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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 (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 ^[1-4] They could be toxic to aquatic life when released in the environment ^[5-9], even at very
41 low concentrations (parts-per-trillion to parts-per-billion) in aquatic systems. ^[10, 11] 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. ^[1-4,12] 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. ^[13] Antibiotics are of particular
47 concern because their presence in natural waters could contribute to the rise of antibiotic
48 resistance in microorganisms. ^[14-19]

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 6.5mg L^{-1} .^[21, 22] 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.^[17, 20] 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.^[7, 23]

58 Several techniques such as ozonation, photocatalysis or UV/H₂O₂ 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.^{[24,}

61 ^{25]} 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.^[26-28] 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^{*}), can react with the contaminant in
68 the interfacial region or in the bulk solution.^[29] 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.^[30] 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. ^[23, 31, 32]

78 There are not many previous studies concerning the sonolysis of CIP and its combination with
79 H₂O₂ 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. ^[33] Xiao et
81 al. ^[11] 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. ^[11] 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⁻¹) enzyme loading. As compared to conventional method, this technique not only
88 increases CIP degradation rate but also reduces degradation time. ^[34] Moreover, it was
89 observed that pH affected the ultrasonic degradation rate of aqueous CIP solution. ^[35]

90 In previous studies, Quesada et al. ^[30] 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 H₂O₂ 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 ^[36] and
95 paracetamol ^[32] degradation when concentrations of H₂O₂ and Fe²⁺ 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 H₂O₂ 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 H₂SO₄, 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 FeSO₄·7H₂O (99.5%), potassium iodide (99.5%), sodium hydroxide (99%) and sodium sulfite
110 (98%) obtained from Sigma-Aldrich, and hydrogen peroxide (30% wt v⁻¹), 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⁻⁰.
124 Sono-Fenton experiments were carried out with a relation of concentrations of H₂O₂/Fe²⁺
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 H₂SO₄. The wastewater
132 was characterized by Standard Method for the examination of water and wastewater. ^[37] 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, Na₂SO₃, and NaOH (each 0.1 M) was used to
136 quench the reaction in the samples when H₂O₂ 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⁻¹ 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 (R²= 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⁻¹.
152 Degradation experiments were performed at an initial CIP concentration of 100 mg L⁻¹, 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 C₀ 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 TOC₀ 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⁻¹ 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. [30] De Bel et al. [33] 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. [11, 38, 39] 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. [39] Other authors have reported faster
186 degradation of organic compounds at 200-600 kHz frequencies . [11, 39-42] 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. [43]

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⁻¹), in comparison with 801
197 kHz ($k_1 = 0.0055$ min⁻¹) and 1081 kHz ($k_1 = 0.0018$ min⁻¹).

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.m³ mol⁻¹ at 25°C [11]) and
206 low water solubility (Log K_{ow} = 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, Cl₂ and chlorine-containing radicals (Cl•, CCl₃• and :CCl₂), having strong oxidizing
212 property, which will markedly accelerate the degradation of levofloxacin in aqueous solution.

213 [44] It was reported^[46] 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 ^[33, 35, 47-49].
220 The highest pseudo first-order rate constant obtained in this work is comparable with the
221 reported value by De Bell and collaborators. ^[33]

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 H₂O₂ as a radical promoter***

230 Few reports about the combination of ultrasound with H₂O₂ on the fluoroquinolones
231 degradation have been found. ^[48] It is well documented in the literature that during aqueous
232 sonolysis, hydroxyl radicals are produced and recombined into H₂O₂ at the bubble-liquid
233 interface and/or in the bulk liquid. ^[50, 51] In general, H₂O₂ is expected to promote degradation

234 since it may be decomposed by US and/or react with H[•] generated by water sonolysis thus
235 generating additional HO[•] according to Equations 6 and 7. [7, 52] For this reason, the degradation
236 of organic compounds maybe augmented by an increase in the H₂O₂ dose. [53]

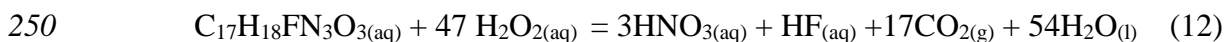


239 where US refers to the ultrasonic irradiation.

240 Hydroxyl radicals can (i) degrade organic compounds, (ii) react with H₂O₂ (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 H₂O₂ addition
248 on CIP sonolysis. The stoichiometric amount of the required H₂O₂ for the complete oxidation
249 of CIP in aqueous solution was calculated according to Equation 12:



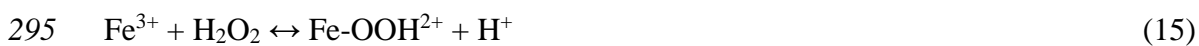
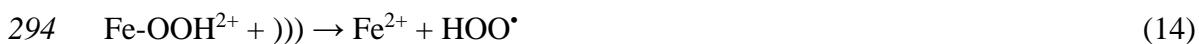
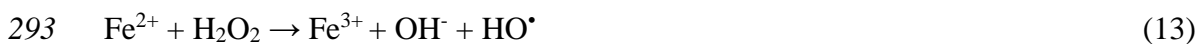
251 After one hour of reaction under stoichiometric conditions, a low CIP degradation was found:
252 5.9% under silent conditions . The influence of the oxidant concentration on CIP degradation
253 and mineralization was studied to understand the phenomena better. Experimental runs were
254 conducted with different concentrations of H₂O₂ 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 H₂O₂. 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, H₂O₂ 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 Fe²⁺ 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⁻¹,
298 F=580 kHz, P = 30.6 W, T = 30°C, pH= 3) at different concentrations of H₂O₂ and Fe²⁺
299 corresponding to a H₂O₂/Fe²⁺ ratio between 2 and 10, following a 3² 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 Fe²⁺ (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 Fe²⁺ 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 H₂O₂ 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 H₂O₂ and H₂O₂/Fe²⁺ 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 H₂O₂
 325 concentration and H₂O₂/Fe²⁺ 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 mgL^{-1} and pH

351 adjustment to 3 (WW-02). As CIP is the major organic compound in this matrix, biochemical
352 oxygen demand (BOD₅), chemical oxygen demand (COD) and TOC concentration increased
353 when it was added. However, the BOD₅/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⁻¹ CIP aqueous solution with
356 BOD₅/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 H₂O₂ and
360 H₂O₂/Fe²⁺ 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 H₂O₂/COD ratio as in the study with the
362 synthetic solution (31.8 mM H₂O₂ and H₂O₂/Fe²⁺ ratio of 6).

363 Figure 7 shows the CIP degradation and mineralization ([CIP]₀: 100 mg L⁻¹, T: 30°C, pH₀=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 BOD₅ removal was
377 14.2% (Table 4), the COD and TOC removal were higher than 50% and the BOD₅/COD ratio
378 increased from 0.21 to 0.36, showing an increase in biodegradability. ^[35] 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 H₂O₂ and H₂O₂/Fe²⁺ 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.; Hermecz, 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/H₂O₂ 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/H₂O₂ system with Fe₃O₄ 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.; Poulios, 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-Fe₂O₃/SBA-
569 15-H₂O₂). 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 O₃, H₂O₂, 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 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

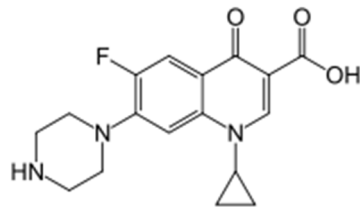
633 **Figure 5.** Degradation and mineralization trend in the US/ H_2O_2 process ($F = 580 \text{ kHz}$ y $P =$
634 21.7 W , $\text{pH} = 3$, $t = 60 \text{ min}$)

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 H_2O_2 concentrations: 14.2 mM (\circ/\bullet) and 31.8 mM (\square/\blacksquare).
640 Experimental conditions: ($[CIP]_0$: 100 mg L^{-1} , T: 30 °C, $\text{pH}_0=3$)

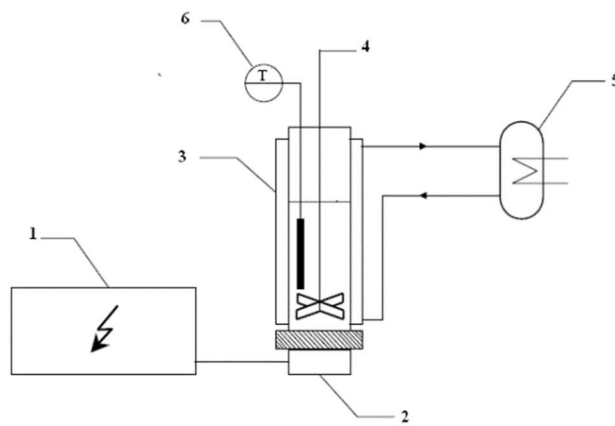
641

642 **Figures**



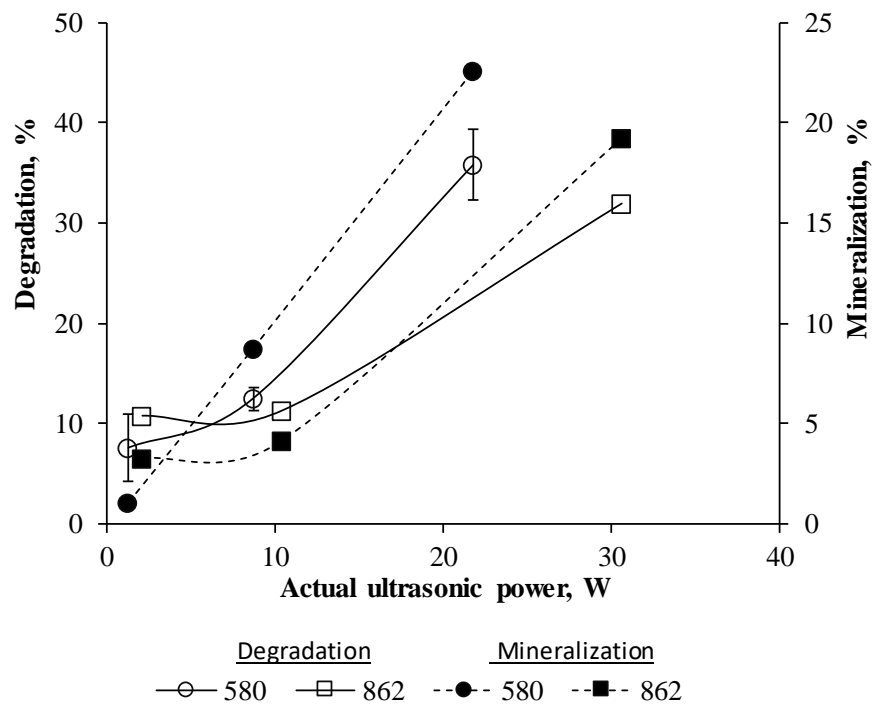
643

644 Fig 1.



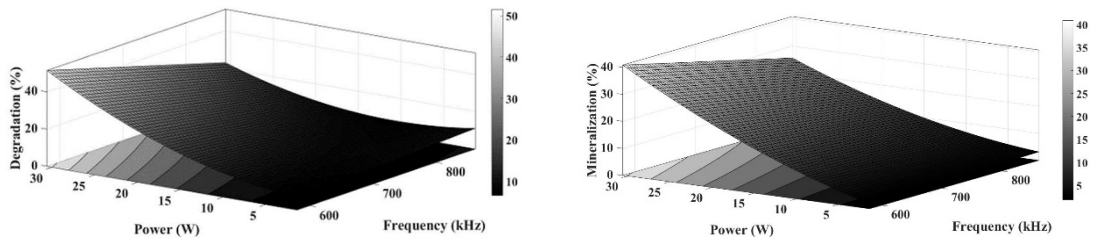
645

646 Fig 2.



647

648 Fig. 3.



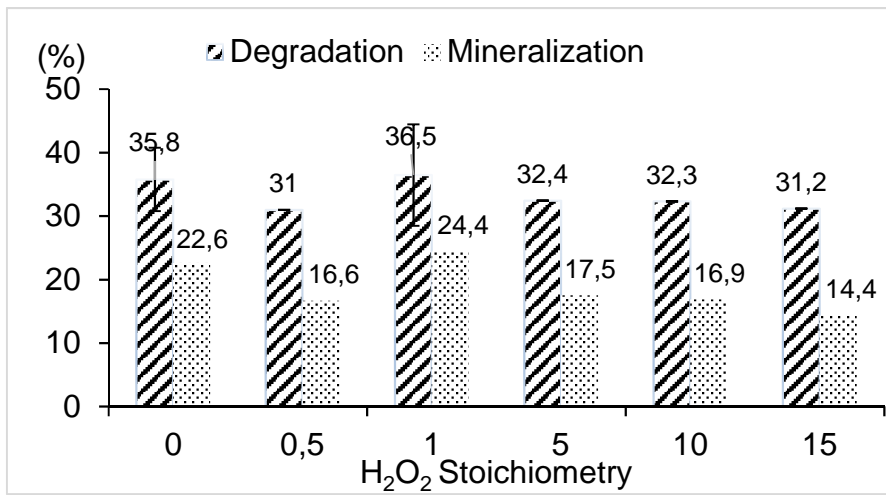
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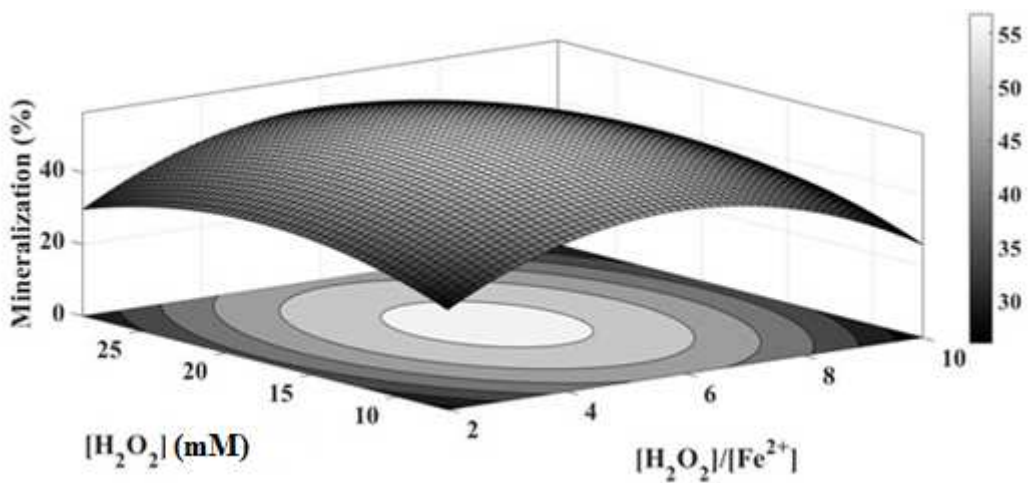
652 Fig. 4

653



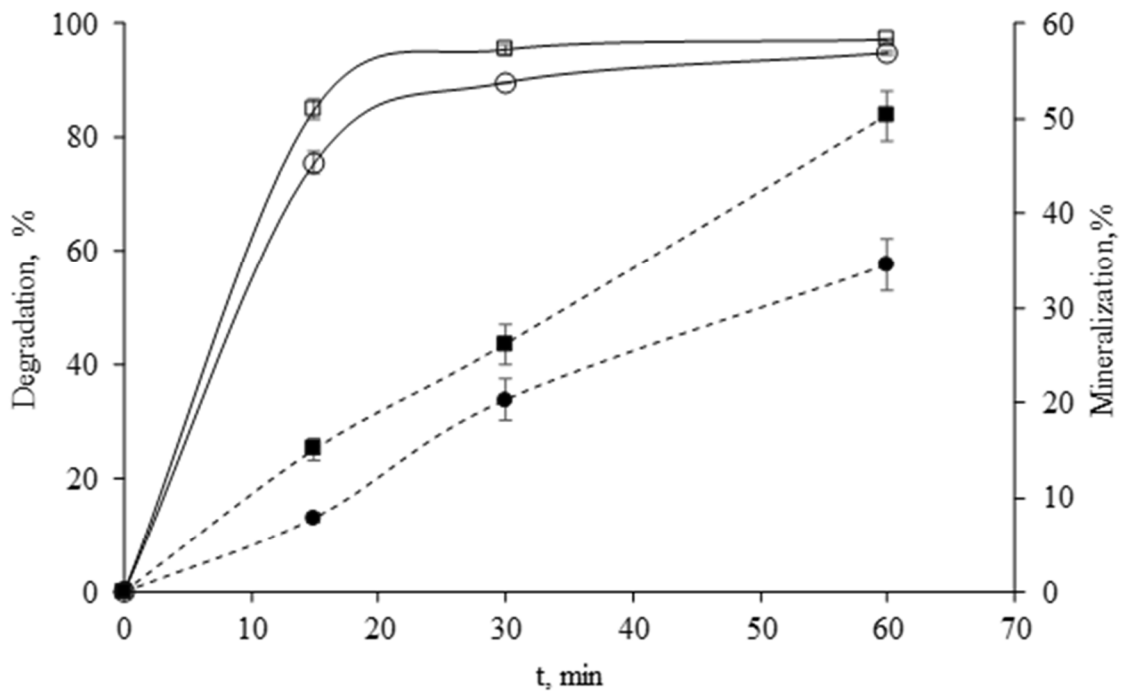
654

655 Fig 5.



656

657 Fig 6.



658

659 Fig 7.

660

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)

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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⁻¹, T: 30 °C, pH₀=3)

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Frequency (kHz)	P _{min} (W) (value)	P _{med} (W) (value)	P _{max} (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 Fe²⁺/H₂O₂ on CIP sonochemical degradation (t=15 min) and mineralization
 677 (t=60 min), (F=580 kHz, P = 30.6 W, [CIP]₀= 100 mg L⁻¹, T = 30°C, pH₀= 3). *Fenton
 678 reaction without ultrasound

Row	c(H ₂ O ₂) mM	c(H ₂ O ₂)/c(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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681 **Table 4.** Physico-chemical characteristics of WW matrix before and after treatment by sono-
 682 Fenton process ($[CIP]_0$: 100 mg L⁻¹, T: 30 °C, pH₀=3)

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

^aAverage of three sampling results; ^bAverage 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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<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).
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<i>Regression analysis</i>				
Parameter	Estimate	Error	t-statistic	p-value
Constant	-13.2	20.8	-0.63	0.571
H_2O_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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