Degradation of gestodene (GES)–17α-ethinylestradiol (EE2) mixture by electrochemical oxidation

Hugo Alejandro Nájera-Aguilar, Rubén Fernando Gutiérrez-Hernández, Rocío González de los Santos, Carlos García-Lara, Roger Méndez-Novelo and María Neftalí Rojas-Valencia

ABSTRACT

Evidence of the negative effects of several pharmaceutical molecules, such as hormones and steroids, on the environment can be observed throughout the world. This paper presents the results of the anodic oxidation of the mixture of gestodene steroid hormones and 17 α-ethinylestradiol present in aqueous medium. The tests were conducted in an undivided cell containing a working volume of 50 mL, using a Na_2SO_4 solution as support electrolyte and boron-doped diamond electrodes. The experiments were adjusted to the structure of a 3^3 factorial design. The evaluated factors were: support electrolyte concentration (0.02, 0.05, and 0.10 M), pH of the reaction media (2, 3, and 4), and current density (16, 32, and 48 mA cm^{-2}). Under the optimum conditions (0.02 M Na_2SO_4, pH 4, and current density of 32 mA cm^{-2}), the degradation of at least 93% of the initial concentration of gestodene and 17α-ethinylestradiol was reached in a reaction time of 5 and 10 min, respectively. The complete degradation of both molecules required 15 min of reaction. Under these conditions, the degradation profile of the pharmaceutical mixture as each one of the active ingredients, followed a pseudo-first order kinetic behavior ($k_{mix} = 0.0321$, $k_{GES} = 0.4206$, and $k_{EE2} = 0.3209$ min^{-1}).

Key words | anodic oxidation, electro-oxidation, gestodene–17α-ethinylestradiol removal, oxidation advanced processes, steroid hormones

Hugo Alejandro Nájera-Aguilar
Rocío González de los Santos
Carlos García-Lara
Escuela de Ingeniería Ambiental,
Facultad de Ingeniería de la Universidad de
   Ciencias y Artes de Chiapas,
Lib. Norte Pte. No. 1150, Colonia Lajas Maciel,
Tuxtla Gutiérrez,
Chiapas C.P. 29039,
México

Rubén Fernando Gutiérrez-Hernández
   (corresponding author)
Departamento de Ingeniería Química y Bioquímica,
Instituto Tecnológico de Tapachula,
Km. 2 carretera a Puerto Madero,
Tapachula, Chiapas C.P. 30700,
México
E-mail: *rgutierrez@ittapachula.edu.mx*

Roger Méndez-Novelo
Facultad de Ingeniería,
Universidad Autónoma de Yucatán,
Av. Industrias no contaminantes por Periférico Nte.
   s/n, Mérida, Yucatán,
México

María Neftalí Rojas-Valencia
Universidad Nacional Autónoma de México,
   Instituto de Ingeniería, Coordinación de
   Ingeniería Ambiental,
Cd. de México C.P. 04510,
México

INTRODUCTION

In the last few years, a wide spectrum of molecules capable of affecting, to a greater or lesser extent, the endocrine system of several living organisms, including human beings, have been identified in the environment (Liu *et al.* 2011; Sahoo *et al.* 2012). Among these compounds can be included: steroid hormones such as gestodene (GES), 17α-ethinylestradiol (EE2), 17β-estradiol (E2), and drospirenone; β-blockers such as metoprolol; and pesticides such as 2,4-dichlorophenoxyacetic acid. Evidence has been gathered relating these types of molecules to the increase in

the prevalence of cancers and malformations in human reproductive organs (Dickerson & Gore 2007), and to feminization, masculinization, and malformation of the reproductive system of lower organisms such as fish, birds, and reptiles (Brian *et al.* 2007). For this reason, they are generally identified as endocrine disrupting compounds (EDCs).

Due to the severe consequences related to the presence of EDCs, a great number of research groups have worked on the evaluation of technologies that may help reduce their

presence in the environment. Among them are biological processes, combined biological–physicochemical processes, and the so-called advanced oxidation processes (AOPs). Fenton and photo-Fenton systems (Colombo *et al.* 2011), heterogenous photocatalysis (Czech & Rubinowska 2013), and several electrochemical processes, such as anodic oxidation and electro-Fenton system (Sirés *et al.* 2010), among others, belong to the AOPs group. Compared to conventional processes, their main advantage is that they achieve a profound transformation of the chemical structure of the contaminants, and do not only transfer them from one form or medium to another (Liu *et al.* 2009).

The mixture of GES and EE2, two steroid hormones, is frequently and intensively used as an oral contraceptive (Matějíček & Kubáň 2007). This explains its widespread presence in the environment (Velicu & Suri 2009), and the interest of various research groups to evaluate technologies that are appropriate for its degradation. Such is the case of Zhang *et al.* (2012), who reported the effectiveness of ozone in the degradation of the EE2 molecule, achieving a 94.7% removal of an initial concentration of $100 \, \mu g \, L^{-1}$, using $9 \, mg \, L^{-1}$ of ozone, pH 6, $10 \, mg \, L^{-1}$ of natural organic matter and $20 \, mg \, L^{-1}$ of suspended solids. On the other hand, Frontistis & Mantzavinos (2012) evaluated the sonodegradation of $110 \, \mu g \, L^{-1}$ of EE2, observing a direct relationship between the rate of degradation of the molecule and the density of sonication power, while an inverse relationship with the system temperature was observed. It was also observed that organic matter delays the degradation process in an acidic medium (pH 3), while it accelerates it in a neutral medium (pH 7.8).

Frontistis *et al.* (2011) evaluated the anodic oxidation of $100 \, \mu g \, L^{-1}$ of EE2, using a zirconium cathode and a boron-doped diamond (BDD) anode. The authors achieved the complete degradation of EE2 in 7 min using a current density of $2.1 \, mA \, cm^{-2}$. The degradation of EE2, alone or mixed with E2, was studied by Guedes *et al.* (2008). These authors evaluated the ozonation and O_3/H_2O_2 processes. With the first process, they removed 99.7 and 100% of EE2 and E2, respectively, from a mixture having an initial concentration of $10 \, \mu g \, L^{-1}$. These results were achieved when the reaction medium operated at pH 3 and $25 \, mg \, L^{-1}$ of ozone. When the estrogens were treated separately, the results were similar, resulting in efficiencies greater than 99% for both compounds. In the O_3/H_2O_2 process, the addition of H_2O_2 did not improve estrogen removal. Currently, the study of the degradation of GES–EE2 mixture is insufficient. Only a few investigations have reported the degradation of the GES–EE2 mixture alone or in the presence of other hormones (Fu *et al.* 2007; Rokhina *et al.* 2012). Fu *et al.* (2007) evaluated the destruction of the mixture of eight molecules ($10 \, \mu g \, L^{-1}$ each one) using ultrasound (20 kHz). After 25 min of treatment, a degradation of about 80% of the total mixture, 82% of EE2, and 70% of GES was observed. The authors also evaluated the effect of the pH on the reaction medium (pH 3, 7, and 9) and observed that the greatest removal was achieved in acidic conditions. Moreover, the degradation kinetics of each molecule followed a pseudo-first order reaction profile.

On the other hand, Rokhina *et al.* (2012) evaluated the ozonation of 12 hormones, among them, EE2 and GES. The hormone mixture had an initial concentration of $100 \, \mu g \, L^{-1}$ of each one and degradation percentages above 99% were achieved with a 1 min treatment using an ozone dose of $5 \, mg \, L^{-1}$. In view of this information, in the present article, data obtained from the degradation of the GES–EE2 mixture through anodic oxidation using BDD electrodes are shown. The tests were performed using the initial GES/EE2 concentration ratio present in pharmaceutical formulations of oral contraceptives. Parameters such as supporting electrolyte concentration, pH of the reaction medium, and the current supply to the system were controlled in order to determine the conditions in which the greater degradation percentage was achieved.

METHODOLOGY

Reagents

The analytical grade chemical substances, such as sodium sulfate, as well as the reagents used in the chemical oxygen demand (COD) determination were supplied by Sigma-Aldrich. The high-performance liquid chromatography (HPLC) grade solvents used in the chromatographic determinations were acquired from Sigma-Aldrich. The GES–EE2 working solutions were prepared using pharmaceutical formulations obtained

from a local pharmacy store. In the preparation of each one of the working solutions, distilled water was used.

Electrolytic system

All the anodic oxidation tests of the GES–EE2 mixture were conducted in an undivided electrolytic cell with a reaction volume of 50 mL, using a Na_2SO_4 solution as supporting electrolyte. Considering the study reported by Frontistis *et al.* (2011), in all the cases, the initial concentration of the mixture was adjusted at 625 μg L^{-1} of GES and 250 μg L^{-1} of EE2, this mixture presenting an initial COD average concentration of 713 mg L^{-1} and a standard deviation of 20.5 mg L^{-1}. As anode and cathode, parallel BDD electrodes (Adamant Technologies, Switzerland) having a working surface of 2.5×2.5 cm^2, separated by a distance of 2 cm, were used. The pH of the reaction medium was adjusted using 10% H_2SO_4. The current was supplied and controlled through a power supply unit (Extech Instruments Model 382270) operated under open potential. The reaction medium was kept at all times at room temperature ($26 \pm 2\ °C$), under constant agitation (850 rpm) and in complete darkness.

Experimental design and data analysis

The degradation tests were conducted in batches according to a 3^3 factorial design, generating a total of 27 different treatments. The studied factors were: supporting electrolyte (Na_2SO_4) concentrations (0.02, 0.05, and 0.10 M); pH of the reaction medium (pH 2, 3, and 4); and current density (16, 32, and 48 mA cm^{-2}). Each one of these treatments was performed in triplicate. The GES–EE2 mixture was dissolved in the reaction medium and, in all the cases, a 10-min medium homogenization period was permitted prior to current induction, which started the oxidative process. The degradation of the GES–EE2 mixture was monitored through the quantification of the COD present in the samples taken from the reaction medium. The COD removal percentage was determined using Equation (1). The data obtained from both the oxidation tests and the witness tests were analyzed by analysis of variance (ANOVA) with a level of significance $\alpha = 0.05$. Before performing the analysis of variance, the assumptions of normality, homoscedasticity, and independence were evaluated. Under the conditions that gave the highest

percentage of COD removal, additional tests where the two metabolites were monitored using reversed phase-HPLC (RP-HPLC) were performed.

$$\% \text{ Rem [COD]} = 100 * \left(1 - \frac{[\text{COD}]_f}{[\text{COD}]_0} \right) \tag{1}$$

where $[\text{COD}]_f =$ COD after a reaction time and $[\text{COD}]_0 =$ COD at the beginning of the oxidative process.

Witness tests

Witness tests were performed in order to ensure that the removal of COD present in the reaction medium could be attributed to the anodic oxidation and not to other uncontrolled factors, such as adsorption or evaporation. These tests were conducted under the same conditions in which the oxidation of the GES–EE2 mixture was evaluated (medium pH, supporting electrolyte concentration, agitation, darkness, and reaction time), the only difference being that in these tests the system did not receive electric current. During the reaction time of the witness tests, the reaction medium was monitored every 20 min and the residual COD of these samples was quantified.

Determination of the COD

The COD was determined using the closed reflex colorimetric method (APHA 2012). The organic matter was digested at 150 °C during 2 hours using potassium dichromate. The chromium ions produced were measured in a spectrophotometer UV/Vis (Hach DR-6000) at 605 nm.

Chromatographic method

The chromatographic quantification of GES and EE2 active ingredients was based on the method proposed by Nautiyal & Ramakrishna (2014), using RP-HPLC (Flexar Quaternary LC Plataform, Perkin Elmer), equipped with a UV/Vis detector. Metabolite reading was performed at 210 nm. The determination was conducted with a 10-min isocratic program using a mobile phase of acetonitrile:methanol:water (35:15:50), at a flow rate of 1.5 mL min^{-1}, an injection volume of 10 μL and a Hypersil ODS 5 μm column, 4×250 mm, supplied by Agilent Technologies. The characteristic

peak of EE2 is shown at 5.85 min, while the GES peak is observed at 5.38 min (Figure 1).

RESULTS AND DISCUSSION

The type and concentration of the supporting electrolyte, current density, electrode type and material, and pH of the reaction medium are among the main parameters controlling the efficiency of the anodic oxidation (De Amorim *et al.* 2013; Rabaaoui *et al.* 2013). A first set of tests was developed in order to determine, within a group of 27 different treatments, the conditions of pH, supporting electrolyte concentration, and current density supplied to the system, that would lead to the greatest degradation of the GES–EE2 mixture measured as a COD removal percentage (Equation (1)), as well as to evaluate the possible interaction between the factors, i.e., the dependence of the effect of one factor in the presence of the other factors. The slight variation observed in the residual COD concentration quantified in the witness tests did not reach a level of significance ($\alpha = 0.05$, d.f. $= 6$, F $= 0.556$, $p = 0.758$), and thus the COD removal observed in the reaction medium during the degradation tests can be attributed to the anodic oxidation. The results obtained in this first set of tests show that the anodic oxidation is a promising alternative for reducing the concentration of the GES–EE2 mixture in aqueous medium.

Anodic oxidation process

The analysis of variance of the results obtained from the anodic oxidation of the GES–EE2 mixture was performed after verifying the assumptions of normality, homoscedasticity, and independence. This analysis shows that both the current density as well as the pH and concentration of the supporting electrolyte have a significant influence on the oxidative process ($\alpha = 0.05$, d.f. $= 2$, $F_{Na2SO4} = 14.16$, $F_{Current} = 41.71$, $F_{pH} = 36.98$, $p \leq 0.001$ in the three cases). Moreover, it also allowed the observation that there is no interaction between the studied factors ($\alpha = 0.05$, d.f. $= 8$, F $= 26.8$, $p = 0.688$). The COD reduction percentage, which is the parameter used for monitoring the GES–EE2 mixture oxidation ranged from $70.83 \pm 5.87\%$ to $92.11 \pm 5.53\%$ (Table 1). Treatments 6, 15, 24, and 25 showed mixture degradation percentages greater than 90% and, according to the Tukey media comparison test (level of significance $\alpha = 0.05$), there is no significant difference among them. The anodic oxidation on non-active electrodes, such as the BDD electrodes, can be explained through the set of Equations (2)–(4) (Panizza & Cerisola 2009). The process initiates with the oxidation of the water molecule and the consequent generation of the OH free
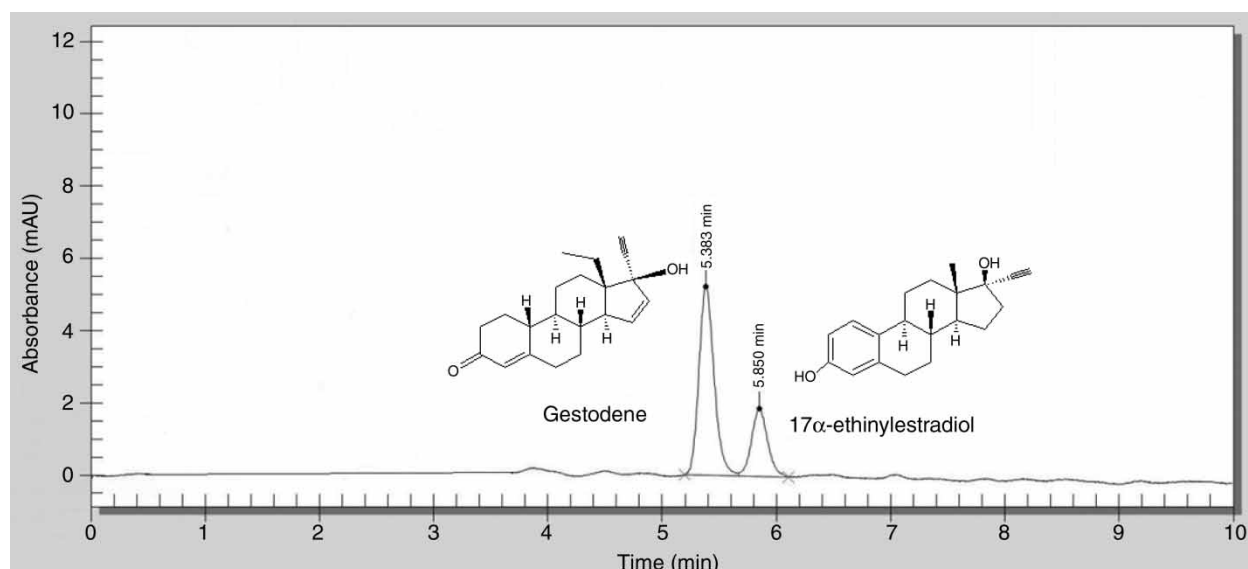

Figure 1 │ Typical chromatogram of the mixture of active ingredients and molecular structure of GES and EE2.

Table 1 | Media comparison through the Tukey test with a level of significance $\alpha = 0.05$

Treatment	[Na$_2$SO$_4$] M	Current mA	pH	COD removal % $\bar{X} \pm \sigma^2$	Tukey $p <$ 0.05
1	0.02	100	2	73.95 ± 3.15	AB
2	0.02	100	3	76.82 ± 2.86	ABCD
3	0.02	100	4	78.93 ± 1.51	ABCDEF
4	0.02	200	2	84.66 ± 3.55	BCDEFGH
5	0.02	200	3	89.90 ± 2.98	GH
6	0.02	200	4	92.11 ± 5.53	H
7	0.02	300	2	86.45 ± 2.85	CDEFGH
8	0.02	300	3	83.31 ± 0.17	BCDEFGH
9	0.02	300	4	82.67 ± 0.86	BCDEFGH
10	0.05	100	2	70.83 ± 5.87	A
11	0.05	100	3	78.19 ± 3.84	ABCDE
12	0.05	100	4	89.01 ± 0.97	FGH
13	0.05	200	2	75.80 ± 3.16	ABC
14	0.05	200	3	85.82 ± 5.44	CDEFGH
15	0.05	200	4	91.00 ± 1.22	H
16	0.05	300	2	71.47 ± 0.83	A
17	0.05	300	3	83.52 ± 5.21	BCDEFGH
18	0.05	300	4	87.43 ± 1.96	DEFGH
19	0.10	100	2	79.29 ± 6.83	ABCDEFG
20	0.10	100	3	74.74 ± 4.91	AB
21	0.10	100	4	89.71 ± 1.43	FGH
22	0.10	200	2	88.39 ± 3.36	EFGH
23	0.10	200	3	87.55 ± 4.04	DEFGH
24	0.10	200	4	91.35 ± 0.92	H
25	0.10	300	2	90.04 ± 0.97	GH
26	0.10	300	3	88.07 ± 1.31	EFGH
27	0.10	300	4	88.52 ± 1.58	EFGH

radical, this radical being the main oxidizing species present in the oxidative process. The ˙OH establishes a weak interaction with the BDD anode surface, allowing an easy reaction with the organic compound present that normally ends in the mineralization of the molecule (Martínez & Ferro 2006).

$$BDD + H_2O \rightarrow BDD[\dot{O}H]_{ads} + H^+ + e^- \qquad (2)$$

$$\begin{aligned}
&\text{Organic compound} + BDD[\dot{O}H]_{ads} \\
&\quad \rightarrow mCO_2 + nH_2O + H^+ + e^- + BDD
\end{aligned} \qquad (3)$$

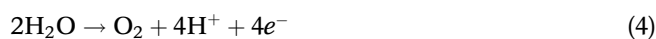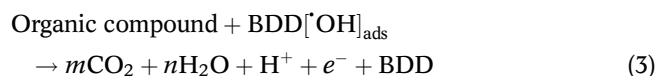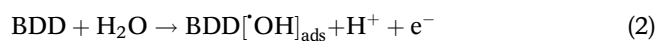$$2H_2O \rightarrow O_2 + 4H^+ + 4e^- \qquad (4)$$

Figure 2 shows COD removal percentages through anodic oxidation. It can be observed that when the density of the current supplied to the system was 16 and 32 mA cm^{-2}, a direct relationship between current density and the efficiency of the anodic oxidation was achieved, i.e., the greater the current density, the greater the percentage of COD removal. This is congruent with the observations made in similar systems studied by others (Frontistis *et al.* 2011; Sun *et al.* 2012). This direct relationship leads to thinking that, under these conditions, the process is controlled by current density which is below its limiting value and the observed behavior can be explained through Equations (2) and (3), where it is noticed that the greater the current supplied to the system, the greater the generation of [˙OH]$_{ads}$ (Equation (2)), and thus, the greater the percentage of removal of the organic compound (Equation (3)). With a current density of 48 mA cm^{-2}, it was observed that the COD removal reached a maximum and then stabilized in some cases, while in other cases, it decreased compared to the results obtained with 32 mA cm^{-2}. This can be attributed to the predominance of collateral or parasitic reactions (Souza *et al.* 2011), such as the oxygen evolution reaction (Equation (4)), that competes with Equation (1). On the other hand, the relationship between efficiency of the anodic oxidation and current density was not observed at 48 mA cm^{-2}. This confirms that, under these conditions, the oxidative system efficiency is not controlled by current density, which indicates that this factor is above or at least close to its limiting value.

In Figure 2, the direct relationship between pH and the removal of COD present in the reaction medium, mainly at low densities (16 to 32 mA cm^{-2}), can be seen, while at 48 mA cm^{-2} this relationship can only be observed when the concentration of the supporting electrolyte in the reaction medium was 0.05 M (8.70 mS cm^{-1}). The analysis of variance showed an interaction between the pH of the reaction medium and the supporting electrolyte ($\alpha = 0.05$, d.f. = 4, F = 4.35, $p = 0.004$). This can be observed in Figure 2, where 0.05 M Na$_2$SO$_4$, independently of the current density applied to the system, permitted a greater effect of the pH on the COD percentage removal. In the same figure, it can be seen that, at a supporting electrolyte concentration of 0.02 M (3.58 mS cm^{-1}), independently of the current density, pH variation does not lead to a significant difference in the removal of the reaction medium. At 0.10 M Na$_2$SO$_4$
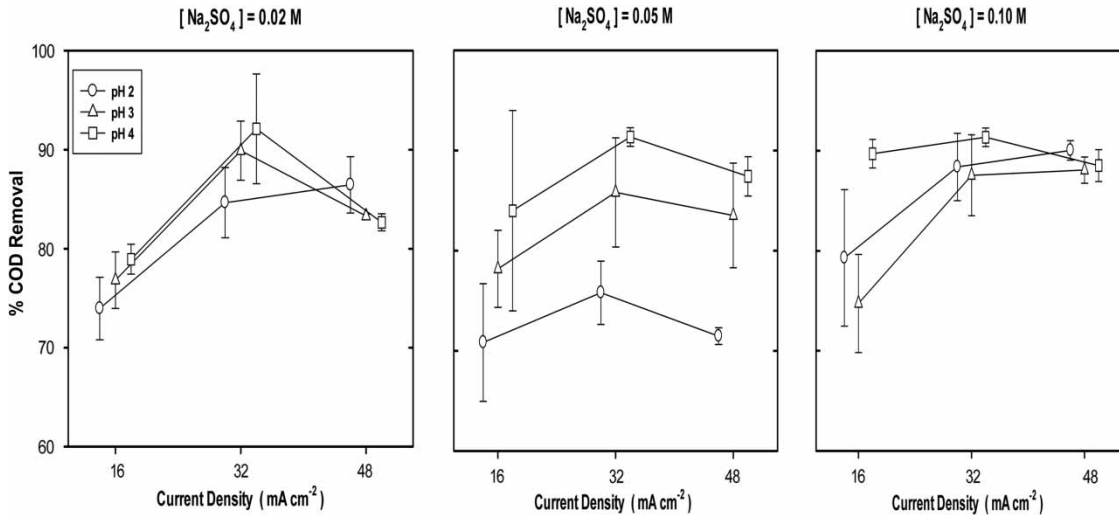
Figure 2 | COD removal in the 27 initial treatments following the structure of a 3^3 factorial design. The initial average concentration was 713.72 mg L^{-1} of COD with a variability of 20.5 mg L^{-1} of COD.

$(16.06 \text{ mS cm}^{-1})$, low current densities show a significant pH effect on the COD removal efficiency, an effect that diminishes with the application of an increased current density to the system.

Reaction kinetics

The analysis of rate reaction was conducted under the conditions of treatment 6, supporting electrolyte concentration of 0.02 M Na_2SO_4, 32 mA cm^{-2} of current density supplied to the system, and pH of the reaction medium adjusted to

4. Under these conditions, the average COD removal reached 92.11% with a variability, expressed as standard deviation, of 5.53%. COD removal was monitored during 120 min. However, after 80 min, no significant difference was observed compared to the sample taken at 100 min ($\alpha = 0.05$, g.l. $= 1$, F $= 0.1$, $p = 0.768$). The profile observed with these samples followed the behavior of a pseudo-first order reaction kinetics (Figure 3(a)), with an apparent kinetic coefficient $k = 0.0321 \text{ min}^{-1}$ (Figure 3(b)). In the case of the degradation of each one of the active ingredients (Figure 4), 15 min were required to achieve the
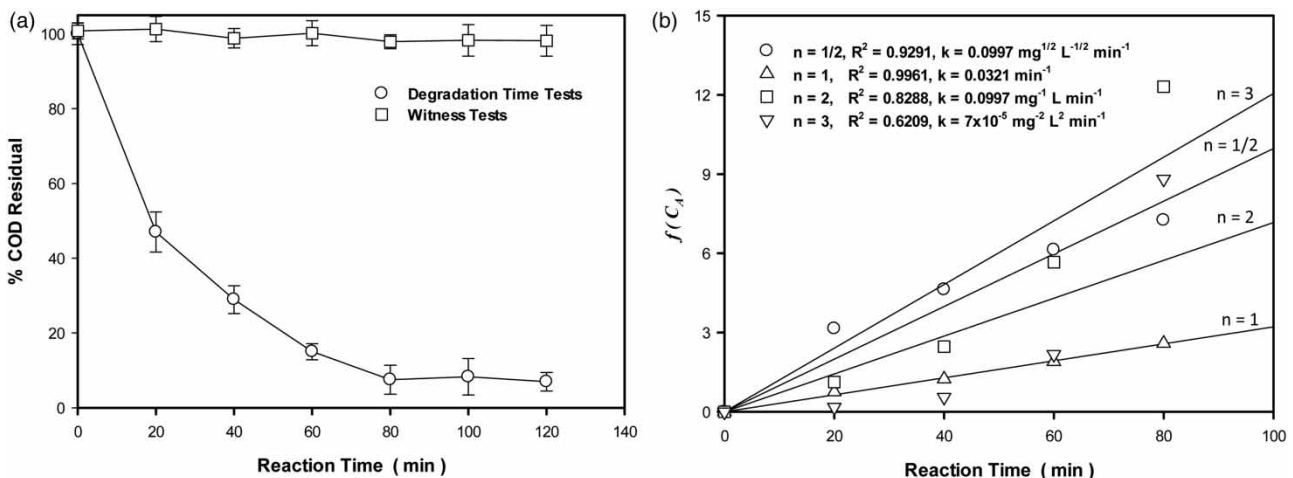

Figure 3 | (a) Profile of COD removal under the conditions of treatment 6. (b) Apparent kinetic coefficient: for $n = \frac{1}{2}$ and $n = 1$, $f(C_A) =$ corresponding; for $n = 2$, the k value is divided by 100 and for $n = 3$, it is divided by 1,000.
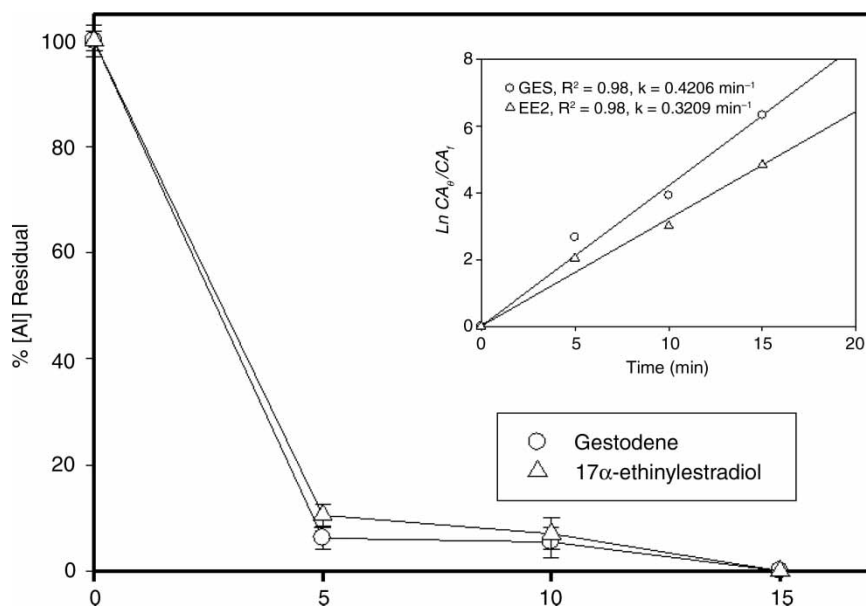
Figure 4 │ Profile of degradation and kinetic coefficient of each one of the active ingredients (GES and EE2).

complete degradation of both molecules. The removal of 93.8% of the initial concentration of GES was reached within the first 5 min, while a similar removal (93%) of EE2 was achieved after 10 min of reaction. The degradation of both active ingredients followed a pseudo-first order reaction profile, the kinetic coefficient of GES was $k = 0.4206$ min^{-1} and that for EE2 was $k = 0.3209$ min^{-1}. Kinetics of the same order were determined by Frontistis et al. (2011) and Zhang et al. (2010) when they degraded one of the components of the mixture (EE2) through a photo-assisted AOP; and by Frontistis & Mantzavinos (2012) when they degraded the same component through sonication. Generally, the AOPs have reported degradation kinetics of this order (Zhang et al. 2010; Sahoo et al. 2012). In the case of the anodic oxidation of the GES–EE2 mixture, a pseudo-first order kinetics was expected because it involves bimolecular reactions, such as the organic oxidation reaction expressed by Equation (3). On the other hand, Equation (2) ensures a high and constant concentration of physisorbed OH free radical on the surface of the BDD electrode, and this meets the main condition for the bimolecular reaction of pseudo-first order: one of the reacting species, the OH free radical, is found in constant and much higher concentration that the second reacting species, the organic contaminants.

Effect of the concentration

It is well known that the initial concentration of the reacting species has an important influence on the kinetics of a reaction. In order to study this effect in the anodic oxidation of the GES–EE2 mixture, three different initial concentrations of the pharmaceutical formulation, 400, 713, and 1,000 mg COD L^{-1} were evaluated under the conditions of treatment 6. The analysis of these results allowed the observation that, independently from the initial concentration, the degradation profile followed the behavior of a pseudo-first order kinetic, which adjusts to the following model $-r_A = kC_A$. In Figure 5(a), the inverse relationship between the initial concentration of the mixture and the kinetic coefficient value can be seen, i.e., $k_{1,000} = 0.0278 < k_{713} = 0.0321 < k_{400} = 0.0372$ min^{-1}. Zhang et al. (2010) observed a similar behavior. According to them, when EE2 was degraded using a photo-assisted system, the increase of the EE2 initial concentration from 0.61 to 1.96 mg L^{-1} led to a decrease of the kinetic coefficient value from 0.091 to 0.0377 min^{-1}. Figure 5(b) shows the profile of COD removal rate vs. time: the highest reaction speeds occur in the first minute of the reaction and, as the reaction time increases, COD removal rate decreases. This was expected because, in pseudo-first order kinetics, the reaction rate depends on the concentration and probability of
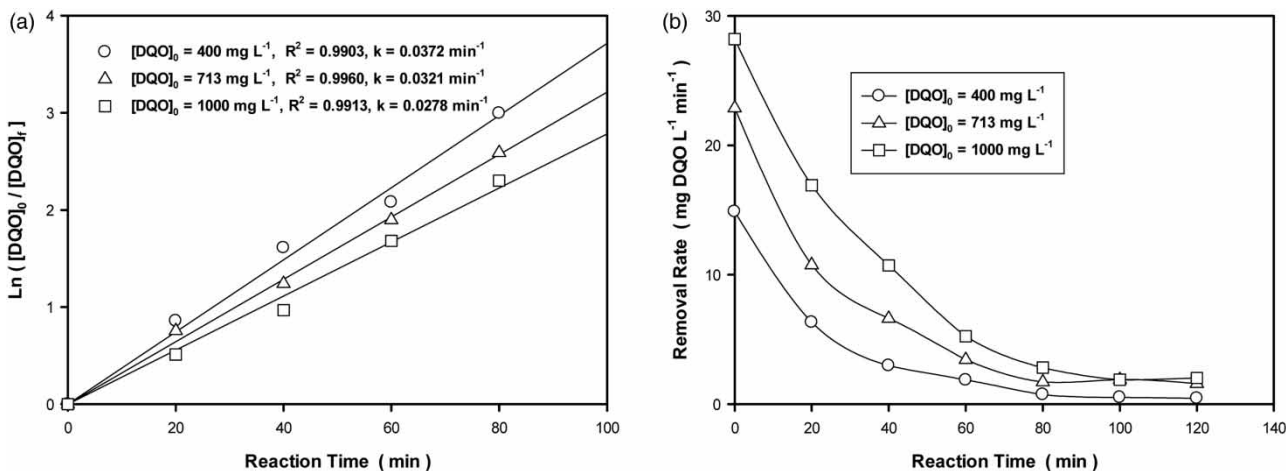
Figure 5 | (a) Apparent kinetic coefficient of the anodic oxidation of the mixture under three different initial concentrations. (b) Effect of the initial concentration of the mixture on the velocity of reaction.

collision between reacting species. With a greater reaction time, this probability decreases since the concentration of the reactants diminishes, which leads to a reduction of the degradation speed.

CONCLUSIONS

The anodic oxidation with BDD electrodes efficiently degraded both the pharmaceutical formulation mixture and the GES and EE2 active ingredients mixture. To degrade at least 93% of the active ingredient in GES and EE2, 5 and 10 min were required, respectively, while 15 min were necessary to achieve a 100% degradation of both molecules. Evidence was presented indicating that the studied factors (pH, supporting electrolyte concentration, and induced current) have a significant influence on the degradation of the GES–EE2 mixture, and follow a pseudo-first order kinetic profile. These results strengthen the arguments according to which anodic oxidation is a technology capable of degrading GES mixed with EE2 in an aqueous medium and can reduce the level of pollution caused by EDCs.

REFERENCES

APHA 2012 *Standard Methods for the Examination of Water and Wastewater*, 22nd edn. American Public Health Association/ American Water Works Association/Water Environment Federation, Washington, DC, USA, pp. 5–20.

Brian, J. V., Harris, C. A., Scholze, M., Kortenkamp, A., Booy, P. & Lamoree, M. 2007 Evidence of estrogenic mixture effects on the reproductive performance of fish. *Environ. Sci. Technol.* **41**, 337–344.

Colombo, R., Ferreira, T. C. R., Alves, S. A. & Lanza, M. R. V. 2011 Photo-Fenton degradation of the insecticide esfenvalerate in aqueous medium using a recirculation flow-through UV photoreactor. *J. Hazard. Mater.* **198**, 370–375.

Czech, B. & Rubinowska, K. 2013 TiO$_2$-assisted photocatalytic degradation of diclofenac, metoprolol, estrone and chloramphenicol as endocrine disruptors in water. *Adsorption* **19**, 619–630.

De Amorim, L. F. M., Cordeiro, D. D., Crispim, B. R., de Souza, G. E., Santos, S. I. & Angnes, L. 2013 Electrochemical remediation of 17α-ethinylestradiol. *J. Chem. Chem. Eng.* **7**, 344–350.

Dickerson, S. M. & Gore, A. C. 2007 Estrogenic environmental endocrine-disrupting chemical effects on reproductive neuroendocrine function and dysfunction across the life cycle. *Rev. Endocr. Metab. Disord.* **8**, 143–159.

Frontistis, Z. & Mantzavinos, D. 2012 Sonodegradation of 17a-ethynylestradiol in environmentally relevant matrices: laboratory-scale kinetic studies. *Ultrason. Sonochem.* **19**, 77–84.

Frontistis, Z., Brebou, C., Venieri, D., Mantzavinosa, D. & Katsaounis, A. 2011 BDD anodic oxidation as tertiary wastewater treatment for the removal of emerging micropollutants, pathogens and organic matter. *J. Chem. Technol. Biotechnol.* **86**, 1233–1236.

Fu, H., Suri, R., Chimchirian, R., Helmig, E. & Constable, R. 2007 Ultrasound-induced destruction of low levels of estrogen hormones in aqueous solutions. *J. Environ. Sci. Technol.* **41**, 5869–5874.

Guedes, M. M., Bila, M. & Márcia, D. 2008 Degradation and estrogenic activity removal of 17β-estradiol and 17α-

ethinylestradiol by ozonation and O_3/H_2O_2. *Sci. Total Environ.* **407**, 105–115.

Liu, Y., Gan, X., Zhou, B., Xiong, B., Li, J., Dong, C., Bai, J. & Cai, W. 2009 Photoelectrocatalytic degradation of tetracycline by highly effective TiO_2 nanopore arrays electrode. *J. Hazard. Mater.* **171**, 678–683.

Liu, Z., Arogo, O. J., Pruden, A. & Knowlton, K. 2011 Occurrence, fate and removal of synthetic oral contraceptives (SOCs) in the natural environment: a review. *Sci. Total Environ.* **409**, 5149–5161.

Martínez-Huitle, C. A. & Ferro, S. 2006 Electrochemical oxidation of organic pollutants for the wastewater treatment: direct and indirect processes. *Chem. Soc. Rev.* **35**, 1324–1340.

Matějíček, D. & Kubáň, V. 2007 High performance liquid chromatography/ion-trap mass spectrometry for separation and simultaneous determination of ethynylestradiol, gestodene, levonorgestrel, cyproterone acetate and desogestrel. *Anal. Chim. Acta.* **588**, 304–315.

Nautiyal, K. & Ramakrishna, K. 2014 Analytical method development and validation for simultaneous determination and quantification of ethinyl estradiol and gestodene in combined tablet dosage form by RP-HPLC. *J. Chem. Pharm. Res.* **6**, 74–80.

Panizza, M. & Cerisola, G. 2009 Direct and mediated anodic oxidation of organic pollutants. *Chem. Rev.* **109**, 6541–6569.

Rabaaoui, N., Moussaoui, Y., Allagui, M. S., Ahmed, B. & Elaloui, E. 2013 Anodic oxidation of nitrobenzene on BDD electrode: variable effects and mechanisms of degradation. *Sep. Purif. Technol.* **107**, 318–323.

Rokhina, E. V., Vattikonda, N. S., Johnson, C. & Suri, R. P. S. 2012 Ozonation of a mixture of estrogens and progestins in

aqueous solution: interpretation of experimental results by computational methods. *Chemosphere* **89**, 1323–1329.

Sahoo, C., Gupta, A. K. & Pillai, I. M. S. 2012 Heterogeneous photocatalysis of real textile wastewater: evaluation of reaction kinetics and characterization. *J. Environ. Sci. Health A* **47**, 2109–2119.

Sirés, I., Oturan, N. & Oturan, M. A. 2010 Electrochemical degradation of β-blockers. Studies on single and multicomponent synthetic aqueous solutions. *Water Res.* **44**, 3109–3120.

Souza, J. P. D., Martínez-Huitle, C. A. & Ribeiro, D. S. 2011 Electrochemical treatment for removing petroleum polycyclic aromatic hydrocarbons (PAHs) from synthetic produced water using a DSA-type anode: preliminary results. *Sustain. Environ. Res.* **21**, 329–335.

Sun, M., Reible, D. D., Lowry, G. V. & Gregory, K. B. 2012 Effect of applied voltage, initial concentration and natural organic matter on sequential reduction/oxidation of nitrobenzene by graphite electrodes. *Environ. Sci. Technol.* **46**, 6174–6181.

Velicu, M. & Suri, R. 2009 Presence of steroid hormones and antibiotics in surface water of agricultural, suburban and mixed-use areas. *Environ. Monit. Assess.* **154**, 349–359.

Zhang, Z., Feng, Y., Liu, Y., Sun, Q., Gao, P. & Ren, N. 2010 Kinetic degradation model and estrogenicity changes of EE2 (17α-ethinylestradiol) in aqueous solution by UV and UV/H_2O_2 technology. *J. Hazard. Mater.* **181**, 1127–1133.

Zhang, H., Zhu, H., Wen, X. & Si, X. 2012 Degradation behavior of 17α-ethinylestradiol by ozonation in the synthetic secondary effluent. *J. Environ. Sci.* **24**, 228–233.