### 139 *Chemical analysis*

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

148 A total organic carbon (TOC) analysis was performed using a TOC-LCPN Shimadzu analyzer  
149 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.

$$M(\%) = \frac{TOC_0 - TOC}{TOC_0} * OC_0 \quad (2)$$

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

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

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

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

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

194

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

198 Sonochemical reactions would be favored by an increase in US power at a fixed frequency. It  
199 is widely accepted that higher ultrasonic power input increases the frequency of cavitation,  
200 the number of active cavitation bubbles, the size of individual bubbles, as well as the rate of  
201 generation and concentration of hydroxyl radicals. [44] During ultrasonic irradiation, two main  
202 reactions occur: (1) pyrolysis due to the high temperature and pressure in the gas phase, and  
203 (2) hydroxyl radical attack in the bubble-liquid interface and/or in the bulk liquid. Gas phase  
204 pyrolytic reactions are considered to play a minor role in the case of non-volatile solutes.  
205 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  
206 low water solubility (Log K<sub>ow</sub> = 0.28 [45]), it has been demonstrated that the attack of hydroxyl  
207 radicals on CIP molecules is the dominant reaction. [33, 35] Recent studies revealed the  
208 intensification of the sonochemical degradation of levofloxacin at 20 kHz using carbon  
209 tetrachloride as a rate enhancer. [44] The formation of °Cl radicals will lead to a series of  
210 recombination reactions conducting to the formation of additional active species, such as  
211 HClO, Cl<sub>2</sub> and chlorine-containing radicals (Cl•, CCl<sub>3</sub>• and :CCl<sub>2</sub>), having strong oxidizing  
212 property, which will markedly accelerate the degradation of levofloxacin in aqueous solution.

213 [44] It was reported<sup>[46]</sup> that the improvement of US power had a positive effect on the  
214 degradation rate of the antibiotic, until an optimal power dissipation. Beyond this value,  
215 cavitation activity and pollutant degradation, are either slightly affected or decreases. This  
216 optimal power is dependent on the reactor configuration and on the particular  
217 system/pollutant.

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

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

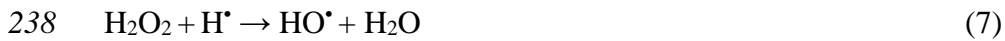
$$\text{deg} = -6.032 + 0.021 F - 0.004 F * P + 2.612 P + 0.039 P * P \quad R^2 = 99.73\% \quad (4)$$

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

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

230 Few reports about the combination of ultrasound with H<sub>2</sub>O<sub>2</sub> on the fluoroquinolones  
231 degradation have been found. <sup>[48]</sup> It is well documented in the literature that during aqueous  
232 sonolysis, hydroxyl radicals are produced and recombined into H<sub>2</sub>O<sub>2</sub> at the bubble-liquid  
233 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<sup>•</sup> generated by water sonolysis thus  
235 generating additional HO<sup>•</sup> 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<sub>2</sub>O<sub>2</sub> dose. [53]

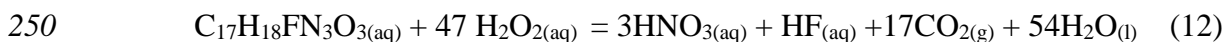


239 where US refers to the ultrasonic irradiation.

240 Hydroxyl radicals can (i) degrade organic compounds, (ii) react with H<sub>2</sub>O<sub>2</sub> (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<sub>2</sub>O<sub>2</sub> addition  
248 on CIP sonolysis. The stoichiometric amount of the required H<sub>2</sub>O<sub>2</sub> 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<sub>2</sub>O<sub>2</sub> 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<sub>2</sub>O<sub>2</sub>. This was verified by comparing the means of CIP degradation by

257 Student test (for  $\alpha=0.05$ ). When ultrasound is applied without  $H_2O_2$  the degradation and  
258 mineralization (35.8% and 22.6% respectively) were similar to the results obtained for one  
259 time the stoichiometric amount of  $H_2O_2$  (36.5% and 24.4% respectively), the highest values  
260 obtained when hydrogen peroxide was added. In some of the experiments, the addition of  
261  $H_2O_2$  showed a detrimental effect on US-driven CIP degradation in comparison to the  
262 performance of the ultrasound-driven process alone.

263 As previously stated here, despite the generation of hydroxyl radicals by its own sonolysis,  
264 the hydrogen peroxide can act as a hydroxyl radical scavenger, producing the much less  
265 reactive hydroperoxyl radicals (Eq. 8). The hydroxyl radicals in excess will be recombined  
266 forming water or hydrogen peroxide (Eqs. 9-11). At pH 3, the addition of different  
267 stoichiometric amounts of  $H_2O_2$  does not improve the CIP sonolysis process. Several authors  
268 reported this negative influence of  $H_2O_2$  in organic pollutant sonodegradation. [36, 52]  
269 Manousaki et al. [52] studied the degradation of sodium dodecyl benzene sulfonate in water  
270 by ultrasonic irradiation at 20 and 80 kHz and found a detrimental effect of hydrogen  
271 peroxide on the substrate degradation, besides the above-mentioned scavenging effect: the  
272 pollutant removal occurred mainly in the interfacial region, and thus the beneficial effect of  
273 extra hydroxyl radicals (Eq. 7) would be of marginal importance, even close to the cavitation  
274 bubbles, due to the thermal decomposition of hydrogen peroxide molecules to oxygen and  
275 water. Nevertheless, other authors claim that the addition of  $H_2O_2$  has a positive effect on the  
276 degradation of various organic compounds. [30, 32, 48, 59-61] The presence of an optimal amount  
277 of  $H_2O_2$  for the sonochemical degradation of the target compounds can occur, but it is  
278 difficult to determine the optimal concentration for each compound. [59, 60, 62] It is because the  
279 experimental conditions varied widely and a very limited range of  $H_2O_2$  concentrations was  
280 used in most previous studies. [61] Under our experimental conditions, this optimum amount of  
281  $H_2O_2$  was not found.

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

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



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

306 An additional ultrasonic experiment was carried out, to evaluate the effect of adding only  
 307 iron, using 2.37 mM of Fe<sup>2+</sup> without additional amount of hydrogen peroxide. In this  
 308 condition the CIP degradation at 15 minutes was 18.5%, higher than the value obtained in  
 309 single sonication experiment but much lower than in the case of hydrogen peroxide was also  
 310 added together with ferrous salt (98.4%, row 7 table 3). This result can be explained by the  
 311 formation of hydrogen peroxide during sonication in water. However, it is known that the  
 312 amount of generated H<sub>2</sub>O<sub>2</sub> is not significant comparing with those added as Fenton reagent.  
 313 [66, 67]

314 The mineralization for the sono-Fenton process was also higher than for ultrasonic oxidation  
 315 alone (row 1 in Table 3) and for sonolysis with hydrogen peroxide (rows 2 in Table 3). The  
 316 best mineralization was obtained when 14.2 mM of H<sub>2</sub>O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup> ratio 6 (row 7 in  
 317 Table 3) were used. An additional experiment was carried out at the same conditions of row 7  
 318 (Table 3) without ultrasound (Fenton reaction). It can be seen, that at 15 min the degradation  
 319 of the sono-Fenton process was practically the same for both processes. With regard to the  
 320 mineralization, sono-Fenton gave better results than the Fenton process: for example at 60  
 321 min, the mineralization rate was 30 % higher for sono-Fenton than for Fenton alone (62 vs.  
 322 30.3). This result shows that ultrasonic radiation combined with Fenton reagent enhances the  
 323 mineralization of aqueous solution.

324 A mathematical model describing the mineralization behavior at 60 min as a function of H<sub>2</sub>O<sub>2</sub>  
 325 concentration and H<sub>2</sub>O<sub>2</sub>/Fe<sup>2+</sup> concentration ratio is proposed as follows:

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



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

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

335 The water treatment by AOPs can be affected by the presence of inorganic and organic  
336 components in the water matrix, significantly slowing the degradation of the target pollutants.  
337 [70-71] Several authors have reported the role of organic components on the sonochemical  
338 degradation of persistent contaminants that appears to be a complex task which need to be  
339 experimentally verified for different systems. [7, 72-77] On the one hand, the presence of an  
340 organic matrix reduces the sonochemical degradation of target contaminants. [7, 72-74] On the  
341 other hand, the presence of organic matter did not affect the sonochemical degradation of  
342 methyl tert-butyl ether, [76] perfluorooctane sulfonate and perfluorooctanoate. [77] In order to  
343 investigate the efficiency of the sono-Fenton degradation of CIP in real application, some  
344 experiments with a real wastewater matrix (WW) were performed. In the case of Fenton  
345 chemistry, the presence of organic and inorganic compounds in WW may hamper this  
346 reaction by scavenging hydroxyl radicals and/or forming iron complex. [7, 78] A positive effect  
347 has also been reported, phenolic compounds that WW may contain could reduce ferric ion to  
348 ferrous ion and thus enhance Fenton reaction. [76]

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

351 adjustment to 3 (WW-02). As CIP is the major organic compound in this matrix, biochemical  
352 oxygen demand (BOD<sub>5</sub>), chemical oxygen demand (COD) and TOC concentration increased  
353 when it was added. However, the BOD<sub>5</sub>/COD ratio decreased from 0.33 to 0.21 showing a  
354 decrease in the biodegradability of CIP-doped matrix WW-02. De Bel et al. [35]  
355 experimentally demonstrated the low degradability of the 15 mgL<sup>-1</sup> CIP aqueous solution with  
356 BOD<sub>5</sub>/COD ratio of only 0.06. The suspended solid concentration in WW-02 also decreased,  
357 due to the solubility of some solids with pH decreasing. The real matrix was treated by the  
358 sono-Fenton process. Two different series of experiments were carried out: (i) under the best  
359 conditions obtained during CIP degradation in aqueous solution (14.2 mM H<sub>2</sub>O<sub>2</sub> and  
360 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  
361 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  
362 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).

363 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)  
364 by the sono-Fenton process in a real WW matrix for both series of experiments. The  
365 degradation and mineralization of CIP are higher when a higher concentration of hydrogen  
366 peroxide is used. Nevertheless, even under this condition in a real matrix WW-02,  
367 degradation of both CIP and TOC by sono-Fenton is significantly hampered in WW. The  
368 degradation of CIP at 15 min and mineralization at 60 min are less important in real  
369 conditions (13.6% and 18.9%), than for synthetic water. This result shows the inhibition of  
370 CIP degradation and mineralization in a real WW matrix, as reported before for the sonolysis  
371 of CIP and other persistent pollutants in different organic matrices. [7, 70-72]

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

376 resistance in natural systems. On the other hand, in the best cases, the BOD<sub>5</sub> removal was  
377 14.2% (Table 4), the COD and TOC removal were higher than 50% and the BOD<sub>5</sub>/COD ratio  
378 increased from 0.21 to 0.36, showing an increase in biodegradability. <sup>[35]</sup> This result is very  
379 promising because it opens the perspective of using ultrasound and sono-Fenton as a  
380 pretreatment of biological process in a WWTP for eliminating persistent organic pollutants.

### 381 **Conclusion**

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

389 The addition of hydrogen peroxide, as a radical promoter, does not markedly improve the  
390 sonolysis process in the range of operating studied conditions. In contrast, CIP degradation  
391 and mineralization are highly improved in the case of the US/Fenton system. The optimal  
392 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  
393 at least a 60% mineralization rate. The degradation of both CIP and TOC by sono-Fenton  
394 was significantly hampered in a real waste water matrix. However, the pollutant degradation,  
395 COD and TOC removals can be considered as efficient in the real matrix, with an increase in  
396 the biodegradability of the wastewater. These results show that sono-Fenton oxidation can be  
397 considered as a promising pretreatment process for wastewater containing pharmaceutical  
398 compounds.

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405 **References**

406

407 [1] Rivera-Utrilla, J.; Sánchez-Polo, M.; Ferro-García, M. Á.; Prados-Joya, G.; Ocampo-  
408 Pérez, R. Pharmaceuticals as emerging contaminants and their removal from water. A  
409 review. *Chemosphere*. **2013**, *93*, 1268-1287.

410 [2]. Padhye, L. P.; Yao, H.; Kung'u, Francis T.; Huang, Ch.H.; Year-long evaluation on  
411 the occurrence and fate of pharmaceuticals, personal care products, and endocrine  
412 disrupting chemicals in an urban drinking water treatment plant. *Water Res.* **2014**, *51*,  
413 266-276.

414 [3]. Andreu, V.; Gimeno García, E.; Pascual, J. A.; Vazquez-Roig, P.; Picó, Y. Presence of  
415 pharmaceuticals and heavy metals in the waters of a Mediterranean coastal wetland:  
416 Potential interactions and the influence of the environment. *Sci. Total Environ.* **2016**,  
417 *540*, 278-286.

418 [4] Alves Monteiro, M.; Ferraz Spisso, B.; dos Santos, Rodrigues Martins Pastor J.; da  
419 Pinto Costa, R.; Gomes Ferreira, R.; Ulberg Pereira, M.; da Silva Miranda, T.; de  
420 Rodrigues Geraldino de Andrade, B.; d'Avila, L. A. Occurrence of antimicrobials in  
421 river water samples from rural region of the State of Rio de Janeiro, Brazil. *J. Environ.*  
422 *Protect.* **2016**, *7*, 230-241.

- 423 [5] Lloret, L.; Eibes, G.; Lú Chau, T. A.; Moreira, M. T.; Feijoo, G.; Lema, J. M.  
424 Laccase-catalyzed degradation of anti-inflammatories and estrogens. *Biochem. Eng. J.*  
425 **2010**, *51*, 124-131.
- 426 [6] Santos, L. H.; Araújo, A. N.; Fachini, A.; Pena, A.; Delerue Matos, C.; Montenegro,  
427 M. C. Ecotoxicological aspects related to the presence of pharmaceuticals in the  
428 aquatic environment. *J. Hazard. Mater.* **2010**, *175*, 45-95.
- 429 [7] Ziyilan, A.; Ince N. H. The occurrence and fate of anti-inflammatory and analgesic  
430 pharmaceuticals in sewage and fresh water: treatability by conventional and non-  
431 conventional processes. *J. Hazard. Mater.* **2011**, *187*, 24-36.
- 432 [8] Taylor, D.; Senac, T. Human pharmaceutical products in the environment—The  
433 “problem” in perspective. *Chemosphere.* **2014**, *115*, 95-99.
- 434 [9] Pereira, A. M.; Silva, L. J. G.; Meisel, L. M.; Lino, C. M.; Pena, A. Environmental  
435 impact of pharmaceuticals from Portuguese wastewaters: geographical and seasonal  
436 occurrence, removal and risk assessment. *Environ. Res.* **2015**, *136*, 108-119.
- 437 [10] Homem, V.; Santos, L. Degradation and removal methods of antibiotics from aqueous  
438 matrices—a review. *J. Environ. Manage.* **2011**, *92*, 2304-2347.
- 439 [11] Xiao, R.; Heb, Z.; Diaz, D.; Yang, G.; Weavers, L. Sonochemical degradation of  
440 ciprofloxacin and ibuprofen in the presence of matrix organic compounds. *Ultrason.*  
441 *Sonochem.* **2014**, *21*, 428-435.
- 442 [12] Zuccato, E.; Castiglioni, S.; Fanelli, R.; Bagnati, R.; Reitano, G.; Calamari, D. Risks  
443 related to the discharge of pharmaceuticals in the environment: further research is  
444 needed. *Pharmaceuticals in the Environment*; Springer, 2004, 431-437.
- 445 [13] Quesada Peñate I.; Jáuregui Haza U. J.; Wilhelm A. M.; Delmas H. Contaminación de  
446 las aguas con productos farmacéuticos. Estrategias para enfrentar la problemática.  
447 *CENIC Ciencias Biológicas.* **2009**, *40*, 173-179.

- 448 [14] Kümmerer, K. Significance of antibiotics in the environment. *J. Antimicrob.*  
449 *Chemother.* **2003**, *52*, 5-7.
- 450 [15] Graham, D. W.; Olivares Rieumont, S.; Knapp, Ch. W.; Lima, L.; Werner, D.; Bowen,  
451 E. Antibiotic resistance gene abundances associated with waste discharges to the  
452 Almendares River near Havana, Cuba. *Environ. Sci. Technol.* **2010**, *45*, 418-424.
- 453 [16] Knapp, C. W.; Lima, L.; Olivares Rieumont, S.; Bowen, E.; Werner, D.; Graham, D.  
454 W. Seasonal variations in antibiotic resistance gene transport in the Almendares River,  
455 Havana, Cuba. *Frontiers in microbiology.* **2012**, *3*, 396.
- 456 [17] Martínez, J. L. Antibiotics and antibiotic resistance genes in natural environments.  
457 *Science.* **2008**, *321*, 365-367.
- 458 [18] Larsson, D. J. Antibiotics in the environment. *Upsala journal of medical sciences*,  
459 **2014**, *119*, 108-112.
- 460 [19] Li, X.; Wang, W.; Dou, J.; Gao, J.; Chen, S.; Quan, X.; Zhao, H. Dynamic adsorption  
461 of ciprofloxacin on carbon nanofibers: Quantitative measurement by in situ  
462 fluorescence. *J. Water Process Eng.* **2016**, *9*, 14-20.
- 463 [20] Ingerslev, F.; Halling - Sørensen, B. Biodegradability properties of sulfonamides in  
464 activated sludge. *Environ. Toxicol. Chem.* **2000**, *19*, 2467-2473.
- 465 [22] Hughes, S. R.; Kay. P.; Brown, L. E. Global synthesis and critical evaluation of  
466 pharmaceutical data sets collected from river systems. *Environ. Sci. Technol.* **2012**,  
467 *47*, 661-677.
- 468 [23] Li, W.; Nanaboina, V.; Zhou, Q.; Korshin, G. V. Effects of Fenton treatment on the  
469 properties of effluent organic matter and their relationships with the degradation of  
470 pharmaceuticals and personal care products. *Water Res.* **2012**, *46*, 403-412.
- 471 [24] Mason, T. Industrial sonochemistry: potential and practicality. *Ultrasonics.* **1992**, *30*,  
472 192-196.

- 473 [25] Kotronarou, A.; Mills, G.; Hoffmann, M. R. Decomposition of parathion in aqueous  
474 solution by ultrasonic irradiation. *Environ. Sci. Technol.* **1992**, *26*, 1460-1462.
- 475 [26] Koda, S.; Kimura, T.; Kondo, T.; Mitome, H. A standard method to calibrate  
476 sonochemical efficiency of an individual reaction system. *Ultrason. Sonochem.* **2003**, *10*,  
477 149-156.[27] Gogate, P. R.; Sutkar, V. S.; Pandit, A. B. Sonochemical reactors: important  
478 design and scale up considerations with a special emphasis on heterogeneous systems. *Chem.*  
479 *Eng. J.* **2011**, *166*, 1066-1082.
- 480 [28] Suslick, K. S. Sonochemistry. *Science.* **1990**, *247*, 1439-1446.
- 481 [29] Mason, T.; Lorimer, J.; Bates, D. Quantifying sonochemistry: casting some light on a  
482 'black art'. *Ultrasonics.* **1992**, *30*, 40-42
- 483 [30] Quesada Peñate, I.; Julcour Lebigue C.; Jáuregui Haza U. J.; Wilhelm, A. M.; Delmas,  
484 H. Sonolysis of levodopa and paracetamol in aqueous solutions. *Ultrason. Sonochem.*  
485 **2009**, *16*, 610-616.
- 486 [31] Fick, J.; Söderström, H.; Lindberg, R. H.; Phan, Ch.; Tysklind, M.; Larsson, D. G.  
487 Contamination of surface, ground, and drinking water from pharmaceutical  
488 production. *Environ. Toxicol. Chem.* **2009**, *28*, 2522-2527.
- 489 [32] Cruz González, G.; González Labrada, K.; Milián Rodríguez, Y.; Quesada Peñate, I.;  
490 Colín Luna, J. A.; Ramírez Muñoz, J.; Jáuregui Haza, U. J. Enhancement of  
491 paracetamol degradation by sono-Fenton process. *Int. J. Chem. Mat. Environ. Res.*  
492 **2015**, *2*, 37-45.
- 493 [33] De Bel, E.; Janssen, C.; De Smet, S.; Van Langenhove, H.; Dewulf, J. Sonolysis of  
494 ciprofloxacin in aqueous solution: Influence of operational parameters. *Ultrason.*  
495 *Sonochem.* **2011**, *18*, 184-189.
- 496 [34] Sutar, R. S.; Rathod, V. K. Ultrasound assisted Laccase catalyzed degradation of  
497 Ciprofloxacin hydrochloride. *J. Ind. and Eng. Chem.* **2015**, *31*, 276-282.

- 498 [35] De Bel, E.; Dewulf, J.; De Witte, B.; Van Langenhove, H.; Janssen, C. Influence of  
499 pH on the sonolysis of ciprofloxacin: biodegradability, ecotoxicity and antibiotic  
500 activity of its degradation products. *Chemosphere*. **2009**, *77*, 291-295.
- 501 [36] Lastre-Acosta, A. M.; Cruz González, G.; Nuevas Paz, L.; Jáuregui Haza, U. J.;  
502 Teixeira Silva Costa, A. C. Ultrasonic degradation of sulfadiazine in aqueous  
503 solutions. *Environ. Sci. and Pollut. Res.* **2015**, *22*, 918-925.
- 504 [37] Cleceri, L.; Greenberg, A.; Eaton, A. Standard methods for the examination of water  
505 and wastewater. American Public Health Association, American Water Works  
506 Association, and Water Environment Association, Washington, DC, USA, 1998.
- 507 [38] Petrier, C.; David, B.; Laguian, S. Unexpected frequency effects on the rate of  
508 oxidative processes induced by ultrasound. *J. Amer. Chem. Soc.* **1992**, *114*, 3148-  
509 3150.
- 510 [39] Petrier, C.; David, B.; Laguian, S. Ultrasonic degradation at 20 kHz and 500 kHz of  
511 atrazine and pentachlorophenol in aqueous solution: Preliminary results.  
512 *Chemosphere*. **1996**, *32*, 1709-1718.
- 513 [40] Pétrier, C.; Francony, A. Ultrasonic waste-water treatment: incidence of ultrasonic  
514 frequency on the rate of phenol and carbon tetrachloride degradation. *Ultrason.*  
515 *Sonochem.* **1997**, *4*, 295-300.
- 516 [41] Weavers, L. K.; Malmstadt, N.; Hoffmann, M. R. Kinetics and mechanism of  
517 pentachlorophenol degradation by sonication, ozonation, and sonolytic ozonation.  
518 *Environ. Sci. Technol.* **2000**, *34*, 1280-1285.
- 519 [42] Golash, N.; Gogate, P. R. Degradation of dichlorvos containing wastewaters using  
520 sonochemical reactors. *Ultrason. Sonochem.* **2012**, *19*, 1051-1060.
- 521 [43] Wu, T. Y.; Guo, N.; Teh, C. Y.; Hay, J. X. W. Advances in ultrasound technology for  
522 environmental remediation; Springer Science & Business Media, **2012**, 95-104.



- 523 [44] Guo, W.; Shi, Y.; Wang, H.; Yang, H.; Zhang, G. Intensification of sonochemical  
524 degradation of antibiotics levofloxacin using carbon tetrachloride. *Ultrason.*  
525 *Sonochem.*, **2010**, *17*, 680-684.
- 526 [45] Takács Novák, K.; Józán, M.; Hermech, I.; Szász, G. Lipophilicity of antibacterial  
527 fluoroquinolones. *Int. J. of Pharmaceutics*. **1992**, *79*, 89-96.
- 528 [46] Bagal, M. V.; Gogate, P. R. Wastewater treatment using hybrid treatment schemes  
529 based on cavitation and Fenton chemistry: a review. *Ultrason. Sonochem.* **2014**, *21*, 1-  
530 14.
- 531 [47] Ou, H.; Ye, J.; Ma, S.; Wei, C.; Gao, N.; He, J. Degradation of ciprofloxacin by UV  
532 and UV/H<sub>2</sub>O<sub>2</sub> via multiple-wavelength ultraviolet light-emitting diodes: Effectiveness,  
533 intermediates and antibacterial activity. *Chem. Eng. J.* **2016**, *289*, 391-401.
- 534 [48] Wei, H.; Ye, J.; Ma, S.; Wei, Cha.; Gao, N.; He, J. Intensification of levofloxacin  
535 sono-degradation in a US/H<sub>2</sub>O<sub>2</sub> system with Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles. *Chinese*  
536 *Chem. Eng. J.* **2015**, *23*, 296-302.
- 537 [49] Gad-Allah, T. A.; Ali, M. E.; Badawy, M. I. Photocatalytic oxidation of ciprofloxacin  
538 under simulated sunlight. *J. Hazard. Mater.* **2011**, *186*, 751-755.
- 539 [50] Hamdaoui, O.; Naffrechoux, E. Sonochemical and photosonochemical degradation of  
540 4-chlorophenol in aqueous media. *Ultrason. Sonochem.* **2008**, *15*, 981-987.
- 541 [51] Velegraki, T.; Poulis, I.; Charalabaki, M.; Kalogerakis, N.; Samaras, P.; Mantzavinos,  
542 D. Photocatalytic and sonolytic oxidation of acid orange 7 in aqueous solution. *Appl.*  
543 *Catal., B: Environ.* **2006**, *62*, 159-168.
- 544 [52] Manousaki, E.; Psillakis, E.; Kalogerakis, N.; Mantzavinos, D. Degradation of sodium  
545 dodecylbenzene sulfonate in water by ultrasonic irradiation. *Water Res.* **2004**, *38*,  
546 3751-3759.

- 547 [53] Mohajerani, M.; Mehrvar, M.; Ein-Mozaffari, F. Recent achievements in combination  
548 of ultrasonolysis and other advanced oxidation processes for wastewater treatment.  
549 Int. J. Chem. Reactor Eng. **2010**, *8*, 5367-5382.
- 550 [54] Gogate, P. R. Treatment of wastewater streams containing phenolic compounds using  
551 hybrid techniques based on cavitation: a review of the current status and the way  
552 forward. Ultrason. Sonochem. **2008**, *15*, 1-15.
- 553 [55] Chakma, S.; Moholkar, V. S. Investigations in synergism of hybrid advanced  
554 oxidation processes with combinations of sonolysis+ fenton process+ UV for  
555 degradation of bisphenol A. Ind. Eng. Chem. Res. **2014**, *53*, 6855-6865.
- 556 [56] Rayaroth, M. P.; Aravind, U. K.; Aravindakumar, C. T. Degradation of  
557 pharmaceuticals by ultrasound-based advanced oxidation process. Environ. Chem.  
558 Letters. **2016**, *14*, 259-290.
- 559 [57] Méndez Arriaga, F.; Torres Palma, R. A.; Pétrier, C.; Esplugas, S.; Gimenez, J.;  
560 Pulgarin, C. Ultrasonic treatment of water contaminated with ibuprofen. Water Res.  
561 **2008**, *42*, 4243-4248.
- 562 [58] Neyens, E.; Baeyens, J. A review of classic Fenton's peroxidation as an advanced  
563 oxidation technique. J. Hazard. Mater. **2003**, *98*, 33-50.
- 564 [59] Mehrdad, A.; Hashemzadeh, R. Ultrasonic degradation of Rhodamine B in the  
565 presence of hydrogen peroxide and some metal oxide. Ultrason. Sonochem.. **2010**, *17*,  
566 168-172.
- 567 [60] Bremner, D. H.; Molina, R.; Martínez, F.; Melero, J. A.; Segura, Y. Degradation of  
568 phenolic aqueous solutions by high frequency sono-Fenton systems (US-Fe<sub>2</sub>O<sub>3</sub>/SBA-  
569 15-H<sub>2</sub>O<sub>2</sub>). Appl. Catal., B: Environ. **2009**, *90*, 380-388.
- 570 [61] Lim, M.; Son, Y.; Khim, J. The effects of hydrogen peroxide on the sonochemical  
571 degradation of phenol and bisphenol A. Ultrason. Sonochem. **2014**, *21*, 1976-1981.

- 572 [62] Ku, Y.; Tu, Y. H.; Ma, Ch. M. Effect of hydrogen peroxide on the decomposition of  
573 monochlorophenols by sonolysis in aqueous solution. *Water Res.* **2005**, *39*, 1093-  
574 1098.
- 575 [63] Neppolian, B., Jung, H.; Choi, H.; Lee, J. H.; Kang, J. W. Sonolytic degradation of  
576 methyl tert-butyl ether: the role of coupled Fenton process and persulphate ion. *Water*  
577 *Res.* **2002**, *36*, 4699-4708.
- 578 [64] Liang, J., Komarov, S.; Hayashi, N.; Kasai, E. Improvement in sonochemical  
579 degradation of 4-chlorophenol by combined use of Fenton-like reagents. *Ultrason.*  
580 *Sonochem.* **2007**, *14*, 201-207.
- 581 [65] Lin, J. G.; Ma, Y. S. Oxidation of 2-chlorophenol in water by ultrasound/Fenton  
582 method. *J. Environ. Eng.* **2000**, *126*, 130-137.
- 583 [66] Weissler A. Formation of hydrogen peroxide by ultrasonic waves: free radicals. 1959,  
584 *81*, 1077-1081.
- 585 [67] Jiang, Y.; Petrier C.; Waite, T. D. Kinetics and mechanisms of ultrasonic degradation of  
586 volatile chlorinated aromatics in aqueous solutions. *Ultrason. Sonochem.* **2002**, *9*,  
587 317–323.
- 588 [68] Bobu, M.; Yediler, A.; Siminiceanu, I.; Zhang, F.; Schulte Hostede, S. Comparison of  
589 different advanced oxidation processes for the degradation of two fluoroquinolone  
590 antibiotics in aqueous solutions. *J. Environ. Sci. Health, Part A.* **2013**, *48*, 251-262.
- 591 [69] Snyder, S. A.; Westerhoff, P.; Yoon, Y.; Sedlak, D. L. Pharmaceuticals, personal care  
592 products, and endocrine disruptors in water: implications for the water industry.  
593 *Environ. Eng. Sci.* **2003**, *20*, 449-469.
- 594 [70] Westerhoff, P.; Aiken, G.; Amy, G.; Debroux, J. Relationships between the structure  
595 of natural organic matter and its reactivity towards molecular ozone and hydroxyl  
596 radicals. *Water Res.* **1999**, *33*, 2265-2276.

- 597 [71] Huber, M. M.; Gobel, A.; Joss, A.; Hermann, N.; Loffler, D.; McArdell, Ch. S.; Ried,  
598 A.; Siegrist, H.; Ternes, T. A. von Gunten, U. Oxidation of pharmaceuticals during  
599 ozonation of municipal wastewater effluents: a pilot study. *Environ. Sci. Technol.*  
600 **2005**, *39*, 4290-4299.
- 601 [72] Taylor, E.; Cook, B.; Tarr, M. Dissolved organic matter inhibition of sonochemical  
602 degradation of aqueous polycyclic aromatic hydrocarbons. *Ultrason. Sonochem.*,  
603 **1999**, *6*, 175-183.
- 604 [73] Laughrey, Z.; Bear, E.; Jones, R.; Tarr, M. A. Aqueous sonolytic decomposition of  
605 polycyclic aromatic hydrocarbons in the presence of additional dissolved species.  
606 *Ultrason. Sonochem.* **2001**, *8*, 353-357.
- 607 [74] Lu, Y.; Weavers, L. K. Sonochemical desorption and destruction of 4-chlorobiphenyl  
608 from synthetic sediments. *Environ. Sci. Technol.* **2002**, *36*, 232-237.
- 609 [75] Goskonda, S.; Catallo, W. J.; Junk, T. Sonochemical degradation of aromatic organic  
610 pollutants. *Waste Manage.* **2002**, *22*, 351-356.
- 611 [76] Cheng, J.; Vecitis, Ch. D.; Park, H.; Mader, B. T. Hoffmann, M. R. Sonochemical  
612 degradation of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in  
613 landfill groundwater: environmental matrix effects. *Environ. Sci. Technol.* **2008**, *42*,  
614 8057-8063.
- 615 [77] Kang, J. W.; Hung, H. M.; Lin, A.; Hoffmann, M. R. Sonolytic destruction of methyl  
616 tert-butyl ether by ultrasonic irradiation: the role of O<sub>3</sub>, H<sub>2</sub>O<sub>2</sub>, frequency, and power  
617 density. *Environ. Sci. Technol.* **1999**, *33*, 3199-3205.
- 618 [78] Tokumura, M.; Sugawara, A.; Raknuzzaman, M.; Habibullah Al Mamun, Md.;  
619 Masunaga, S. Comprehensive study on effects of water matrices on removal of  
620 pharmaceuticals by three different kinds of advanced oxidation processes.  
621 *Chemosphere.* **2016**, *159*, 317-325.



623 **List of Figure Captions**

624 **Figure 1.** Molecular structure of CIP

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

627 **Figure 3.** Influence of ultrasonic frequency and actual ultrasonic power on CIP degradation  
628 and mineralization after 120 min. Open markers with solid line represent degradation and  
629 filled markers with dash line represent mineralization. Experimental conditions: ( $[CIP]_0$ : 100  
630  $\text{mg L}^{-1}$ , T: 30 °C,  $\text{pH}_0=3$ )

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

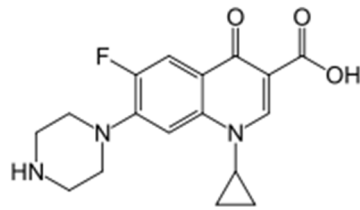
633 **Figure 5.** Degradation and mineralization trend in the US/ $\text{H}_2\text{O}_2$  process ( $F = 580 \text{ kHz}$  y  $P =$   
634  $21.7 \text{ W}$ ,  $\text{pH} = 3$ ,  $t = 60 \text{ min}$ )

635 **Figure 6.** Response surface as a function concentration of  $[\text{H}_2\text{O}_2]$  and the relation of  
636  $c(\text{H}_2\text{O}_2)/c(\text{Fe}^{2+})$

637 **Figure 7.** CIP degradation and mineralization by sono-Fenton process in a real WW matrix.  
638 Open markers with solid line represent degradation and filled markers with dash line mean  
639 mineralization for two different  $\text{H}_2\text{O}_2$  concentrations: 14.2 mM ( $\circ/\bullet$ ) and 31.8 mM ( $\square/\blacksquare$ ).  
640 Experimental conditions: ( $[CIP]_0$ : 100  $\text{mg L}^{-1}$ , T: 30 °C,  $\text{pH}_0=3$ )

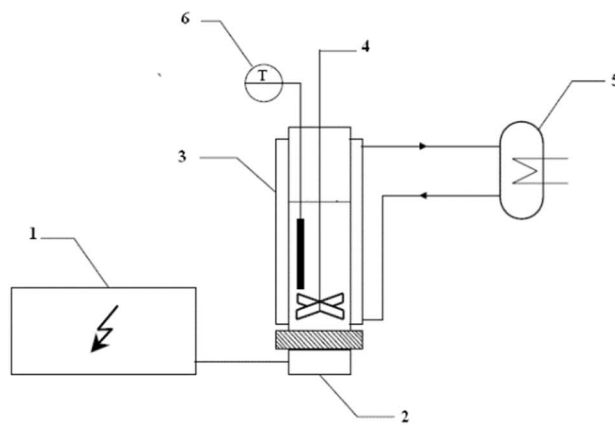
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642 **Figures**



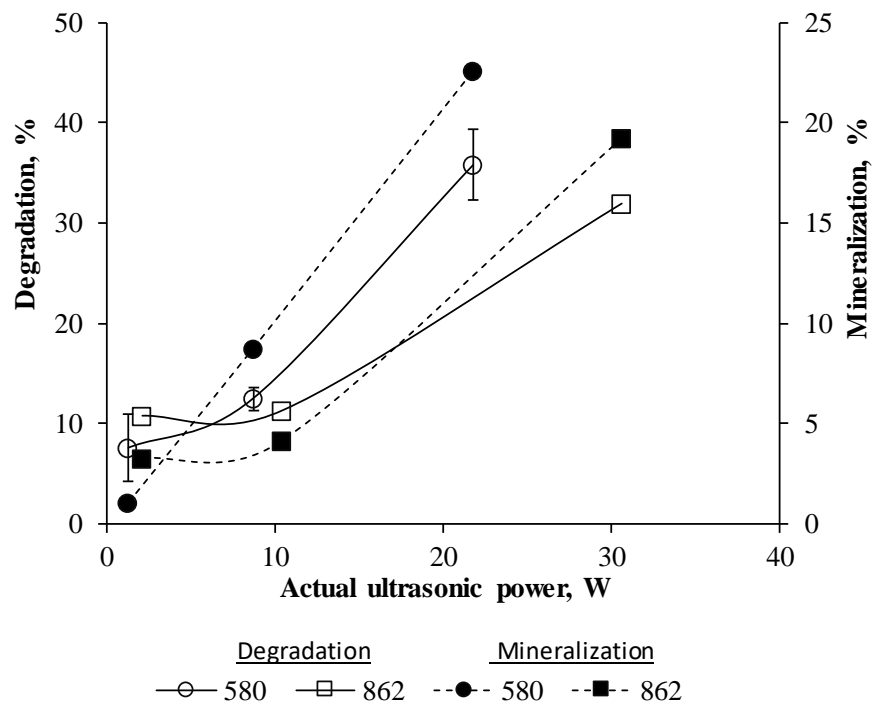
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644 Fig 1.



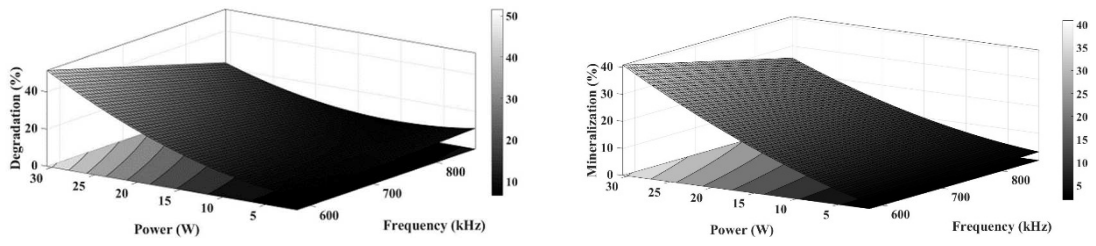
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646 Fig 2.



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648 Fig. 3.



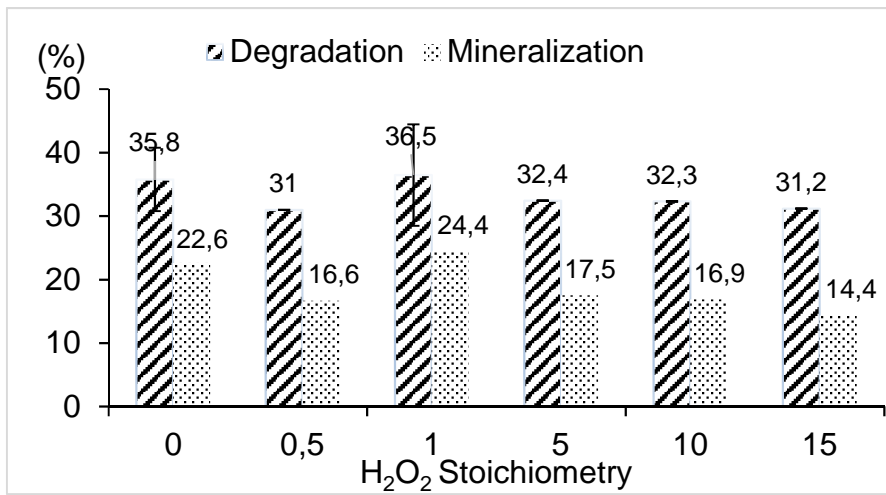
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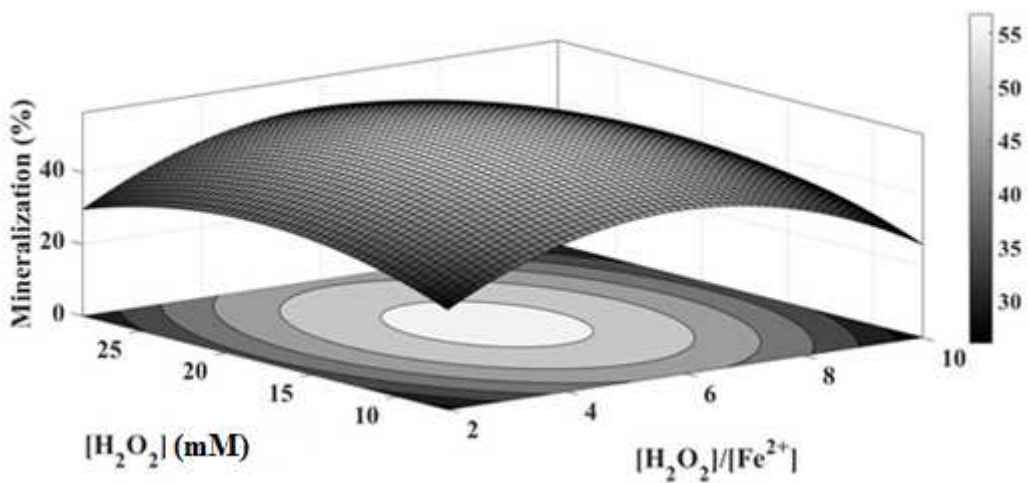
652 Fig. 4

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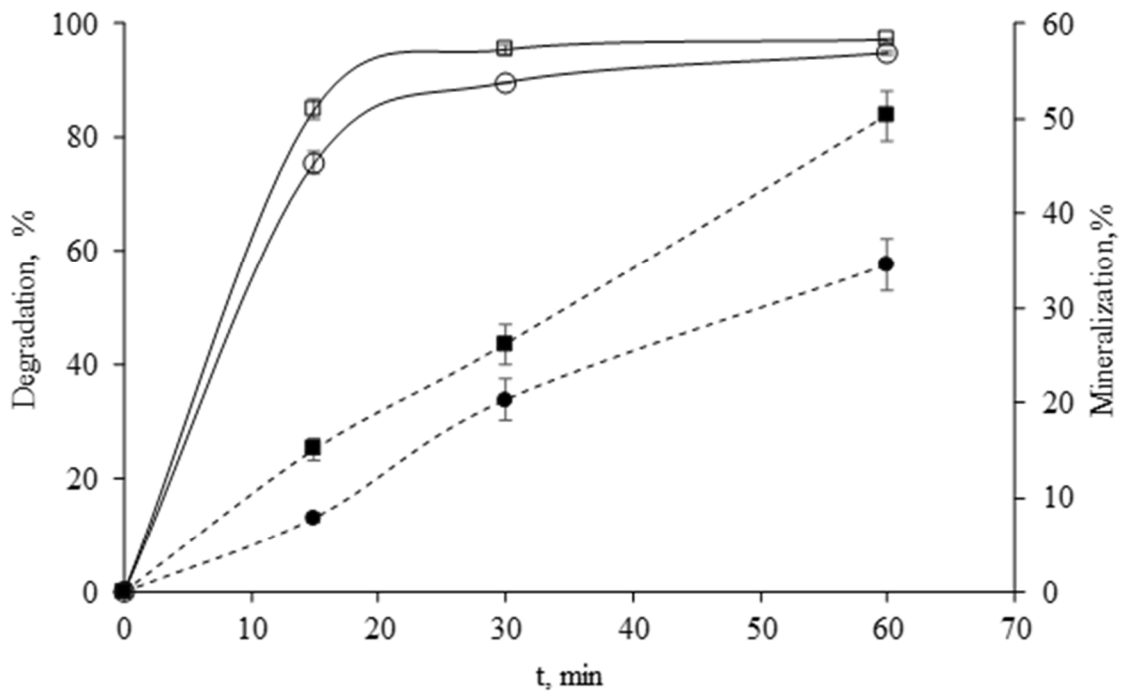
655 Fig 5.



656



657 Fig 6.



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659 Fig 7.

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661 **Tables**

662 **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)

663

664 **Table 2.** Degradation pseudo first-order rate constant for three different ultrasonic power at

665 frequency 580-862 kHz ( $[CIP]_0$ : 100 mg L<sup>-1</sup>, T: 30 °C, pH<sub>0</sub>=3)

666

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)

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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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680

681 **Table 4.** Physico-chemical characteristics of WW matrix before and after treatment by sono-  
 682 Fenton process ( $[CIP]_0$ : 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

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685 **Supporting informat**

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687 **Table 1S.** Regression and variance analysis for equation 4 (Degradation as function of

688 ultrasonic frequency and power).

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690

<i>Regression analysis</i>				
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
<i>Analysis of variance</i>				
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				

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

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<i>Regression analysis</i>				
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
<i>Analysis of variance</i>				
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				

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702 **Table 3S.** Regression and variance analysis for equation 17 (Mineralization as function of  
 703 hydrogen peroxide concentration and  $\text{H}_2\text{O}_2/\text{Fe}^{2+}$  concentration ratio for sono-Fenton reaction).  
 704

<i>Regression analysis</i>				
Parameter	Estimate	Error	t-statistic	p-value
Constant	-13.2	20.8	-0.63	0.571
$\text{H}_2\text{O}_2$	3.12	2.19	1.42	0.25
$\text{H}_2\text{O}_2/\text{Fe}^{+2}$	13.86	4.61	3.01	0.057
$\text{H}_2\text{O}_2^* \text{H}_2\text{O}_2$	-0.09	0.06	-1.49	0.233
$\text{H}_2\text{O}_2^* \text{H}_2\text{O}_2/\text{Fe}^{+2}$	0.007	0.09	0.07	0.946
$\text{H}_2\text{O}_2/\text{Fe}^{+2*} \text{H}_2\text{O}_2/\text{Fe}^{+2}$	-1.18	0.35	-3.31	0.045
<i>Analysis of variance</i>				
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				

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