Electro-oxidation of diclofenac at boron doped diamond: Kinetics and mechanism

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ABSTRACT

Diclofenac is a common anti-inflammatory drug. Its electrochemical degradation at boron doped diamond electrode was investigated in aqueous solution. The degradation kinetics and the intermediate products were studied. Results showed that electro-oxidation was effective in inducing the degradation of diclofenac with 30 mg/L initial concentration, ensuring a mineralization degree of 72% after a 4 h treatment with the applied bias potential of 4.0 V. The effects of applied bias potential and addition of NaCl on diclofenac degradation were investigated. Different degradation mechanisms of diclofenac were involved at various applied bias potentials. With the addition of NaCl, some chlorination intermediates including dichlorodiclofenac were identified, which lead to the total organic carbon increase compared with the electrolysis process without NaCl addition at the reaction initial period. The main intermediates including 2,6-dichlorobenzenamine, 2,5-dihydroxybenzyl alcohol, and benzoic acid are identified at the time of 2 h. 1-(2,6-Dichlorocyclohexa-2,4-dienyl)indolin-2-one were also identified. These intermediates disappeared gradually with the extension of reaction time. Small molecular acids were identified finally. Based on these results, a degradation pathway of diclofenac was proposed.

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1. Introduction

In recent years, pharmaceutical drugs have emerged as a novel class of water contaminants. Public and scientific concern is increasing steadily because of their potential impact on human health and the environment even at trace levels [1,2]. These drugs are specifically designed to elicit a biological response. Thus, it has been suggested that some drugs can inflict biological harm even at trace concentrations, with possible synergistic effects. Many pharmaceutical compounds are not effectively removed by conventional wastewater treatment processes, thus passing the compounds to surface waters that receive wastewater effluent [3,4].

Physical and chemical remediation technologies such as filtration, adsorption, coagulation–flocculation, and flotation have been used to remove some pharmaceutical compounds [5]. On the other hand, advanced oxidation processes have been largely investigated for their degradation [6–11]. Recently, anodic oxidation with electronically conductive diamond anode is a new advanced oxidation process with many advantages as compared to other known chemical and photochemical processes [12,13]. A large quantity of hydroxyl radicals can be produced from water electrolysis at diamond surfaces. And, the diamond surface does not interact with these radicals, and, as a consequence, these radicals can only couple

to form oxygen or oxidize the contaminants in the aqueous solution. It has been shown that the electrochemical oxidation with BDD anodes achieves a very high current efficiency as compared to other electrochemical treatments, and very high conversions of the organic carbon into carbon dioxide [14–16].

Diclofenac is a popular non-steroidal anti-inflammatory drug widely used to treat inflammatory and painful diseases of rheumatic and non-rheumatic origin. It has been detected in many municipal sewage treatment plant effluents [17]. Some studies indicated that diclofenac can induce some adverse effects on aquatic life [18,19]. And, in combination with other pharmaceuticals present in water samples, the toxic effect can be considerably increased [20]. Recently, removal of diclofenac from polluted and drinking water by AOPs has been reported [4,21,22]. But, only photo-Fenton treatment achieved total mineralization [22]. And, electrochemical degradation of diclofenac has not been reported. Its molecular structure is shown below.

Diclofenac

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Fig. 1. Cyclic voltammograms of diclofenac with various concentrations at BDD electrode (A) and glass carbon electrode (B) (0.1 M Na₂SO₄ electrolyte).

In the present work, electrochemical oxidation of diclofenac in aqueous solution at BDD electrode was investigated, which has not been reported previously. Degradation intermediates were identified and a possible degradation pathway was proposed. And, largely different effects of applied bias and the addition of NaCl on diclofenac degradation were observed and explored. Relatively high initial concentrations of diclofenac were tested in order to investigate the effectiveness of BDD electro-oxidation process in removing diclofenac in aqueous solutions and to assess the nature and toxic variation of the main intermediates along the mineralization route. This latter aspect is of particular relevance, since potentially toxic species may be produced by incomplete degradation of diclofenac and their assessment is important if the method should be applied for water treatment.

2. Materials and methods

Diclofenac was purchased from Sigma–Aldrich Chemie (Steinheim, Germany). Stock solutions of diclofenac were prepared with Milli-Q purified water (Millipore). All chemicals used were reagent grade. Highly BDD electrode used in this work were purchased by CSEM (Switzerland) and synthesized on single crystal p-type Si (100) wafers, with resistivity of 0.1 Ω cm, by the hot filament chemical vapour deposition technique. It consists of a coating of nano-polycrystalline boron-doped diamond (BDD) film with the thickness of 2 μm (Fig. S1).

Degradation experiments were performed in a rectangular (50 mm × 50 mm × 100 mm) reactor, which is made from quartz

glass. The reactor contained a 100 mL reaction solution allowing 3.5 cm of the electrode to be immersed into the solution. The electrochemical reaction employed a basic electrochemical system (Princeton Applied Research) connected with a counter-electrode (Pt wire, 70 mm in length with a 0.4-mm diameter), a working electrode (the BDD electrode, active area of 12 cm²), and a reference electrode (a saturated calomel electrode (SCE)). About 0.1 mol/L (M) Na₂SO₄ aqueous solution was used as electrolyte solution.

Initial concentration of diclofenac solution was 30 mg/L and was analyzed by reversed-phase high performance liquid chromatogram (HPLC) with a Hitachi HPLC apparatus (Diode Array Detector L-2450, Column Oven L-2300, and Pump L-2130). The pH value was determined to be 8.5. Diclofenac was determined by isocratic elution with 50% aqueous buffer solution with 10 mM ammonium formate/50% acetonitrile. The flow rate was 1.0 mL/min and the detection wavelength was set at 280 nm. The concentration of total organic carbon (TOC) was analyzed using a multi N/C 3000 TOC analyzer (Analyti Jena AG, Germany). Prior to injection into the TOC analyzer, the samples were filtrated with 0.45 μm Millipore filter. All experiments were carried out at least in duplicate. The reported

Fig. 2. Electro-oxidation of diclofenac at BDD electrode at various reaction times: (A) variation of HPLC spectra and (B) UV–vis spectra of diclofenac reaction solution (initial diclofenac concentration 30 mg/L; applied bias potential, 4.0 V; 0.1 M Na₂SO₄ electrolyte).

Table 1
Potential intermediates identified in the electro-oxidation of diclofenac detected by GC–MS.

Retention time/min	Intermediates	Molecular structure
8.229 ^a	2-Hydroxyl-propanoic acid
8.900 ^b	Hydroxyl-acetic acid
12.948 ^a	Glycol
14.818 ^a	Malonate
15.655 ^a	2,6-Dichlorobenzenamine
16.153 ^a	Benzoic acid
18.058 ^{a,b}	Glycerol
18.335 ^{a,b}	Butanedioic acid
18.678 ^a	2-Amino-benzoic acid
21.756 ^b	Hexanoic acid

Table 1 (Continued)

Retention time/min	Intermediates	Molecular structure
21.822 ^b	Oxalic acid
22.226 ^c	Furan-2,5-diol
29.424 ^c	2,5-Dihydroxyl-benzaldehyde
31.180 ^{c,d}	2,5-Dihydroxybenzyl alcohol
34.848 ^{c,d}	2,5-Dihydroxyl-benzeneacetic acid
41.811 ^{a,d}	1-(2,6-Dichlorocyclohexa-2,4-dienyl)indolin-2-one

Reaction time: ^a2 h; ^b4 h; ^c1 h; ^d0.5 h (30 mg/L diclofenac; 4.0 V applied bias potential; 0.1 M Na₂SO₄ electrolyte).

average values are within the experimental error of $\pm 3\%$. For gas chromatography–mass spectroscopy (GC–MS) analysis, the residue was trimethylsilylated with 0.2 mL of anhydrous pyridine, 0.1 mL of hexamethyldisilazane, and 0.05 mL of chlorotrimethylsilane at room temperature. GC–MS analysis was carried out on an Agilent 6890GC/5973MSD with a DB-5 MS capillary column. Liquid chromatography/electrospray-time-of-flight mass spectrometry (LC/EIS-TOF-MS) with negative ionization was used to detect diclofenac chlorination products. Separation was not

used. LC/TOF-MS accurate mass spectra were recorded from 50 to 1000 *m/z*.

The toxicity of an initial diclofenac solution and of aqueous samples collected at different reaction time was evaluated by monitoring changes in the natural emission of the luminescent bacteria *Vibrio fischeri* when challenged with toxic compounds. Briefly, samples were tested in medium containing 2% sodium chloride, in five dilutions and luminescence was recorded after 5 and 15 min of incubation at 15 °C. The inhibition of the luminescence, compared

The initial concentration of diclofenac was 30 mg/L. At the reaction time of 0.5, 1, 2, 3, and 4 h, the concentration of diclofenac was reduced to 18.3, 10.6, 5.1, 1.9, and 1.1 mg/L. Nearly complete abatement of diclofenac is observed within 4 h. And, 72% diclofenac is mineralized within 4 h based on the TOC analysis. It can be seen from Fig. 2(A) that some near peaks appear with the decrease of diclofenac concentration. And the intensity of new peaks decreases with the extension of reaction time. These results suggested that the intermediates were produced at the initial reaction time, which were degraded with the extension of reaction process. As shown in Fig. 2(B), the decrease in UV-vis absorbance of the reaction solution furthermore confirms the above conclusion.

3.3. Identification of intermediates and proposed degradation pathways

The main intermediates of diclofenac generated during the BDD electro-oxidation process were identified by GC–MS with library spectra (Table 1). It is observed that 2,6-dichlorobenzeneamine and benzoic acid are identified at the reaction time of 2 h. 1-(2,6-Dichlorocyclohexa-2,4-dienyl)indolin-2-one are also identified. These intermediates disappear at the reaction time of 4 h. Many small molecular acids such as hydroxyl-acetic acid, 2-hydroxyl-propanoic acid, malonate, butanedioic acid, hexanoic acid, and oxalic acid are identified. Based on these results, it can be concluded that diclofenac was degraded by cleavage of C–N bond firstly. And, some aromatic compounds are formed, which are degraded by ring open way. Finally, some small molecular acids are produced. A proposed electro-oxidation pathway of diclofenac with the applied bias potential of 4.0 V was given in Scheme 1. At the same time, the degradation intermediates of diclofenac with the 2.5 V applied bias potential at 4 h was also identified. Similar aromatic compounds and small molecular acids are also identified, which indicated that the reaction pathways of diclofenac at 4.0 and 2.5 V are similar.

3.4. Effect of applied bias potential

Furthermore, the effect of applied bias potential on diclofenac degradation was investigated. Fig. 3 shows the electrochemical degradation of diclofenac at various applied bias potentials ranging from 0.8 to 4.0 V. Degradation of diclofenac is observed at all applied bias potentials; the degradation rate increases with the increasing bias potential. Two possible mechanisms were taken into account to explain the degradation behavior of diclofenac (Fig. 3(A)), involving direct oxidation and indirect oxidation mediated by reactive oxidants (ROs) generated during the electrolysis of H₂O [23–25]. At the meantime, diclofenac concentration vs. volume-normalized charge quantity was presented in Fig. 3(B). It can be seen that the specific charge consumed for diclofenac degradation increases with increasing applied bias potential, which means that increasing applied bias potential causes acceleration of O₂ evolution reaction, which will consume charge quantity.

No remarkable degradation of diclofenac was achieved at anodic potential below 1.2 V, for which H₂O electrolysis nearly cannot occur, which indicated that the contribution of direct oxidation is not significant. The other possible mechanism responsible for the diclofenac degradation is indirect oxidation mediated by several oxidants produced from the oxidation of water. ROs such as $\cdot\text{OH}$, O₃, H₂O₂, and $\cdot\text{O}_2^-$ can be considered as candidate oxidants [26]. The most common oxidation is the $\cdot\text{OH}$ radicals formed by the one-electron oxidation of water. Additionally, other ROs can also be responsible for the diclofenac degradation. As shown in Fig. S2, the impedance spectra with the bias potential of 1.3 V is different from that with the potential of 2.5 and 4.0 V, which indicates that the degradation mechanism of diclofenac at 1.3 V may be different from that at 2.5 and 4.0 V [27,28]. Fig. 4 presents Bode phase plots in the blank NaCl electrolyte and in a 30 mg/L diclofenac solution at a current potential of 2.5 V. Each peak in the Bode phase plot corresponds to a reaction that affects the impedance to current flow. The first peak centered near 1000 Hz in the blank electrolyte corresponding to H₂O oxidation [29]. In the diclofenac solutions, several unresolved peaks centered near 1 and 100 Hz are observed which are the reaction results involving electrochemical oxidation of diclofenac and its reaction products. The chronoamperometry results (Fig. 5) have shown that the BDD electrode is rapidly deactivated during anodic polarization in the potential of 0.9 V, which may be attributed to electrode fouling by polymeric products. However, in the potential region of water electrolysis, diclofenac oxidation

Fig. 3. Electro-oxidation of diclofenac at BDD electrode at various reaction times: (A) effect of applied bias potential and (B) effect of charge quantity on diclofenac degradation (initial diclofenac concentration, 30 mg/L; 0.1 M Na₂SO₄ electrolyte).

involves active intermediates that can avoid electrode deactivation. In this region, the amount of electrogenerated ROs and the nature of oxidation products can be controlled by a proper choice of the applied current density. In particular, at low current density and high diclofenac concentration, low diclofenac conversion are

Fig. 4. Bode phase plots in 0.1 M NaCl electrolyte in the presence and absence of diclofenac at a bias potential of 2.5 V.

Fig. 5. Potentiostatic $I-t$ curves in a stirred reaction solution recorded at several applied potential (initial diclofenac concentration, 30 mg/L; 0.1 M Na_2SO_4 electrolyte).

formed; while at high current density and low diclofenac concentration, most of diclofenac are mineralized into CO_2 .

3.5. Effect of NaCl on diclofenac degradation kinetics and pathway

It can be seen from Fig. 6 that the addition of Cl^- slows down the degradation rate of diclofenac and TOC removal rate. Because the potential of Cl_2 evolution is below than that of O_2 evolution, Cl_2 evolution will lead to the decrease rate of H_2O electrolysis. As a result, the amount of $\cdot\text{OH}$ generated from H_2O electrolysis is reduced. Thus, the rates of diclofenac degradation and TOC removal will be decreased.

As shown in Fig. 7(A) and (B), HPLC and UV-vis spectra variation with the reaction time in the diclofenac electro-oxidation in NaCl solution is different from that in Na_2SO_4 solution (Fig. 2(A) and (B)), which indicate that some different intermediates may be produced. It is known that electrochemical oxidation of Cl^- produces hypochlorous acid (HOCl) or the hypochlorite ion (OCl^-) depending on the solution pH. Cl_2 is the main chlorine species at $\text{pH} < 3$; HOCl in the region $3 \leq \text{pH} \leq 7$, and OCl^- at $\text{pH} > 7$ [30]. The pH value of the initial diclofenac solution was determined to be 6.7. Thus, HOCl can be produced. And, some undesirable organic chloride compounds may be formed. Dichlorodiclofenac was identified using TOF-MS analytic method. The analytic results of TOF-MS were shown in Fig. S3. The results were consistent with that reported by Miyamoto et al. [31]. These chlorinated intermediates may be responsible for the slow TOC removal rate as shown in Fig. 6. Although available analytical information does not allow the precise position of the HOCl attack to be predicted, considerations concerning the reactivity of the different sites on the diclofenac molecule [21] suggest chlorination of C-5, which is para to the NH substitute as the

Fig. 6. Variation of diclofenac concentration and TOC in electro-oxidation process in the presence of 0.1 M NaCl (a) and Na_2SO_4 (b) (initial diclofenac concentration, 30 mg/L; applied bias potential, 4.0V).

most probable option on the basis of their electrophilic character and frontier electron densities (FED) theory. This hypothesis is consistent with previous publications [31]. Subsequently, these chlorination intermediates were degraded, which was supported by the GC-MS analysis.

Fig. 7. Electro-oxidation of diclofenac at BDD electrode at various reaction times: (A) variation of HPLC spectra and (B) UV-vis spectra of diclofenac electro-oxidation process (initial diclofenac concentration, 30 mg/L; applied bias potential, 4.0V; 0.1 M NaCl electrolyte).

During the electro-oxidation process in Na₂SO₄ electrolyte, the generation of intermediates increases until a maximum concentration is reached. Subsequently, these intermediates are degraded. It can be related to the toxicity results. The toxicity of the solution at different reaction time at 4.0 V was measured. The inhibition rate was 65, 89, 76, and 23% corresponding to the reaction time of 0, 2, 4, and 12 h. The increase in the inhibition of the bacteria test goes with the increase in toxic intermediates. A maximum value of inhibition percentage is observed at 2 h. After that, a decrease appears due to the diminishing concentration of toxic intermediates. Even if a correlation between the intermediates formed and the toxicity can be seen, it has not been possible to assess which molecule is responsible for the toxicity. These observations clearly demonstrate that transformation intermediates are more toxic than single diclofenac at the initial reaction period. When the reaction time was extended to 12 h, the inhibition was 23%, which indicated that BDD electro-oxidation is efficient in reducing the toxicity of diclofenac aqueous solution.

4. Conclusions

It has been exhibited that the electro-oxidation using BDD electrode is effective in inducing diclofenac degradation. The diclofenac degradation was found to follow the reaction pathways leading to hydroxylated intermediates and C–N cleavage intermediates through competitive routes. Subsequent oxidative ring cleavage leads to carboxylic acid fragments. At the low applied bias potential, direct electro-oxidation of diclofenac did not occur although there was anode oxidation peak in the CV curve. Electro-oxidation degradation of diclofenac is mainly performed by the active radicals produced in the anode electro-oxidation process with the application of high bias potential. Addition of NaCl into the diclofenac reaction solution decreases the TOC removal rate at the reaction initial period. And, some chlorination products were identified. Inhibition of the bacteria increased with the reaction time at the initial reaction phase and gradually decreased with the extension of reaction time. Transformation intermediates at the initial reaction period were more toxic than single diclofenac.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.electacta.2009.02.059.

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