Advanced oxidation of real sulfamethoxazole + trimethoprim formulations using different anodes and electrolytes

Juan C. Murillo-Sierra[a], Ignasi Sirés[b], Enric Brillas[b,*], Edgar J. Ruiz-Ruiz[a], Aracely Hernández-Ramírez[a,*]

[a] *Universidad Autónoma de Nuevo León, Facultad de Ciencias Químicas, Av. Universidad, Ciudad Universitaria, San Nicolás de los Garza, Nuevo León, Mexico.*

[b] *Laboratori d'Electroquímica dels Materials i del Medi Ambient, Departament de Química Física, Facultat de Química, Universitat de Barcelona, Martí i Franquès 1-11, 08028 Barcelona, Spain.*

*Corresponding author. E-mail: brillas@ub.edu (E. Brillas)

E-mail: aracely.hernandezrm@uanl.edu.mx (A. Hernández-Ramírez)

Abstract

A commercial sulfamethoxazole + trimethoprim formulation has been degraded in 0.050 M Na_2SO_4 at pH 3.0 by electrochemical oxidation with electrogenerated H_2O_2 (EO-H_2O_2), electro-Fenton (EF), photoelectro-Fenton with a 6-W UVA lamp (PEF) and solar photoelectro-Fenton (SPEF). The tests were performed in an undivided cell with an IrO_2-based, Pt or boron-doped diamond (BDD) anode and an air-diffusion cathode for H_2O_2 electrogeneration. The anode material had little effect on the accumulated H_2O_2 concentration. Both drugs always obeyed a pseudo-first-order decay with low apparent rate constant in EO-H_2O_2. Much higher values were found in EF, PEF and SPEF, showing no difference because the main oxidant was always $^{\bullet}OH$ formed from Fenton's reaction between H_2O_2 and added Fe^{2+}. The solution mineralization increased in the sequence EO-H_2O_2 < EF < PEF < SPEF regardless of the anode. The IrO_2-based and Pt anodes behaved similarly but BDD was always more powerful. In SPEF, similar mineralization profiles were found for all anodes because of the rapid removal of photoactive intermediates by sunlight. About 87% mineralization was obtained as maximum for the powerful SPEF with BDD anode. Addition of Cl^- enhanced the decay of both drugs due to their quicker reaction with generated active chlorine, but the formation of persistent chloroderivatives decelerated the mineralization process. Final carboxylic acids like oxalic and oxamic were detected, yielding Fe(III) complexes that remained stable in EF with BDD but were rapidly photolyzed in SPEF with BDD, explaining its superior mineralization ability.

Keywords: Electrochemical oxidation; Electro-Fenton; Photoelectro-Fenton; Sulfamethoxazole; Sunlight; Trimethoprim

1. Introduction

Over the last two decades, there has been an increasing concern about the presence of substances classified as emerging contaminants in water. Their long-term effects on humans or aquatic organisms are still unknown. Pharmaceuticals, which are defined as prescription, over the counter and veterinary drugs to prevent or treat human and animal diseases, are among these pollutants (Thiele-Bruhn and Beck, 2005; Ebele et al., 2017). In particular, the wide use of antibiotics favors their presence in the aquatic environment and, even at trace concentrations, they may induce the development of resistant bacteria or genes (Sirés and Brillas, 2012; Dias et al., 2014).

Sulfamethoxazole ($C_{10}H_{11}N_3O_3S$, 4-amino-N-(5-methyl-3-isoxazolyl)benzene-sulfonamide) and trimethoprim ($C_{14}H_{18}N_4O_3$, 2,4-diamino-5-(3,4,5-trimethoxybenzyl)-pyrimidine) (see molecular structures in Fig. 1) are two drugs prescribed for treating bacterial infections in humans, being commonly available as a unique commercial formulation (Dias et al., 2014). Approximately 15% and 60% of sulfamethoxazole and trimethoprim are excreted from the human body in their original form. As a result, metabolites and non-metabolized residues of both drugs have been detected in surface water at μg L^{-1} levels (Hirsch et al., 1999).

Most drugs from a wide spectrum of therapeutic classes enter in natural aquatic environments mainly conveyed by the effluents of sewage treatment plants due to the inefficacy of conventional water treatment technologies. Sulfamethoxazole and trimethoprim have been degraded by biological treatments, but after relatively long residence times (3-20 days) (Pérez et al., 2005). The degradation of both drugs by photolysis has been reported as well (Ryan et al., 2011). The main drawback of these processes is the production of metabolites that could be more recalcitrant or toxic than parent molecules.

Electrochemical advanced oxidation processes (EAOPs) such as electrochemical oxidation (EO), EO with electrogenerated H_2O_2 (EO-H_2O_2), electro-Fenton (EF), photoelectro-Fenton (PEF) and solar photoelectro-Fenton (SPEF) have been successfully applied to the remediation of wastewater containing drugs (Sirés and Brillas, 2012; Feng et al., 2013; Moreira et al., 2017). Their oxidation power is based on their ability to generate hydroxyl radical ($^{\bullet}OH$) as strong oxidant to attack the organic pollutants, which depends on parameters like electrode material, applied current and electrolyte composition. Several authors degraded synthetic sulfamethoxazole solutions by EO with a boron-doped diamond anode (BDD) in 1 M Na_2SO_4 (Martín de Vidales et al., 2012) and in chloride + sulfate mixtures (Boudreau et al., 2010) and with a mixed oxide anode ($Ti/Ru_{0.3}Ti_{0.7}O_2$) in 0.1 M NaCl at pH 3.0 (Hussain et al., 2015). Fast decay of the drug and partial mineralization were found in all cases, with formation of chloroderivatives in the presence of Cl^-. In contrast, Dirany et al. (2010, 2011) described the total mineralization of sulfamethoxazole solutions with 0.2 mM Fe^{2+} at pH 3.0 by EF using a BDD/carbon-felt cell. Wang et al. (2011) compared the degradation of up to 300 mg L^{-1} sulfamethoxazole in sulfate medium by EO, EO-H_2O_2, EF and PEF with UVA light using a Ti/RuO_2 anode and a carbon fiber cathode, attaining a maximum mineralization of 80% after 360 min of PEF at 0.36 A. Under similar conditions, Zhang et al. (2016) reported the same mineralization for 200 mg L^{-1} trimethoprim after 360 min of SPEF under optimum pH 3.0, 1.0 mM Fe^{2+} and current density (j) of 18 mA cm^2. For this drug, optimum conditions of pH 3, j = 207 mA cm^{-2} and 0.49 M Na_2SO_4 were found for the EO treatment with BDD (González et al., 2011). Mansour et al. (2015) tried to optimize the EF process with a Pt/carbon-felt cell, but they only reached 12% mineralization. Moreira et al. (2014) reported partial mineralization of near 78% by PEF and SPEF for 20 mg L^{-1} trimethoprim in 7.0 g L^{-1} Na_2SO_4 with 2 mg L^{-1} Fe^{2+} at pH 3.0 using a BDD/air-diffusion cell. However, only a reduced number of articles examined the EO treatment of mixtures of drugs,

like sulfamethoxazole with ciprofloxacin in sulfate and chloride media using a BDD anode (Lan et al., 2017), with diclofenac in phosphate and sulfate media using a Pt anode (Sifuna et al., 2016) and with trimethoprim using a BDD anode (Amorim et al., 2013). In the latter case, 1.0 L of 250 mg L^{-1} sulfamethoxazole + 50 mg L^{-1} trimethoprim in 0.1 M Na_2SO_4 were treated in a flow cell at 5 L min^{-1} to achieve a partial mineralization of 90% at pH 5.0 after 3 h at j = 36 mA cm^{-2}. More research efforts are then required to evaluate the oxidation ability and viability of more powerful EAOPs to destroy such mixtures upon use of different anode materials and electrolytes.

This work aims to study the degradation of sulfamethoxazole + trimethoprim mixtures by EO-H_2O_2, EF, PEF and SPEF. The comparative oxidation power of all these treatments with three different anodes, namely a metal oxide (IrO_2-based), Pt and BDD, and an air-diffusion cathode has been examined. The decay kinetics of each drug and the mineralization degree have been analyzed to establish the best anode and the most efficient EAOP. The effect of electrolyte composition including sulfate and/or chloride has been clarified. Final carboxylic acids have been detected to explain the oxidation ability of the Fenton-based processes.

2. Experimental

2.1. Reagents

Mixtures of sulfamethoxazole + trimetrophim were prepared from the commercial formulation Bactrim®. Analytical standards of both drugs were purchased from Sigma-Aldrich. Sodium sulfate, sodium chloride, iron(II) sulfate heptahydrate and sulfuric acid (to adjust the pH to 3.0) were of analytical grade provided by Panreac and Fischer. Ultrapure Millipore Milli-Q water (resistivity > 18 MΩ cm) was used to prepare all solutions. Other chemicals were of analytical or HPLC grade supplied by Panreac and Riedel de Häen.

109 *2.2. Electrochemical system*

110 The EO-H_2O_2, EF, PEF and SPEF trials were carried out in a conventional undivided
111 tank reactor of 200 mL capacity, surrounded with a jacket to keep the solution temperature at
112 30 ºC through thermostated water recirculation. Solutions of 130 mL vigorously stirred with a
113 magnetic bar, were degraded in the cell. Three anodes of 3 cm^2 area were alternately used for
114 each EAOP: a BDD thin film on Si (NeoCoat), a Pt sheet (99.99% purity, SEMPSA) and an
115 IrO_2-based plate (NMT Electrodes). The latter electrode was mainly composed of IrO_2 with a
116 minor proportion of Ta_2O_5 as stabilizer. A 3 cm^2 carbon-PTFE air-diffusion electrode from
117 Sainergy Fuel Cell was always used as the cathode. It was mounted as previously reported
118 (Guinea et al., 2010) and fed with air pumped at 1 L min^{-1} for continuous H_2O_2 generation.
119 The interelectrode gap was about 1 cm. Trials were made at constant j = 33.3 mA cm^{-2}
120 supplied by an Amel 2049 potentiostat-galvanostat. This j value was selected because it is
121 high enough to achieve a large mineralization of organics in our electrolytic system, as
122 previously reported (Coria et al., 2014; Steter et al., 2016). The cell voltage was monitored
123 with a Demestres 601BR digital multimeter. The EF, PEF and SPEF assays were performed
124 in the presence of 0.50 mM Fe^{2+}, since this is the optimum content found for such EAOPs in
125 this kind of cell (Ruiz et al., 2011). The PEF trials were ran by illuminating the solution with
126 a Philips TL/6W/08 fluorescent that supplied UVA light with λ_{max} = 360 nm and power
127 density of 5 W m^{-2}, measured with a Kipp&Zonen CUV 5 UV radiometer. The SPEF assays
128 were performed for 4 h upon direct sunlight irradiation in clear and sunny days of summer
129 2017 in our laboratory of Barcelona, starting at noon. The average solar irradiance in the UV
130 range was 32.6 W m^{-2}.

131 *2.3. Analytical procedures*

132 The solution pH was determined with a Crison GLP 22 pH-meter. The H_2O_2 content was
133 obtained from the light absorption of its Ti(IV) complex using an Unicam UV/Vis

spectrophotometer at λ = 408 nm (Welcher, 1975). Samples withdrawn from treated solutions were filtered with Whatman 0.45 μm PTFE filters before analysis.

The sulfamethoxazole and trimethoprim concentrations were determined by reversed-phase high-performance liquid chromatography (HPLC). In the EF, PEF and SPEF assays, samples were immediately diluted with 50% vol. acetonitrile to the sample to stop the degradation process. The analyses were carried out by injecting aliquots into a Waters 600 liquid chromatograph, fitted with a BDS Hypersil C18, 250 mm × 4.6 mm (i.d.), column at 25 ºC, and coupled to a Waters 996 photodiode array detector set at λ = 270 nm. A 70:30 (v/v) acetonitrile:water (KH_2PO_4 10 mM, pH 3) mixture was eluted at 1.0 mL min^{-1} as mobile phase. The chromatograms displayed well-defined peaks for sulfamethoxazole and trimethoprim at retention time (t_r) of 3.3 and 3.9 min, respectively. The above chromatograph fitted with a Bio-Rad Aminex HPX 87H, 300 mm × 7.8 mm (i.d.), column at 35 ºC, and the photodiode array detector selected at λ = 210 nm were employed to quantify generated carboxylic acids. The mobile phase was 4 mM H_2SO_4, eluted at 0.6 mL min^{-1}. The chromatograms exhibited peaks for oxalic (t_r = 6.7 min), maleic (t_r = 8.0 min), oxamic (t_r = 9.3 min), formic (t_r = 13.9 min) and fumaric (t_r = 15.5 min) acids. NH_4^+ concentration was measured by the standard indophenol blue method using the previous spectrophotometer. NO_3^- content was quantified by ion chromatography (Pipi et al., 2014).

Total organic carbon (TOC) was obtained by injecting fresh samples to a Shimadzu VCSN TOC analyzer. Total nitrogen (TN) was measured on a Shimadzu TNM-1 unit coupled to the above analyzer. Kinetic and mineralization assays were always replicated and average data are reported. Since the error of all the values obtained within 95% confidence interval was very small (< 2%), no error bars are depicted in figures.

2.4. Mineralization current efficiency

158 A tablet of the formulation Bactrim® (508 mg) was completely dissolved in 2 L of Milli-
159 Q water and the concentration of the two drugs was determined by reversed-phase HPLC
160 upon comparison with pure standards. From this analysis, it was found that the tablet
161 contained 360 mg of sulfamethoxazole and 80 mg of trimethoprim, with 68 mg of additives.
162 Hence, their respective molar fractions were 0.818 and 0.182. This composition agreed with
163 the expected molar ratio 0.80:0.20 from commercial Bactrim® tablets.

164 The TOC of a solution with 50.0 mg L^{-1} sulfamethoxazole + 11.1 mg L^{-1} trimethoprim
165 was 30.1 mg L^{-1}, with a TN of 10.4 mg L^{-1}, which means that both drugs were the only
166 organic components of the tablet. Neither NH_4^+ nor NO_3^- were detected in the initial sample.
167 When 0.050 M Na_2SO_4 and 0.50 mM Fe^{2+} were added to the above solution and EF and SPEF
168 were carried out with an IrO_2-based/air-diffusion cell at pH 3.0 and j = 33.3 mA cm^{-2} for 240
169 min, the final solutions contained 8.6±0.2 mg L^{-1} of NH_4^+ (64.3±0,1% of initial N) and no
170 NO_3^- ions. The final TN value was slightly superior to that accumulated as NH_4^+, suggesting
171 that a small part of initial N was lost as volatile *N*-products, as reported for other *N*-containing
172 targets (Thiam et al. 2015a, 2015b). As a result, reactions (1) and (2) can be written for the
173 theoretical total mineralization of sulfamethoxazole and trimethoprim, respectively:

174 $$C_{10}H_{11}N_3O_3S + 21H_2O \rightarrow 10CO_2 + SO_4^{2-} + 3NH_4^+ + 41H^+ + 42e^- \quad (1)$$

175 $$C_{14}H_{18}N_4O_3 + 25H_2O \rightarrow 14CO_2 + 4NH_4^+ + 52H^+ + 56e^- \quad (2)$$

176 As a plausible approximation, the drug mixture was mineralized with a mean number of
177 electrons n_{mean} = (0.818×42) + (0.182×56) = 44.54, which acted on a mean number of C atoms
178 m_{mean} = (0.818×10) + (0.182×14) = 10.73. The mineralization current efficiency (MCE) for
179 each assay at current I (A) and electrolysis time t (h) was then estimated as (Ruiz et al., 2011):

180 $$\%\ \mathrm{MCE} = \frac{n_{mean}\, F\, V \triangle(\mathrm{TOC})}{4.32\times10^7\, m_{mean}\, I\, t} \times 100 \quad (3)$$

where F is the Faraday constant (96,485 C mol^{-1}), V is the solution volume (L), $\triangle$(TOC) is the TOC decay (mg L^{-1}) and 4.32×10^7 is a conversion factor (3600 s h^{-1} × 12000 mg C mol^{-1}).

3. Results and discussion

3.1. Effect of anode on the degradation of sulfamethoxazole + trimethoprim by EAOPs

3.1.1. H_2O_2 electrogeneration

Three anode materials, namely Pt, IrO_2-based and BDD, were selected to examine the degradation of the drug mixture by EAOPs using an air-diffusion cathode. It has been well-established that at high enough j, all these anodes (M) originate adsorbed hydroxyl radical (M($^\bullet$OH)) at their surface as follows (Boye et al., 2002; Marselli et al., 2003; Panizza and Cerisola, 2009):

$$M + H_2O \rightarrow M(^\bullet OH) + H^+ + e^- \quad (4)$$

This electrogenerated hydroxyl radical is a strong oxidant that attacks most organic pollutants. However, the nature of the anode limits its oxidation ability. Pt and IrO_2-based anodes are active materials in which a large proportion of M($^\bullet$OH) is transformed into a weaker superoxide (MO) that causes the conversion of organics (Scialdone et al., 2009; Coria et al., 2016; Ridruejo et al., 2017). In contrast, BDD is a non-active anode with much larger O_2-overvoltage, producing great amounts of physisorbed BDD($^\bullet$OH) leading to mineralization (Özcan et al., 2008; Brinzila et al., 2014; Olvera-Vargas et al., 2014; Steter et al., 2016).

When an air-diffusion cathode is utilized in an undivided cell, H_2O_2 is efficiently produced from the reduction of injected O_2 gas via reaction (5) (Sirés et al., 2014). The extent of H_2O_2 accumulation depends on its decomposition rate at the anode to yield O_2 gas with formation of the weaker oxidant hydroperoxyl radical (M($HO_2^\bullet$)) as intermediate via reactions (6) and (7) (Brillas et al., 2009).

$$O_{2(g)} + 2H^+ + 2e^- \rightarrow H_2O_2 \quad (5)$$

$$M + H_2O_2 \rightarrow M(HO_2^{\bullet}) + H^+ + e^- \quad (6)$$

$$M(HO_2^{\bullet}) \rightarrow M + O_{2(g)} + H^+ + e^- \quad (7)$$

Large H_2O_2 production is essential in EAOPs based on Fenton's reaction chemistry like EF, PEF and SPEF. To clarify this behavior for the three anodes, 130 mL of 0.050 M Na_2SO_4 at pH 3.0 were electrolyzed under EO-H_2O_2 conditions at j = 33.3 mA cm^{-2} for 360 min. In all cases, the H_2O_2 content in solution increased rapidly at the beginning of electrolysis due to efficient reaction (5), but the accumulation was progressively decelerated by the rise in rate of reaction (6), thus attaining a plateau once the rate of reactions (5) and (6) equated. High and similar steady H_2O_2 concentrations of 23.7, 33.8 and 26.0 mM for the Pt/air-diffusion, IrO_2-based/air-diffusion and BDD/air-diffusion cells, respectively, were obtained at the end of the trials. This means that little effect should be expected from the anode nature on the generation of $^{\bullet}OH$ in the EF, PEF and SPEF treatments of sulfamethoxazole + trimethoprim mixtures.

3.1.2. EO-H_2O_2 process

A first series of assays was performed by treating 130 mL of 50.0 mg L^{-1} sulfamethoxazole + 11.1 mg L^{-1} trimethoprim in 0.050 M Na_2SO_4 at pH 3.0 and j = 33.3 mA cm^{-2} for 360 min. No significant change in pH was found, gradually dropping to final values of 2.6-2.7 by the formation of acidic by-products.

Fig. 2a and b depicts the decay of sulfamethoxazole and trimethoprim concentrations during these treatments. The degradation rate of both drugs was enhanced in the order: IrO_2-based << Pt < BDD. Removals of 52.8% for IrO_2-based, 87.2% for Pt and 96.1% for BDD were finally obtained for the former drug, whereas the latter one dropped by 92.1% for IrO_2-based and disappeared completely after 360 min with Pt and 150 min with BDD. Although weak reactive oxygen species (ROS) like H_2O_2 and $M(HO_2^{\bullet})$ are generated under EO-H_2O_2

conditions, both drugs were pre-eminently destroyed by M(•OH). Our results indicate the much larger oxidation ability of BDD(•OH) compared to IrO_2(•OH) and Pt(•OH) (Panizza and Cerisola, 2009; Thiam et al., 2015a; Steter et al., 2016). All decays obeyed a pseudo-first-order kinetics, as shown in the inset panels of Fig. 2a and b, and the corresponding apparent rate constants (k_{SMX} and k_{TMP}) are summarized in Table 1. The k_{SMX}-value using BDD was about 5- and 2-fold higher than that with IrO_2-based and Pt, respectively, whereas the k_{TMP}-value using BDD was even relatively greater, near 8- and 4.5-fold compared to IrO_2-based and Pt. This corroborates the superiority of BDD over the two active anodes to destroy the drugs, and suggests that a constant and low M(•OH) content attacks both substrates.

A different behavior can be observed in Fig. 2c for the TOC abatement in the three EO-H_2O_2 trials. A very low mineralization (< 5% TOC decay) was finally achieved with the two active anodes, whereas the alternative use of BDD yielded 58.1% mineralization. This was also reflected in the MCE values presented in Fig. 2d. The mineralization current efficiency was very small (< 0.28%) with IrO_2-based and Pt, and varied between 3.4% and 3.7% using BDD, informing about a constant mineralization rate during the treatment.

The aforementioned results demonstrate a clear superiority of BDD(•OH) to destroy sulfamethoxazole and trimethoprim, as well as to mineralize the solutions.

3.1.3. EF process

The drug mixture in 0.050 M Na_2SO_4 at pH 3.0 was further treated under EF conditions with 0.50 mM Fe^{2+}. Again, a slight decay in solution pH to 2.6-2.7 was determined during the 360 min of these assays at 33.3 mA cm^{-2}.

Fig. 3a and b reveals a similar and very fast abatement of both substrates by EF. Sulfamethoxazole disappeared between 12 min with Pt and 8 min with BDD, whereas overall removal of trimethoprim was achieved between 7 and 5 min, respectively. This trend differs largely from the behavior in EO-H_2O_2 (see Fig. 2a and b) and suggests the generation of some

253 stronger oxidant. This species is the homogeneous •OH formed from Fenton's reaction (8)
254 between electrogenerated H_2O_2 and added Fe^{2+}, with optimum pH 2.8 (Brillas et al., 2009;
255 Dirany et al., 2010; Feng et al., 2014). This reaction is propagated by Fe^{2+} regeneration from
256 cathodic Fe^{3+} reduction.

257 $$H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + {}^{\bullet}OH + OH^- \quad (8)$$

258 The concentration decays of Fig. 3a and b also obeyed a pseudo-first-order reaction, as
259 can be seen in their inset panels. Table 1 shows k_{SMX}-values near 0.30 min^{-1} with the active
260 anodes and slightly higher (0.37 min^{-1}) with BDD. The same tendency can be observed for
261 k_{TMP}, with values close to 0.43-0.50 min^{-1} using the former anodes and 0.55 min^{-1} using the
262 latter one. This means that both drugs were competitively degraded by •OH in the bulk and, to
263 a much smaller extent, by M(•OH) generated at each anode surface from reaction (4). The
264 superior oxidation ability of BDD(•OH) compared to IrO_2(•OH) and Pt(•OH) can then explain
265 the slightly greater k_{SMX} and k_{TMP} values found using BDD.

266 Conversely, the TOC removal depended on the anode nature (see Fig. 3c). Slow and
267 similar TOC abatements were obtained with the two active anodes, attaining a mineralization
268 of 36.2% and 40.2% using Pt and IrO_2-based. Much quicker TOC decay was found with
269 BDD, yielding 66.8% mineralization. In all cases, the MCE values dropped at long time (see
270 Fig. 3d) as result of the loss of organic matter and the production of more recalcitrant by-
271 products (Panizza and Cerisola, 2009; Thiam et al., 2015b). Final mineralization current
272 efficiencies of 2.2%, 2.4% and 4.0% with Pt, IrO_2-based and BDD, respectively, were
273 determined. These findings inform about the positive role of BDD(•OH) to mineralize
274 intermediates that are not removed by •OH, making this anode preferable for the EF
275 treatment.

276 *3.1.4. PEF and SPEF processes*

277 The effect of UV radiation was finally examined using PEF and SPEF to treat the drug
278 mixture in 0.050 M Na_2SO_4 with 0.50 mM Fe^{2+} at pH 3.0 and j = 33.3 mA cm^{-2}. Under these
279 conditions, the additional generation of •OH in the bulk is expected from the photolysis of
280 $Fe(OH)^{2+}$, which is the predominant Fe(III) species at pH near 3 (Flox et al., 2007; Ruiz et al.,
281 2011; Sirés et al., 2014):

282 $$Fe(OH)^{2+} + h\nu \rightarrow Fe^{2+} + {}^{\bullet}OH \quad (9)$$

283 However, the concentration decay of both drugs in PEF and SPEF was quite similar to
284 that mentioned in EF, suggesting a minor contribution of •OH induced by reaction (9). This
285 fact can be easily deduced by comparing the analogous k_{SMX} and k_{TMP} values given in Table 1
286 for each anode in these three EAOPs. In contrast, the TOC removal was very different in each
287 system, as shown in Fig. 4a. In PEF, TOC was continuously abated for 300 min, giving rise to
288 66.1%, 68.1% and 84.7% mineralization using IrO_2-based, Pt and BDD, respectively, In
289 SPEF, the same anodes led to 78.5%, 81.3% and 87.4% TOC reduction after 240 min, with no
290 significant mineralization increase from 180 min. For all these trials, the MCE values dropped
291 along electrolysis, being higher in SPEF (see Fig. 4b).

292 It is noticeable that the use of the two active anodes yielded analogous mineralization in
293 PEF, which was greater using BDD. The same behavior was found in SPEF. From the TOC
294 and MCE values listed in Table 1 after 240 min, one can infer for each anode a higher
295 oxidation ability in the sequence: EO-H_2O_2 < EF < PEF < SPEF, always being superior with
296 BDD. The higher mineralization attained by PEF and SPEF compared to EF can be accounted
297 for by the photolysis of photoactive intermediates by UV radiation, such as the
298 photodecomposition of Fe(III) complexes with generated carboxylic acids (Brillas et al.,
299 2009; Pérez et al., 2016; Moreira et al., 2017):

300 $$Fe(OOCR)^{2+} + h\nu \rightarrow Fe^{2+} + CO_2 + R^{\bullet} \quad (10)$$

The fact that organics are more quickly destroyed by SPEF can be related to the high UV intensity provided by sunlight ($\lambda > 300$ nm). This causes a much rapid photodecomposition of intermediates with the consequent rise in mineralization rate. Although the SPEF process with BDD is the most powerful EAOP for the remediation of water containing sulfamethoxazole + trimethoprim, overall mineralization was not achieved because of the accumulation of highly recalcitrant by-products than are quite stable against BDD(•OH), •OH and sunlight.

3.2. Influence of electrolyte composition on SPEF degradation

Cl^- ion is a common species in real wastewater. It can be easily oxidized at the anode of an electrolytic cell to produce the strong oxidant active chlorine (Cl_2/HClO) in acidic medium from reactions (11) and (12) (Sirés et al., 2014; Thiam et al., 2015a; Steter at al., 2016):

$$2Cl^- \rightarrow Cl_{2(aq)} + 2e^- \quad (11)$$

$$Cl_{2(aq)} + H_2O \rightarrow HClO + Cl^- + H^+ \quad (12)$$

To clarify the effect of this ion on the effectiveness of the most powerful process, i.e., SPEF with BDD, the drug mixture was treated in either 0.035 M NaCl + 0.020 M Na_2SO_4 or 0.070 M NaCl, both having a conductivity ~ 10 mS cm^{-1} as that of 0.050 M Na_2SO_4. Fig. 5a and b shows a faster decay of both drugs with increasing Cl^- concentration, meaning that their destruction with active chlorine prevailed over that with BDD(•OH) and •OH produced from reactions (4) and (8), respectively. For example, sulfamethoxazole disappeared in about 10 min using 0.050 M Na_2SO_4, but in only 4 min in 0.070 M NaCl. The inset panel of Fig. 5a highlights the good pseudo-first-order kinetics obtained in all cases, suggesting a reaction with a constant quantity of all oxidants (Cl_2/HClO, BDD(•OH) and •OH). This behavior can also be observed for trimethoprim in the inset panel of Fig. 5b except in 0.070 M NaCl, where bad linear fitting was found. Thus, active chlorine, the most powerful oxidant in this medium, destroyed the major part of the drug very quickly, even before reaching a steady content. Note

that the k_{SMX}-value was 1.12- and 2.65-fold higher in the chloride + sulfate mixture and 0.070 M NaCl, respectively, compared to that in 0.050 M Na_2SO_4 (see Table 1), as result of the increasing generation of active chlorine. This enhancement was even larger for k_{TMP}, which rose 1.30-fold in the chloride + sulfate mixture, evidencing a quicker attack of active chlorine over this molecule. This explains its complex kinetics in 0.070 M NaCl, where much larger content of such oxidant was produced.

For the above assays, Fig. 5c shows a progressive loss of TOC abatement at higher Cl^- concentration, confirmed with the concomitant decay in MCE, as depicted in Fig. 5d. The final TOC and current efficiency dropped from 87.4% and 7.9% in 0.050 M Na_2SO_4 to 65.8% and 6.0% in 0.070 M NaCl (see Table 1). This behavior can be associated to the gradual formation of persistent chloroderivatives that are more hardly oxidized under SPEF conditions (Sirés et al., 2014; Hussain et al., 2015; Thiam et al., 2015a; Steter at al., 2016).

The above findings demonstrate the complex influence of Cl^- on the performance of SPEF with BDD. Although it was beneficial to remove more quickly the parent drugs, the chloroderivatives formed inhibited the mineralization process and hence, low Cl^- contents are preferable to achieve the best mineralization by this EAOP.

3.3. Detection of final carboxylic acids

To corroborate the formation of final carboxylic acids during the mineralization of the sulfamethoxazole + trimethoprim mixtures, solutions with 0.050 M Na_2SO_4 treated by EF and SPEF with BDD at j = 33.3 mA cm^{-2} were analyzed by ion-exclusion HPLC. The chromatograms exhibited peaks corresponding to maleic, fumaric, formic, oxalic and oxamic acids. The two former acids came from the cleavage of the benzene rings and were oxidized to oxalic acid (Brillas et al., 2009; Sirés et al, 2014). Oxamic acid should came from the degradation of *N*-derivatives. Formic, oxalic and oxamic acids were the final by-products,

being directly mineralized to CO_2 (Sirés et al., 2014; Thiam et al., 2015a, 2015b). All these acids were mainly in the form of Fe(III) complexes.

Maleic, fumaric and formic acids were detected as traces (< 0.1 mg L^{-1}), disappearing after 120-180 min. This means that Fe(III)-maleate, Fe(III)-fumarate and Fe(III)-formate complexes were easily oxidized by generated hydroxyl radicals. In contrast, oxalic and oxamic acids were largely produced and persisted for 240 min, as can be seen in Fig. 6a and b, respectively. These acids were accumulated up to 33.1 and 7.50 mg L^{-1} in EF, which accounts for a total TOC of 10.85 mg L^{-1}, corresponding to 60.3% of the solution TOC (18.0 mg L^{-1}, see Fig. 3c). Conversely, only 1.09 mg L^{-1} of oxalic acid and 0.13 mg L^{-1} of oxamic acid were found at the end of SPEF, corresponding to 0.3 mg L^{-1} TOC, i.e., 7.9% of the final solution TOC (see Fig. 4c). Oxalic and oxamic acids were largely accumulated in EF because Fe(III)-oxalate and Fe(III)-oxamate complexes are quite stable against BDD($^\bullet$OH) and $^\bullet$OH, whereas such species were rapidly photodecomposed via reaction (10) in SPEF. This positive action of UV radiation provided by sunlight on final Fe(III)-carboxylate complexes explains the superior oxidation ability of SPEF, although other undetected recalcitrant products (about 12% of initial TOC) remained in the final solution, thus impeding overall mineralization.

4. Conclusions

The decay of sulfamethoxazole and trimethoprim in 0.050 M Na_2SO_4 always agreed with a pseudo-first-order reaction. Their apparent rate constants were very low in EO-H_2O_2, being much higher in EF, PEF and SPEF with small influence of the anode used because they were mainly destroyed by $^\bullet$OH in the bulk. The mineralization process was enhanced in the order: EO-H_2O_2 < EF < PEF < SPEF, regardless of the anode. All methods were more powerful with BDD due to the higher oxidation ability of BDD($^\bullet$OH) compared to IrO_2($^\bullet$OH) and Pt($^\bullet$OH). The difference in TOC abatement using the different anodes was not substantial in SPEF due to the very positive action of natural UV radiation to remove photoactive intermediates. The

most powerful process was SPEF with BDD, although it yielded 87.4% mineralization as maximal owing to the accumulation of very recalcitrant by-products. The presence of Cl^- in the medium accelerated the decay of both drugs by the quicker attack of generated active chlorine, but lower mineralization was reached due to the formation of persistent chloroderivatives. Oxalic and oxamic acids were detected as final carboxylic acids. Their Fe(III) complexes were slowly destroyed by BDD($^\bullet$OH) and $^\bullet$OH in EF, whereas they were rapidly photolyzed in SPEF, thus explaining the superiority of the latter method.

Acknowledgements

The authors thanks financial support from project CTQ2016-8616-R (AEI/FEDER, EU) and CONACyT 181057. Juan C. Murillo-Sierra thanks the fellowship granted by CONACyT (Mexico).

References

Amorim, K.P., Romualdo, L.L., Andrade, L.S., 2013. Electrochemical degradation of sulfamethoxazole and trimethoprim at boron-doped diamond electrode: Performance, kinetics and reaction pathway. Sep. Purif. Technol. 120, 319-327.

Boudreau, J., Bejan, D., Li, S., Bunce, N.J., 2010. Competition between electrochemical advanced oxidation and electrochemical hypochlorination of sulfamethoxazole at a boron-doped diamond anode. Ind. Eng. Chem. Res. 49, 2537-2542.

Boye, B., Michaud, P.A., Marselli, B., Dieng, M.M., Brillas, E., Comninellis, C., 2002. Anodic oxidation of 4-chlorophenoxyacetic acid on synthetic boron-doped diamond electrode. New Diamond Frontier Carbon Technol. 12, 63-72.

Brillas, E., Sirés, I., Oturan, M.A., 2009. Electro-Fenton and related electrochemical technologies based on Fenton's reaction chemistry. Chem. Rev. 109, 6570-6631.

Brinzila, C.I., Monterio, N., Pacheco, M.J., Ciríaco, L., Siminiceanu, I., Lopes, A., 2014. Degradation of tetracycline at a boron-doped diamond anode: influence of initial pH, applied current intensity and electrolyte. Environ. Sci. Pollut. Res. 21, 8457-8465.

Coria, G., Sirés, I., Brillas, E., Nava, J.L., 2016. Influence of the anode material on the degradation of naproxen by Fenton-based electrochemical processes. Chem. Eng. J. 304, 817-825.

Dias, I.N., Souza, B.S., Pereira, H.O.S.J., Moreira, F.C., Dezotti, M., Boaventura, R.A.R., Vilar, V.J.P., 2014. Enhancement of the photo-Fenton reaction at near neutral pH through the use of ferrioxalate complexes: A case study on trimethoprim and sulfamethoxazole antibiotics removal from aqueous solutions. Chem. Eng. J. 247, 302–313.

Dirany, A., Efremova Aaron, S., Oturan, N., Sirés, I., Oturan, M.A., Aaron, J.J., 2011. Study of the toxicity of sulfamethoxazole and its degradation products in water by a bioluminescence method during application of the electro-Fenton treatment. Anal. Bioanal. Chem. 400, 353-360.

Dirany, A., Sirés, I., Oturan, N., Oturan, M.A., 2010. Electrochemical abatement of the antibiotic sulfamethoxazole from water. Chemosphere 81, 594-602.

Ebele, A.J., Abou-Elwafa Abdallah, M., Harrad, S., 2017. Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. Emerg. Contam. 3, 1-16.

Feng, L., Van Hullebusch, E.D., Rodrigo, M.A., Esposito, G., Oturan, M.A., 2013. Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced oxidation processes. A review. Chem. Eng. J. 228, 944-964.

Flox, C., Garrido, J.A., Rodríguez, R.M., Cabot, P.L., Centellas, F., Arias, C., Brillas, E., 2007. Mineralization of herbicide mecoprop by photoelectro-Fenton with UVA and solar light. Catal. Today 129, 29-36.

González, T., Domínguez, J.R., Palo, P., Sánchez-Martín, J., Cuerda-Correa, E.M., 2011. Development and optimization of the BDD electrochemical oxidation of the antibiotic trimethoprim in aqueous solution. Desalination 280, 197-202.

Guinea, E., Garrido, J.A., Rodríguez, R.M., Cabot, P.L., Arias, C., Centellas, F., Brillas, E., 2010. Degradation of the fluoroquinolone enrofloxacin by electrochemical advanced oxidation processes based on hydrogen peroxide electrogeneration, Electrochim. Acta 55, 2101-2115.

Hirsch, R., Ternes, T., Haberer, K,, Kratz, K.-L., 1999. Occurrence of antibiotics in the aquatic environment. Sci. Total Environ. 225, 109-118.

Hussain, S., Gul, S., Steter, J.R., Miwa, D.W., Motheo, A.J., 2015. Route of electrochemical oxidation of the antibiotic sulfamethoxazole on a mixed oxide anode. Environ. Sci. Pollut. Res. 22, 15004-15015.

Lan, Y., Coetsier, C., Causserand, C., Groenen-Serrano, K., 2017. On the role of salts for the treatment of wastewaters containing pharmaceuticals by electrochemical oxidation using a boron doped diamond anode. Electrochim. Acta 231, 309-318.

Mansour, D., Fourcade, F., Soutrel, I., Hauchard, D., Bellakhal, N., Amrane, A., 2015. Mineralization of synthetic and industrial pharmaceutical effluent containing trimethoprim by combining electro-Fenton and activated sludge treatment. J. Taiwan Inst. Chem. Eng. 53, 58-67.

Marselli, B., Garcia-Gomez, J., Michaud, P.A., Rodrigo, M.A., Comninellis, C., 2003. Electrogeneration of hydroxyl radicals on boron-doped diamond electrodes. J. Electrochem. Soc. 150, D79-D83.

Martín de Vidales, M.J., Robles-Molina, J., Domínguez-Romero, J.C., Cañizares, P., Sáez, C., Molina-Díaz, A., Rodrigo, M.A., 2012. Removal of sulfamethoxazole from waters and

445 wastewaters by conductive-diamond electrochemical oxidation. J. Chem. Technol.
446 Biotechnol. 87, 1441-1449.
447 Moreira, F.C., Boaventura, R.A.R., Brillas, E., Vilar, V.J.P., 2017. Electrochemical advanced
448 oxidation processes: A review on their application to synthetic and real wastewaters.
449 Appl. Catal. B: Environ. 202, 217-261.
450 Moreira, F.C., Garcia-Segura, S., Boaventura, R.A,R., Brillas, E., Vilar, V.J.P., 2014.
451 Degradation of the antibiotic trimethoprim by electrochemical advanced oxidation
452 processes using a carbon-PTFE air-diffusion cathode and a boron-doped diamond or
453 platinum anode. Appl. Catal. B: Environ. 160-161, 492-505.
454 Olvera-Vargas, H., Oturan, N., Brillas, E., Buisson, D., Esposito, G., Oturan, M.A., 2014.
455 Electrochemical advanced oxidation for cold incineration of the pharmaceutical
456 ranitidine: Mineralization pathway and toxicity evolution. Chemosphere 117, 644-651.
457 Özcan, A., Şahin, Y., Koparal, A.S., Oturan, M.A., 2008. Propham mineralization in aqueous
458 medium by anodic oxidation using boron-doped diamond anode. Experimental
459 parameters' influence on degradation kinetics and mineralization efficiency. Water Res.
460 42, 2889-2898.
461 Panizza, M., Cerisola, G., 2009. Direct and mediated anodic oxidation of organic pollutants.
462 Chem. Rev. 109, 6541-6569.
463 Pérez, S., Eichhorn, P., Aga, D.S., 2005. Evaluating the biodegradability of sulfamethazine,
464 sulfamethoxazole, sulfathiazole, and trimethoprim at different stages of sewage
465 treatment. Environ. Toxicol. Chem, 24, 1361-1367.
466 Pérez, T., Sirés, I., Brillas, E., Nava, J.L., 2017. Solar photoelectro-Fenton flow plant
467 modeling for the degradation of the antibiotic erythromycin in sulfate medium.
468 Electrochim. Acta 228, 45-56.

Pipi, A.R.F., De Andrade, A.R., Brillas, E., Sirés, I., 2014. Total removal of alachlor from water by electrochemical processes. Sep. Purif. Technol. 132, 674-683.

Ridruejo, C., Salazar, C., Cabot, P.L., Centellas, F., Brillas, E., Sirés, I., 2017. Electrochemical oxidation of anesthetic tetracaine in aqueous medium. Influence of the anode and matrix composition. Chem. Eng. J. 326, 811-819.

Ruiz, E.J., Hernández-Ramírez, A., Peralta-Hernández, J.M., Arias, C., Brillas, E., 2011. Application of solar photoelectro-fenton technology to azo dyes mineralization: Effect of current density, Fe^{2+} and dye concentration. Chem. Eng. J. 171, 385-392.

Ryan, C.C., Tan, D.T., Arnold, W.A., 2011. Direct and indirect photolysis of sulfamethoxazole and trimethoprim in wastewater treatment plant effluent. Water Res. 45, 1280-1286.

Scialdone, O., Randazzo, S., Galia, A., Filardo, G., 2009. Electrochemical oxidation of organics at metal oxide electrode: the incineration of oxalic acid at IrO_2-Ta_2O_5 (DSA-O_2) anode. Electrochim. Acta 54, 1210-1217.

Sifuna, F.W., Orata, F., Okello, V., Jemutai-Kimosop, S., 2016. Comparative studies in electrochemical degradation of sulfamethoxazole and diclofenac in water by using various electrodes and phosphate and sulfate supporting electrolytes. J. Environ. Sci. Health A 51, 954-961.

Sirés, I., Brillas, E., 2012. Remediation of water pollution caused by pharmaceutical residues based on electrochemical separation and degradation technologies: A review. Environ. Int. 40, 212-229.

Sirés, I., Brillas, E., Oturan, M.A., Rodrigo, M.A., Panizza, M., 2014. Electrochemical advanced oxidation processes: today and tomorrow. A review. Environ. Sci. Pollut. Res. 21, 8336-8367.

493 Steter, J.R., Brillas, E., Sirés, I., 2016. On the selection of the anode material for the
494 electrochemical removal of methylparaben from different aqueous media. Electrochim.
495 Acta 222, 1464-1474.
496 Thiam, A. Brillas, E., Centellas, F., Cabot, P.L., Sirés, I., 2015a. Electrochemical reactivity of
497 Ponceau 4R (food additive E124) in different electrolytes and batch cells. Electrochim.
498 Acta 173, 523-533.
499 Thiam, A., Sirés, I., Garrido, J.A., Rodríguez, R.M., Brillas, E., 2015b. Decolorization and
500 mineralization of Allura Red AC aqueous solutions by electrochemical advanced
501 oxidation processes. J. Hazard. Mater. 290, 34-42.
502 Thiele-Bruhn, S., Beck, I.-C., 2005. Effects of sulfonamide and tetracycline antibiotics on soil
503 microbial activity and microbial biomass. Chemosphere 59, 457-465.
504 Wang, A., Li, Y.-Y., Estrada, A.L., 2011. Mineralization of antibiotic sulfamethoxazole by
505 photoelectro-Fenton treatment using activated carbon fiber cathode and under UVA
506 irradiation. Appl. Catal. B: Environ. 102, 378-386.
507 Welcher, F.J., 1975. Standard Methods of Chemical Analysis, 6th ed., vol. 2, R.E. Krieger
508 Publishing Co, Huntington, New York, Part B.
509 Zhang, Y., Wang, A., Tian, X., Wen, Z., Lv, H., Li, D., Li, J., 2016. Efficient mineralization
510 of the antibiotic timethoprim by solar assisted photoelectro-Fenton process driven by a
511 photovoltaic cell. J. Hazard. Mater. 318, 319-328.