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Degradation of Acetaminophen and Its Transformation Products in Aqueous Solutions by Using an Electrochemical Oxidation Cell with Stainless Steel Electrodes

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Abstract: In this study, a novel electrochemical oxidation cell using stainless steel electrodes was found to be effective in oxidizing acetaminophen and its transformation products in short reaction times. Aqueous solutions of 10 mg/L-acetaminophen were prepared at pH 3, 5, 7, and 9. These solutions were electrochemically treated at direct current (DC) densities of 5.7 mA/cm^2, 7.6 mA/cm^2, and 9.5 mA/cm^2. The pharmaceutical and its intermediates/oxidation products were determined by using high pressure liquid chromatography (HPLC). The results showed that electrochemical oxidation processes occurred in the cell. Acetaminophen degradation rate constants increased proportionally with the increase of current intensity. High current densities accelerated the degradation of acetaminophen; however, this effect diminished remarkably at pH values greater than 5. At pH 3 and 9.5 mA/cm^2, the fastest degradation of acetaminophen and its intermediates/oxidation products was achieved. To minimize the wear down of the electrodes, a current density ramp is recommended, first applying 9.5 mA/cm^2 during 2.5 min or 7.6 mA/cm^2 during 7.5 min and then continuing the electrochemical oxidation process at 5.7 mA/cm^2. This strategy will hasten the acetaminophen oxidation, extend the electrode's life, and shorten the reaction time needed to degrade the pharmaceutical and its intermediates/oxidation products. DC densities up to 9.5 mA/cm^2 can be supplied by photovoltaic cells.

Keywords: acetaminophen; anodic oxidation; DC densities; electrochemical oxidation with active chlorine; transformation products

1. Introduction

Acetaminophen is the most common analgesic and antipyretic pharmaceutical prescribed around the world [1–3]. However, acetaminophen presents adverse effects, when over dosed, due to the generation of toxic metabolites when oxidized by reactive oxygen species. Among multiple effects, protein denaturation, lipid peroxidation, and DNA damage can result. The presence and the toxic effects of acetaminophen on microorganisms in aquatic systems have been reported [1]. Acetaminophen and its toxic metabolites have been found in surface waters, wastewater, and drinking water [4].

The formation of intermediates/oxidation products such as hydroquinone, p-aminophenol, p-nitrophenol, 1,4-benzoquinone and, NAPQI (N-acetyl-benzoquinone imine) has been reported in advanced oxidation processes [2,5,6]. These intermediates/oxidation products are of concern because of their toxicity and difficulty to degrade them by conventional methods which are expensive and not viable for practical scaling up. Several studies have been conducted to find an effective

method of acetaminophen degradation in aqueous solutions. Among then can be mentioned chemical [7,8], electrochemical [9–11], sonolysis [12], Fenton [13], photo-Fenton [14–18], solar/TiO_2 and solar/photo-Fenton [19], solar-photoelectro-Fenton [20], ozonation and H_2O_2/UV oxidation [21], ozonation catalyzed with photo-Fenton [18], TiO_2 photocatalysis [22–25], and electrocatalysis [26]. In these studies, partial degradation of acetaminophen was achieved, from 14% [15] to 88% [13], rather than a total mineralization. The reaction time ranged from six minutes [17] to more than six hours [22]. Furthermore, in most of these studies, intermediates/oxidation products produced by the processes were not degraded and were consequently detected at the end of the tests [10,14,21,22]. High voltages between 600 and 1400 V [27] or the continuous feeding of pure O_2 for H_2O_2 generation [17] were required. Because of the hard reaction conditions, the generation of secondary pollutants, and the high operational costs associated with these methods, they are often not a desirable solution for treating the acetaminophen [4]. More recently, new advanced oxidation processes such as UVA/LED/TiO_2 and TiO_2/UVA/LED have been proposed by Xiong and Hu [28,29] to remove acetaminophen. In their former study, when they used UVA/LED alone the degradation of acetaminophen was negligible, but enhanced to non-detectable concentrations within 20 min when TiO_2 was used. In their last study, they found that periodic UVA illumination with small duty cycle (0.2) and short cycle time (20 ms) resulted in high photocatalytic degradation of acetaminophen. Furthermore, the addition of H_2O_2 enhanced the mineralization of the compound. However, in their studies they did not discuss about the intermediates/oxidation products, which is an essential consideration in order to ensure the complete degradation/ mineralization of the acetaminophen and their byproducts.

Sirés and Brillas [30] made a major review of electrochemical separation and degradation technologies for various pharmaceuticals, including acetaminophen. They found that, among the various and different techniques, the solar photoelectro-Fenton process is a promising technique. They also reported that more research is needed for a solid understanding of electrochemical advanced oxidation processes like anodic oxidation, electro-Fenton, and photoelectron-Fenton for pharmaceuticals removal. As seen, there is still work to do if it is considered that some research has shown inconclusive results that some other works are based on processes that would be costly at large scales, and that practical, economic, ecological, and accessible technological solutions are needed.

With this in mind, in this study, the performance of an innovative electrochemical oxidation cell with stainless steel electrodes was assessed to degrade acetaminophen and its transformation products in aqueous solutions prepared using ultrapure water. The effect of four pH values (3, 5, 7, and 9) and three direct current (DC) densities (5.7 mA/cm^2, 7.6 mA/cm^2, and 9.5 mA/cm^2) on the degradation kinetics of acetaminophen and its reaction intermediates/oxidation products was evaluated. Electrochemical processes and mechanisms that occurred inside the cell were identified and described. To minimize the wear down of stainless steel electrodes, an operating strategy for the electrochemical cell was proposed.

2. Materials and Methods

2.1. Chemicals and Materials

Acetaminophen (4-acetamidophenol, 98%), sulfuric acid (H_2SO_4), and potassium hydroxide (KOH) were supplied by Sigma-Aldrich (Toluca, Mexico). Methanol was acquired from J.T. Baker (Center Valley, PA, USA). Acetic acid was provided by Fisher Scientific (Monterrey, Mexico). Ultrapure water was prepared with a Milli-Q water purification system (Bedford, MA, USA).

2.2. Experimental Device

Tests were conducted using a home-built fiberglass electrochemical oxidation device that consisted of a cell integrated by four plates. The upper plate has inlets and valves for water admission and air release. The lower plate has an outlet and a valve for water release (Figure 1). Both internal plates have a hole with the dimensions of 107 mm × 60 mm × 12 mm. With this configuration, the cell

has a total volume of 180 mL. The third plate has a mesh of stainless steel electrodes. The mesh of electrodes was configured and prepared based on a textile technique reported by [31]. The dimension of the mesh was 107 mm × 60 mm and contained 27 electrodes made of 24 American Wire Gauge (AWG) stainless steel wire with a diameter of 0.56 mm, an effective length of 107 mm, and spaced approximately 2.1 mm each. Fourteen electrodes worked as "active" anodes and the other thirteen as cathodes. These electrodes were provided with a terminal to be connected to the power source. In this study, a direct current (DC) power supplier (Kaselco from Seal Beach, CA, USA) was used. This apparatus can provide a voltage between 0 V and 50 V and a current intensity of 0 to 10 A.

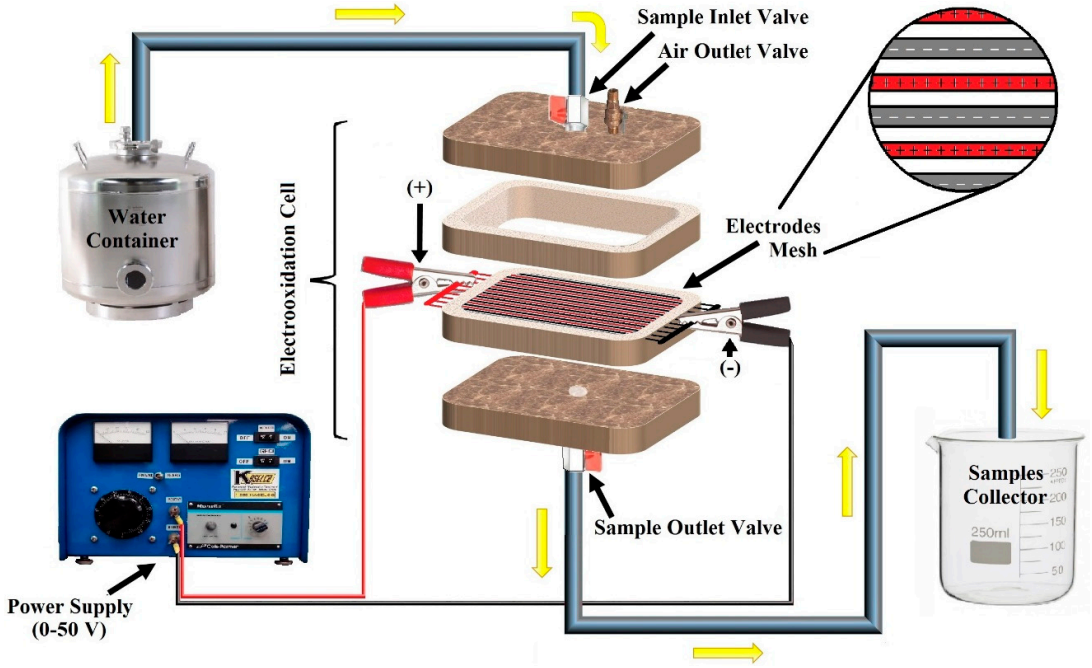

Figure 1. Schematic diagram of the innovative electrochemical oxidation cell.

2.3. Experimental Procedures

Aqueous solutions of 10 mg/L-acetaminophen were prepared using ultrapure water, and their pH was adjusted to achieve values of 3, 5, 7, and 9. The pH of the initial solutions was approximately 5.6. Hydrochloric acid (HCl) was used to adjust the solutions' pH to 3 and 5, and potassium hydroxide (KOH) was used to raise the solutions' pH to 7 and 9. All solutions were treated electrochemically at DC densities of 5.7 mA/cm^2 (6 V), 7.6 mA/cm^2 (12 V), and 9.5 mA/cm^2 (24 V) (Table 1). The reaction time applied for each solution depended on the total time required to achieve the complete degradation of the acetaminophen and its intermediates/oxidation products. Sampling was conducted at 1, 2.5, 5, 7.5, 10, 15, 20, 25, 30, 35, 40, 50, 60, 120, 240, 360, 540, and 900 min after starting the tests. All samples were filtered with 0.45 µm polytetrafluoroethylene (PTFE) syringe filters for further analysis. Determination of acetaminophen and intermediates/oxidation products was conducted by high-pressure liquid chromatography using an Agilent 1200 HPLC-DAD system (Agilent Technologies, Santa Clara, CA, USA). The analytes separation was carried out with a 150 mm × 4.6 mm reverse phase monomeric Zorbax C18 column with 5 µm diameter spherical particles (MAC-MOD Analytical, Wilmington, DE, USA). The method used for the analysis of acetaminophen and its intermediates/oxidation products was adapted from that reported by [32]. The mobile phase consisted of methanol and 1% acetic acid in water (40/60 v/v). The operating conditions of the system were temperature 25 °C, flowrate 1.0 mL/min, and detection at 254 nm.

Table 1. pH and current density conditions for acetaminophen degradation.

Scenario	pH	Current Density (mA/cm^2)	Scenario	pH	Current Density (mA/cm^2)
1		5.7	7		5.7
2	3	7.6	8	7	7.6
3		9.5	9		9.5
4		5.7	10		5.7
5	5	7.6	11	9	7.6
6		9.5	12		9.5

3. Results and Discussion

3.1. Degradation of Acetaminophen in the Innovative Electrochemical Oxidation Cell

When current, at voltage potentials greater than 2 V, is applied to the stainless steel electrodes, electrochemical oxidation processes occurred in the cell. Fe^{2+} was dissolved in the aqueous solution from the anodic oxidation (AO) of stainless steel electrodes by Reaction (1), whereas H_2 gas was generated at the cathodes from proton reduction in acid medium by Reaction (2) or water reduction in alkaline medium by Reaction (3) [30]:

$$Fe \rightarrow Fe^{2+} + 2\,e^{-}, \quad (1)$$

$$2\,H^{+} + 2\,e^{-} \rightarrow H_2\,(g), \quad (2)$$

$$2\,H_2O + 2\,e^{-} \rightarrow 2\,OH^{-} + H_2\,(g), \quad (3)$$

According to [30], in the presence of O_2, dissolved Fe^{2+} is oxidized to insoluble $Fe(OH)_3$ by Reaction (4):

$$4\,Fe^{2+} + 10\,H_2O + O_2\,(g) \rightarrow 4\,Fe(OH)_3\,(s) + 8\,H^{+}, \quad (4)$$

The acetaminophen was subjected to electrochemical oxidation as described below. Evidence of electrochemical oxidation is the formation of reaction intermediates/oxidation products, which is discussed in Section 3.2.

Acetaminophen was successfully degraded by using the innovative electrochemical oxidation cell developed in this study. Figure 2 shows the decay of the acetaminophen at different pH values and current densities. Degradation of acetaminophen was achieved in all scenarios; however, it is evident that faster degradation occurred at lower pH values and greater current densities. At 5.7 mA/cm^2 and pH 3, the total degradation of acetaminophen was achieved in a reaction time of 120 min (2 h), but at pH 5, 7, and 9 the complete degradation took a longer time, beyond the 900 min (15 h). The acetaminophen degradation observed at 15 h was 84% for pH 9 and 92% for pH 5. At 7.6 mA/cm^2, complete degradation of the pharmaceutical at pH 3 was achieved in only 7.5 min, compared with the 120 min required at 5.7 mA/cm^2. At pH 5 and 7, the time needed for the total degradation of acetaminophen was in the order of 570 min (9.5 h) and 900 min (15 h), respectively—much shorter than that at 5.7 mA/cm^2. At pH 9, the time needed for complete degradation of acetaminophen was longer than 900 min (15 h). The degradation reached at this time was approximately 88%—greater than that observed at 5.7 mA/cm^2. Acetaminophen degradation at 9.5 mA/cm^2 was definitely much faster; at pH 3 the total degradation of acetaminophen was reached in only 2.5 min, meanwhile at pH 5 and 7 the total degradation of the pharmaceutical was achieved in 240 min (4 h). At pH 9, the required time for the complete degradation of the compound was 540 min (9 h).

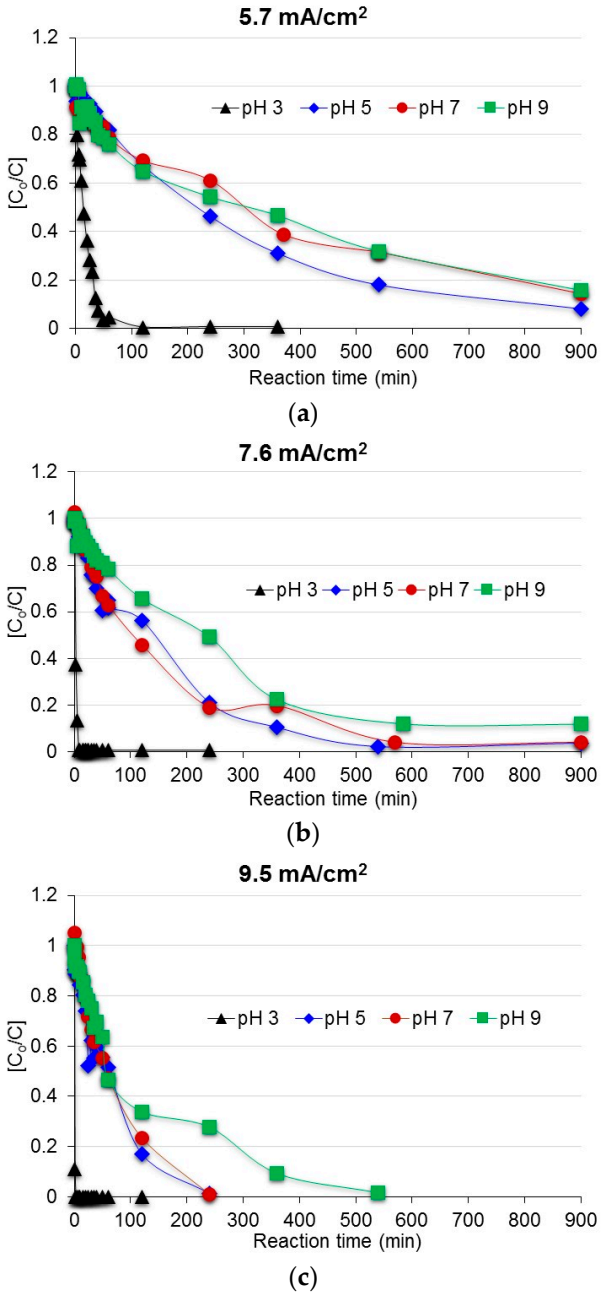

Figure 2. Decay of the acetaminophen at different pH values and current densities. (**a**) DC density: 5.7 mA/cm^2; (**b**) DC density: 7.6 mA/cm^2; (**c**) DC density: 9.5 mA/cm^2.

Kinetics analysis gave more details of the effects of pH and current intensity on the acetaminophen degradation. As seen in Figure 3, degradation rate constants for all pH values increased proportionally to the increase of current intensity. This means that high current densities accelerated the degradation of acetaminophen; however, this effect diminished markedly at pH values greater than 5. On the other hand, pH values lower than 5 enhanced the degradation of acetaminophen, particularly at pH 3. This result is in accordance with the results reported on the literature for electrochemical degradation of acetaminophen and other emergent contaminants (colorants) where pH values on the order of 2.5–3.5 resulted in optimum conditions for degradation [17,27].

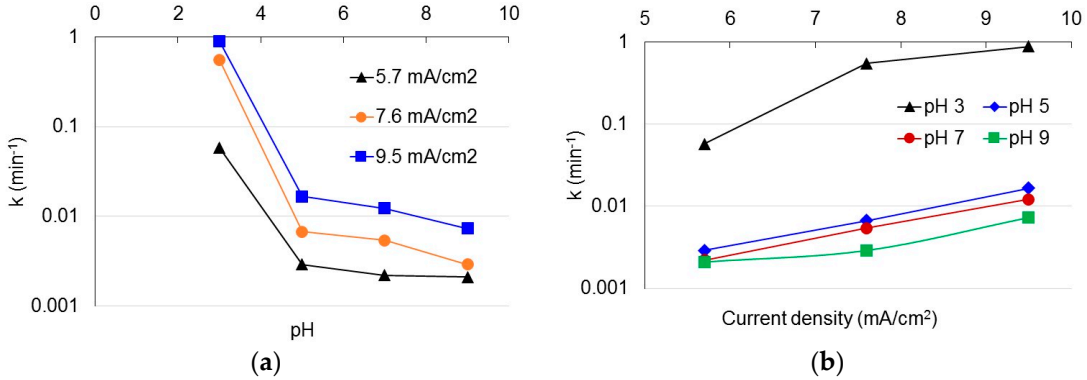

Figure 3. (**a**) Effect of pH and (**b**) current density on degradation rate constants of acetaminophen.

Depending on the pH values and the presence of chloride ions, the oxidation of the acetaminophen in the electrochemical oxidation cell involved different mechanisms. For aqueous solutions, where non-chloride ions were present (pH 7 and 9), or in very low concentration (pH 5), the process was dominated by an anodic oxidation (AO) where the oxidation of the pharmaceutical in the electrochemical oxidation cell might have occurred by direct electron transfer to the anode or by indirect (mediated) oxidation with heterogeneous reactive oxygen species (ROS) formed from water at the anode, such as •OH or "active oxygen" [30,33–35]. Thus, electrochemical conversion, where the acetaminophen was transformed into intermediates by the "active oxygen" species and electrochemical combustion, where the pharmaceutical was mineralized by the •OH might have occurred. According to [30], when high cell voltages are applied, the simultaneous oxidation of the acetaminophen and water are achieved and the anode activity has a strong influence on the selectivity and efficiency of the process yielding either electrochemical conversion or combustion depending on the anode material. Comninellis [35] explained this different behavior by a model that assumes the existence of "active" and "non-active" anodes, respectively. In both kind of anodes, denoted as M, water is oxidized leading to the formation of the hydroxyl radical (M(•OH)) by Reaction (5). In the case of "active" anodes, such as those used in this study (stainless steel), this radical interacts strongly with their surface such that it is transformed into the "active oxygen" species or superoxide MO from Reaction (6).

$$M + H_2O \rightarrow M(\bullet OH) + H^+ + e^-, \quad (5)$$

$$M(\bullet OH) \rightarrow MO + H^+ + e^-, \quad (6)$$

The MO/M pair is a mediator in the electrochemical conversion of the pharmaceutical (R) by Reaction (7).

$$MO + R \rightarrow M + RO, \quad (7)$$

On the other hand, for pH 3, the solution contained chloride ions due to the aqueous dissociation of the HCl into H^+ and Cl^-. Thus, the oxidation under these conditions, usually called electro-oxidation with active chlorine, is based on the direct oxidation of the Cl^- ion at the anode to yield soluble chlorine by Reaction (8), which diffuses away from the anode to be rapidly hydrolyzed and transformed into hypochlorous acid and the chloride ion from Reaction (9):

$$2\,Cl^- \rightarrow Cl_2\,(aq) + 2e^-, \quad (8)$$

$$Cl_2\,(aq) + H_2O \rightleftarrows HClO + Cl^- + H^+, \quad (9)$$

Hypochlorous acid is then in equilibrium with hypochlorite ion at pKa = 7.55:

$$HClO \rightleftarrows ClO^- + H^+, \quad (10)$$

Under equilibrium, Boxall and Kelsall [36] found that the predominant species are Cl_2 until pH near 3, HClO in the pH range 3–8, and ClO^- at pH > 8. Thus, at pH 3, active chlorine species such as Cl_2 and HClO were generated and they attacked the acetaminophen in competition with ROS. According to [30], the mediated oxidation with active chlorine species is faster in acid than in alkaline media because of the higher standard potential of Cl_2 (E^0 = 1.36 V) and HClO (E^0 = 1.49 V) compared to ClO^- (E^0 = 0.89 V). In this study, the degradative action of active chlorine species (pH 3) was greater than that of reactive oxygen species (pH 5, 7, and 9). This was because the degradative action of the "active" anodes (stainless steel electrodes) was strongly enhanced by chloride ions present in the solution since generated active chlorine, alone or in combination with hydroxyl radicals, oxidized the pharmaceutical. This result is in agreement with that reported by [37], who found 80% and 95% acetaminophen destruction in 0.1 M NaCl in 30 min with Ti/RuO_2 and boron doped diamond (BDD) anodes at 80 mA.

3.2. Degradation of Acetaminophen Intermediates/Oxidation Products in the Innovative Electrochemical Oxidation Cell

Anodic oxidation of acetaminophen generates intermediates by the electrochemical conversion of the acetaminophen described by Reaction (3); meanwhile, electro-oxidation with active chlorine produces oxidation products. These compounds were detected in this study and they were also degraded because they could be more toxic than the acetaminophen itself. Chromatograms in Figures 4 and 5 show the acetaminophen degradation and its transformation products at different reaction times for two scenarios, (i) pH 3 with current density 9.5 mA/cm^2; and (ii) pH 9 with current density 9.5 mA/cm^2. Similar chromatograms were obtained for the rest of the scenarios (not included in this document). In general, five main intermediates/oxidation products were detected and denoted as OP 1 to OP 5. At pH 3, four intermediates/oxidation products, OP 1 to OP 3 and OP 5 were detected in all current intensities (Figure 4); meanwhile, in the rest of pH values evaluated only three main oxidation products were observed, OP 1, OP 4, and OP 5 (Figure 5). This means that electro-oxidation with active chlorine produces more intermediates/oxidation products than the anodic oxidation; however, their degradation is faster, as seen in Figures 4 and 5. Identification of these oxidation products was out of the scope of this study; however, OP 1 to OP 4 could correspond to those reported by the literature, such as hydroquinone, p-aminophenol, p-nitrophenol, 1,4-benzoquinone, and NAPQI (N-acetyl-benzoquinone imine) [2]. OP 5 was assessed to be Fe^{2+}, produced during the electro-oxidation process, because its detection level increased at extreme pH values (3 and 9) and as the current and the reaction time increased. OP 1 to OP 4 were successfully degraded in the innovative electrochemical oxidation cell, as seen in Figure 6. It is clear that lower pH values and greater current densities accelerated the degradation of reaction intermediates/oxidation products. At 5.7 mA/cm^2 and pH 3, the degradation achieved at 360 min (6 h) was greater than 96%, and for the rest of the pH values the time required for the complete degradation was greater than 900 min (15 h). At 7.6 mA/cm^2 and pH 3, a reaction time of approximately 240 min (4 h) was required to completely degrade all the intermediate/oxidation products, and for the rest of the pH values the degradation time needed was between 570 min (9.5 h) and 900 min (15 h). At 9.5 mA/cm^2 and pH 3, the degradation of the intermediates/oxidation products was accomplished in 120 min (2 h); meanwhile, at pH 5 and 7 the total degradation was achieved in 240 min (4 h). At pH 9, the required time for the complete degradation of the intermediates/oxidation products was 540 min (9 h). Similar to acetaminophen degradation, the degradative action of active chlorine species (pH 3) was greater than that of reactive oxygen species (pH 5, 7, and 9). This was because the degradative action of the "active" anodes was enhanced by chloride ions present in the solution since generated active chlorine, alone or in combination with hydroxyl radicals, oxidized the reaction intermediates/oxidation products.

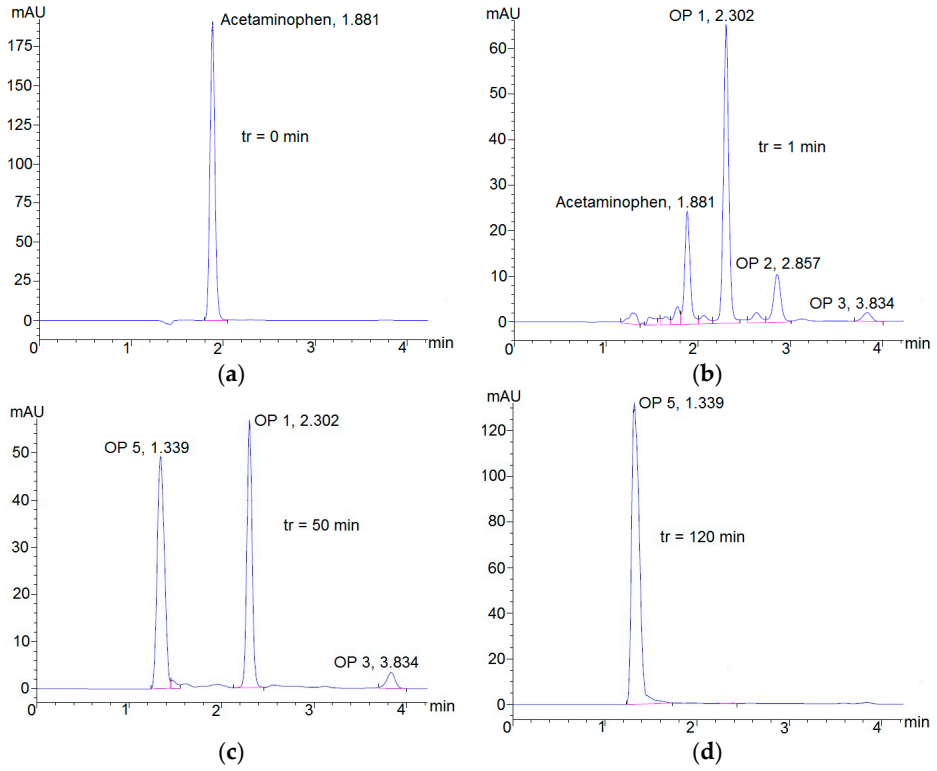

Figure 4. Chromatograms of acetaminophen degradation and its transformation products at different reaction times for the scenario involving pH 3 with a current density 9.5 mA/cm^2. (**a**) tr = 0 min; (**b**) tr = 1 min; (**c**) tr = 50 min; (**d**) tr = 120 min. OP refers to oxidation products.

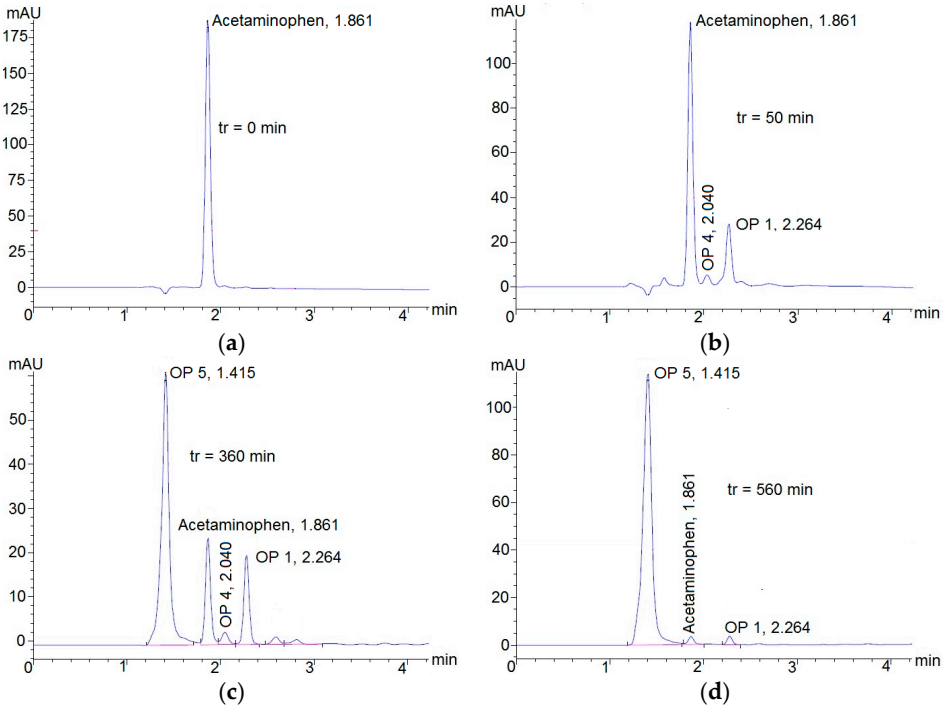

Figure 5. Chromatograms of acetaminophen degradation and its transformation products at different reaction times for the scenario involving pH 9 with a current density 9.5 mA/cm^2. (**a**) tr = 0 min; (**b**) tr = 50 min; (**c**) tr = 360 min; (**d**) tr = 560 min. OP refers to oxidation products.

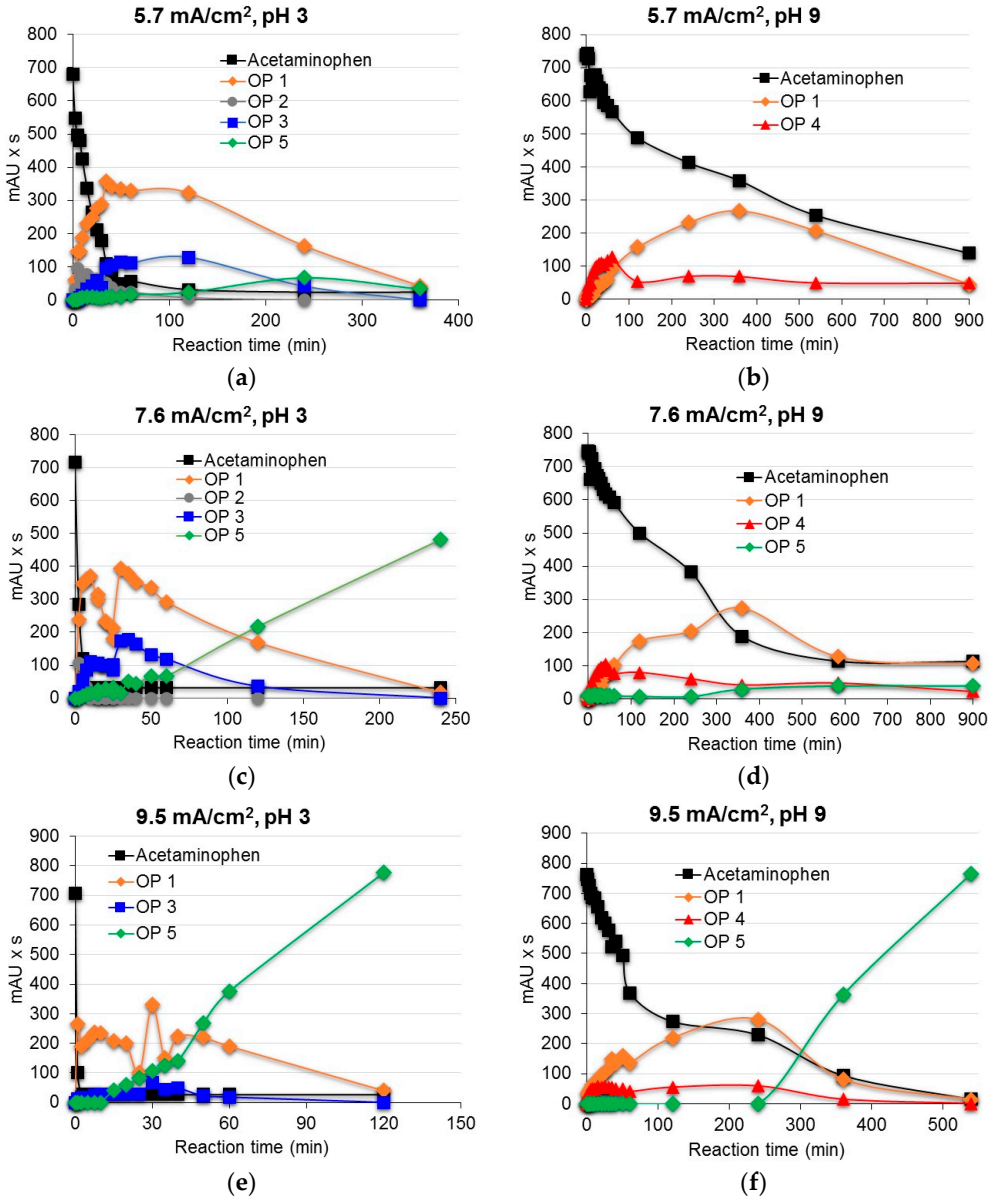

Figure 6. Effect of pH and current density on the degradation of reaction intermediates/oxidation products of acetaminophen. (**a**) 5.7 mA/cm^2 and pH 3; (**b**) 5.7 mA/cm^2 and pH 9; (**c**) 7.6 mA/cm^2 and pH 3; (**d**) 7.6 mA/cm^2 and pH 9; (**e**) 9.5 mA/cm^2 and pH 3; (**f**) 9.5 mA/cm^2 and pH 9.

On the other hand, oxidation of the stainless steel electrodes (OP 5) was mainly observed at 7.6 mA/cm^2 and 9.5 mA/cm^2 and at pH 3 (Figure 6). This process could rapidly wear down the electrodes; therefore, strategies to avoid this process were proposed. Regarding the results obtained in this study (Figure 6), the first alternative consisted of conducting the electrochemical oxidation process under a current density of 5.7 mA/cm^2; however, this condition will imply longer reaction times. Therefore, a more viable alternative was proposed and consisted of operating the electrochemical oxidation cell under a current ramp, applying first 9.5 mA/cm^2 during 2.5 min or 7.6 mA/cm^2 during 7.5 min, and then continuing the electrochemical oxidation process under a current density of 5.7 mA/cm^2. In the first step of the ramp, complete degradation of the acetaminophen will be achieved and the main intermediates/oxidation products will be formed with low wear down of the stainless steel electrodes. In the second step, degradation of intermediates/oxidation products will occur with a minimum oxidation of the electrodes. This operation scheme will enhance the degradation of the

pharmaceutical, extend the life of the electrodes, and shorten the reaction time needed to degrade not only the acetaminophen, but also the intermediates/oxidation products. The combined use of other "active" (Pt, IrO_2, and RuO_2) and "non-active" (PbO_2, SnO_2, and boron doped diamond (BDD)) electrodes has been reported in the literature [30] as a successful strategy to degrade pharmaceuticals and reduce the wear down of the electrodes, even under active chlorine species. However, these electrodes are expensive, thus limiting their practical application.

Moreover, the application of direct current densities up to 9.5 mA/cm^2 allows the potential use of photovoltaic cells to degrade not only pharmaceuticals, but also their intermediates/oxidation products from water and wastewater. This fact makes the novel electrochemical oxidation cell an interesting alternative for degrading environmentally and sustainably emergent contaminants. Undoubtedly, more research is needed to evaluate the performance of the innovative electrochemical oxidation cell when other pharmaceuticals and emergent contaminants have to be removed not only in aqueous solutions but also in raw water for human consumption and wastewater effluents, where the presence of particulate and dissolved organic and inorganic matter may influence the degradation process; however, the results obtained in this study are promising.

4. Conclusions

A novel electrochemical oxidation cell was developed and tested to degrade acetaminophen and its reaction intermediates/oxidation products in aqueous solutions prepared using ultrapure water. The configuration of a mesh with stainless steel electrodes was effective for that purpose, degrading the acetaminophen and the intermediates/oxidation products in very short reaction times. Due to the use of stainless steel electrodes, electrochemical oxidation processes occurred inside the cell. Acetaminophen degradation rate constants increased proportionally to the increase of current density. High current densities accelerated the degradation of acetaminophen; however, this effect diminished markedly at pH values greater than 5. On the other hand, pH values lower than 5 enhanced the degradation of acetaminophen, particularly at pH 3. Formation of four reaction intermediates/oxidation products were detected and also successfully degraded. The degradative action of active chlorine species at pH 3 was greater than that of reactive oxygen species at pH 5, 7, and 9 because the degradative action of the stainless steel electrodes was enhanced by the chloride ions present in the solution. Operating the electrochemical oxidation cell under a current density ramp, applying first 9.5 mA/cm^2 during 2.5 min or 7.6 mA/cm^2 during 7.5 min and then continuing the electrochemical oxidation process under a current density of 5.7 mA/cm^2 will enhance the degradation of the pharmaceutical, extend the life of the electrodes, and shorten the reaction time needed to degrade not only the acetaminophen, but also the intermediates/oxidation products. Direct current densities up to 9.5 mA/cm^2 can be supplied by photovoltaic cells; therefore, the novel electrochemical oxidation cell could be a sustainable technological solution for degrading emergent contaminants.

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Conflicts of Interest: The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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