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On the Degradation of 17-β Estradiol Using Boron Doped Diamond Electrodes

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Abstract: This work focuses on the evaluation of the degradation of 17β-estradiol in a mixture of synthetic urine and methanol, trying to determine in which conditions the hormone can be more easily degraded than the urine compounds. This is in the frame of an overall study in which the pre-concentration stage with adsorption/desorption technology is evaluated to improve electrolysis efficiency. Results show that this pollutant can be efficiently removed from mixtures of urine/methanol by electrolysis with diamond electrodes. This removal is simultaneous with the removal of uric acid (used as a model of natural pollutants of urine) and leads to the formation of other organic species that behave as intermediates. This opens the possibility of using a concentration strategy based on the adsorption of pollutants using granular activated carbon and their later desorption in methanol. Despite methanol being a hydroxyl radical scavenger, the electrolysis is found to be very efficient and, in the best case, current charges lower than 7 kAh·m^{-3} were enough to completely deplete the hormone from urine. Increases in the operation current density lead to faster but less efficient removal of the 17β-estradiol, while increases in the operation flowrate do not markedly affect the efficiency in the removal. Degradation of 17β-estradiol is favored with respect to that of uric acid at low current densities and at high flowrates. In those conditions, direct oxidation processes on the surface of the anode are encouraged. This means that these direct processes can have a higher influence on the degradability of the hazardous species and opens the possibility for the development of selective oxidation processes, with a great economic impact on the degradation of the hazardousness of hospitalary wastewater.

Keywords: 17β-estradiol; boron doped diamond; urine; electrolysis; selective oxidation

1. Introduction

Nowadays, the occurrence of emerging synthetic contaminants in natural bodies of water, such as rivers, lakes and groundwater [1–4] represents an urgent problem not only environmentally but more importantly from the health point of view. Many of these compounds enter the environment through urine or faecal matter [5], the treatment of these biological fluids being a point of increasing interest. Within the emerging contaminants, the group of oestrogens, such as estrone, estriol, 17β-estradiol, 17α-ethinylestradiol and mestranol, is an important group of pollutants because many of them have

shown important interferences with the endocrine system, even in the range of concentrations of ng·L^{-1} [6]. Conventional treatment in municipal wastewater treatment plants is not enough to achieve their removal. In fact, only 60% to 80% of the contaminants are eliminated, because such facilities are not currently designed to remove all contaminants that are present in the water and, as a consequence, the contaminants contained in the effluent flow into natural bodies of water [7].

An important example of this kind of pollutants are the hormones used in therapeutic care, which are often considered as endocrinal disruptors due to their high estrogenic activity. Even at very low concentrations (ng·L^{-1}) [8] they are capable of altering the hormonal equilibrium of living beings. Among them, it is worth mentioning oestrogens, like estrone, estradiol, estriol and ethynylestradiol [9,10], which have diverse clinical uses [11–13]. Despite having many advantages, its use also implies risk factors due to its toxicity, which implies certain adverse effects such as cancer, thromboembolic disease, a greater risk of cardiovascular disease [14]. One representative oestrogen is 17β-estradiol, which is considered the strongest natural oestrogen [9]. Different studies have reported the risk of breast, ovarian and endometrial cancer in humans, severe congenital deformities in children [15] and the contribution to male reproductive disorders [16,17]. Their negative effects are not only related to human health but also to the environment. Fish are sensitive to the concentrations of oestrogen in water, even in parts per trillion (ppt) [18]. Thus, a feminization effect has been observed on rainbow trout and fathead minnow in concentrations as low as 0.3 ng·L^{-1} [19]. Likewise, it has been shown that in higher concentrations the risk of larval or embryonic mortality in clearhead icefish (*Protosalanx hyalocranius*) increases by 60% after 23 days of exposure in concentrations of 1 mg·L^{-1} [20], in addition to having the capacity to interrupt the hypothalamic-pituitary-gonadal axis of Argentinian Silverside (*Odontesthes bonariensis*) in concentrations of 350 ng·L^{-1} [21]. It is also related to the increase in cases of hermaphroditic carp [22]. 17β-estradiol has been found very often in surface water close to treatment plants in Europe [23,24].

To remove this pollutant, advanced oxidation technologies should be proposed. This type of oxidation methodology has proved to be capable of destroying most pollutants because of the formation of many oxidant reagents, the most important of which is the hydroxyl radical [25]. Among them, it is worth highlighting ozonation, photolysis, Fenton's oxidation, sonolysis, heterogenous photocatalysis and electro-oxidation [26]. This last technology consists of the application of electrical energy among two electrodes. This electricity promotes the direct oxidation of the pollutants on the surface of the anode and the production of many oxidants [27,28]. Electrodes can be made of a variety of materials, among which the most common are metals (Ti, Pt) and coatings of metals oxides (RuO_2, IrO_2, etc.) [29,30] or boron-doped diamond [31]. The outstanding properties of these diamond coatings have promoted the development of many applications [32–35]. Efficiencies of this technology are only limited by the low concentration of the pollutants. Thus, in operating over a given concentration, current efficiencies near 100% are typically obtained [36,37].

Recently, a new technique was proposed to improve the efficiency of electrolytic processes [38]. It consists of the concentration of pollutants contained in a waste by adsorption onto granular activated carbon and in the later desorption of the pollutants in an appropriate solvent. In fact, the selection of the solvent is critical because pollutants must be highly soluble in the solvent and this should be easily be recovered after treatment. Regarding this point, methanol was selected for its high solvent capacity for many organics but also because it remains almost unmodified during electrolysis [38–41]. For most organic compounds, the adsorption/desorption process allows us to concentrate pollutant even more than one-fold. On the other hand, it has been found that, despite methanol being a well-known radical scavenger, electrolysis in this media can attain the mineralization of organics with efficiencies that are close to those obtained in aqueous media for the same organic concentration. Taking into account the concentration attained by the adsorption/desorption process, and the fact that the kinetic of the electrolysis of wastes fits well to a first order model, it is easy to explain the important increase in the efficiency that can be reached by combining both processes. Anyway, it is important to obtain more

information about the electrolysis of organics in media containing methanol or mixtures of methanol and water.

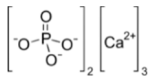
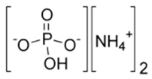
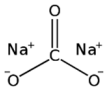
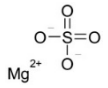
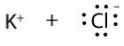
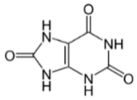
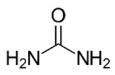
This work focused on the evaluation of the degradation of 17β-estradiol in a mixture of synthetic urine and methanol, trying to determine in which conditions the hormone can be more easily degraded than the urine compounds, because this allows the design of new processes in which the selective removal of the more hazardous compounds can be removed by Advanced Oxidation Processes (AOPs) while more readily degradable organics can be destroyed by the cheaper biological treatments. This research is carried out in the frame of a study in which the pre-concentration stage with adsorption/desorption technology is evaluated. In this work, uric acid is monitored during the treatments in order to compare its degradation with that of the 17β-estradiol. The effect of the two more important operation parameters, flowrate and current density, were evaluated in order to determine the best conditions to produce a higher selectivity in the removal of the hormone.

2. Materials and Methods

Reagents. 17β-estradiol ≥ 98%; *Calcium phosphate* purum p.a., ≥96.0% (calc. as $Ca_3(PO_4)_2$, KT); *Calcium carbonate* BioXtra, ≥99.0%; *Magnesium sulfate* BioReagent, (suitable for cell culture, suitable for insect cell culture); *Potassium chloride* BioXtra, ≥99.0%; Uric acid ≥ 99%, crystalline; *Creatinine anhydrous*, ≥98%; Urea of analytical standard were bought in Sigma Aldrich. Sulfuric acid, 95–97% p.a. EMSURE® ISO and Sodium hydroxide 1 mol·L^{-1} in an aqueous solution were bought in Merck. The 17β-estradiol from Gedeon Richter consisted of 8.1 mL transdermic solution, with 56 sprays per bottle. The deionised water was obtained through a Milli-Q® IQ 7003/7005/7010/7015 water purification system with Elix® EDI technology and UV lamps.

Synthetic urine. In order to carry out the experiment, half the urine was prepared, which comprised of the components detailed in Table 1 [42].

Table 1. Compounds and concentrations present in the synthetic urine.

Name	Structure	Concentration/mg·L^{-1}
Calcium phosphate		28.34
Diammonium phosphate		83.34
Sodium carbonate		166.67
Magnesium sulphate		170
Potassium chloride		1000
Uric acid		50
Creatinine		166.67
Urea		3333.34

Experimental setup. A Diacell® cell equipped with diamond doped with boron (DDB) anode and cathode was used. It was manufactured by Adamant Technologies (Swiss) with an electrodic area of 78.54 cm^2. The diamond coating had a boron content of 500 mg·dm^{-3}, and sp^3/sp^2 217 and

a thickness of 2.83 μm. The cell was connected to a 1 L glass tank were the synthetic waste was recirculated. Operation was in galvanostatic conditions and the current densities were fixed within the range 20–100 $mA \cdot cm^{-2}$.

Characterization of pollutants. 17β-estradiol and uric acid were quantified by an Agilent 1260 Infinity HLPC (Agilent Technologies). An Eclipse Plus C-18 column (4.6 mm × 100 mm; 3.5 μm) was used. Each sample was filtered with Agilent brand 0.2 μm nylon acrodiscs before being injected. For 17β-estradiol, we used 0.4 $mL \cdot min^{-1}$ of 70% acetonitrile and 30% acidified water with formic acid at 0.1% and the wavelength was 280 nm. The injection volume was 20 μL. For the uric acid, we used 1 $mL \cdot min^{-1}$ of 2% acetonitrile and 98% acidified water with formic acid at 0.1% with an injection volume of 10 μL [42].

Calculation of current efficiency. The faradaic efficiencies were calculated to all the cases according reaction (1) and following the Equation (2):

$$C_{18}H_{24}O_2 + 34\ H_2O \rightarrow 18\ CO_2 + 92\ H^+ + 92\ e^- \quad (1)$$

$$E_f(\%) = \frac{F \cdot \Sigma[\Delta n \cdot z]}{I \cdot \Delta t} \cdot 100 \quad (2)$$

where F is the Faraday constant (96,487 C/mol), Δn is the moles of 17β-estradiol removed at time Δt, z is the number of electrons exchanged (92) and I is the current applied.

3. Results and Discussion

Figure 1 shows the changes in the concentration of 17β-estradiol and uric acid in two different treatment tests carried out under the same operation conditions and with the same concentration of these two species. This figure also shows the total amount of intermediates measured over these two tests, which was estimated as the sum of the areas of all intermediates detected by chromatography.

As it can be observed in Figure 1a, uric acid and 17β-estradiol are electrolytically degraded and transformed into other species (summarized in part b of the figure) that behave as intermediates, with a maximum concentration at 200 min, at the moment in which the two main initial organics contained in the waste are removed. From that moment, the concentration of these intermediates starts to decrease. According to literature [43], these may correspond to 2-hydroxyestradiol, 6-hydroxy-estradiol or 17b-dihydroxy-1,4-estradieno-3-one. After that, they can be oxidized to carboxylic acid and then to carbon dioxide. On the other hand, measured concentrations of the three outputs (17β-estradiol, uric acid and summarized intermediates) in the two tests are almost overlapped, which indicates a great reproducibility of the experimental results. Hence, the electrolysis with boron doped diamond anodes attains the successful removal of the hormone 17β-estradiol, even in a complex media such as synthetic urine mixed with methanol, in which methanol may act as a hydroxyl radical scavenger [39–41]. Likewise, it is important to observe how the oxidation products do not behave as final product but as reaction intermediates. At this point, it is important to point out that three main peaks were monitored during the tests and they had the same dynamic response. This removal of organics in methanol media without the formation of stable organic compounds has been previously observed for other species such as the hormone progesterone or the chlorinated organics perchloroethylene and clopyralid [38–41]. In fact, it is important to state the feasibility of the process because the absence of intermediates measured by HPLC indicates mineralization of the raw molecules of pollutant contained in the waste. During the 17β-estradiol degradation process, the degradation can be divided into two parts. The first stage (along the first 20 min) is the most important because it is when the highest concentration of 17β-estradiol is degraded. Afterwards, a slightly different behaviour with degradation at a lower rate can be observed. This could be explained by considering that, due to the very limited solubility of 17β-estradiol, two different species are contained in the waste: micelles containing the hormone and solubilized 17β-estradiol. The first stage may correspond to the degradation of the soluble fraction. It can also be explained because of the competition in the degradation of 17β-estradiol

with intermediates formed. Thus, the decrease in the rate may be explained by the easier oxidation of reaction intermediates in comparison with the raw 17β-estradiol. These two stages are not observed in the case of the uric acid, which has a much higher solubility in water or a much lower competition in the oxidation of uric acid with respect to the intermediates formed in the reaction media.

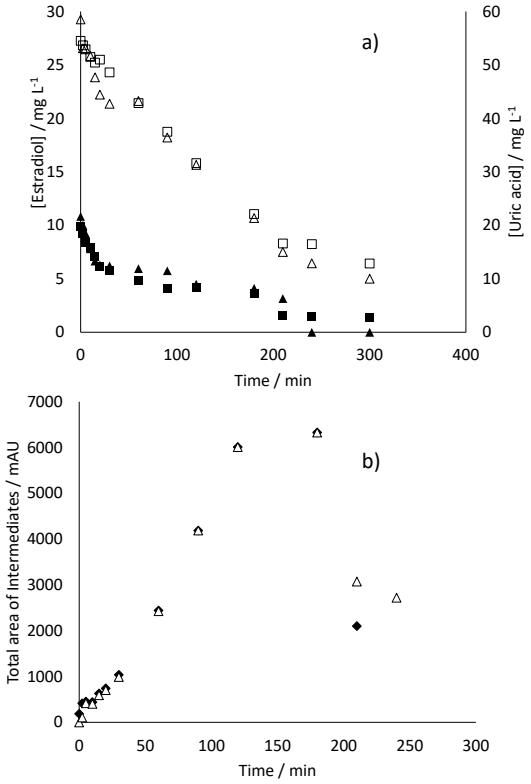


Figure 1. (**a**) Changes in the concentration of 17β-estradiol (black symbols) and uric acid (white symbols) during the electrolysis with Boron Doped Diamond (BDD) anodes of 10 mg·L^{-1} of 17β-estradiol in methanol-urine solutions at 20 mA·cm^{-2} of current density. Flowrate: (▲, △) 8.66 mL·s^{-1}; (■, □) 10.166 mL·s^{-1}. (**b**) Totalized chromatographic area of reaction intermediates during the electrolysis of 10 mg·L^{-1} 17β-estradiol in methanol-urine solutions at 20 mA·cm^{-2} of current density. Flowrate: (♦) 8.66 mL·s^{-1}; (△) 10.166 mL·s^{-1}.

The direct comparison of these results with previous works reported in the literature is not an easy task due to the different nature of the reaction media tested (water vs. urine/methanol) as well as the different reaction conditions. Murugananthan et al., 2007 [44] demonstrated the superiority of diamond electrodes over Pt and glassy carbon anodes to oxidize 17β-estradiol in sulfate media. Pereira et al., 2011 [43] demonstrated that 17β-estradiol can be efficiently removed from water through ozonation, but it leads to the formation of byproducts tan can pose a risk not only to drinking water consumers but also to the environment. More recently, Moraes et al., 2016 [29] synthetized a new electrode for the photoelectrochemical removal of 17b-estradiol from water using ruthenium oxide nanoparticles supported on reduced graphene oxide, obtaining up to 92.2% of removal after 60 min of photo-electrocatalytic treatment.

Figures 2 and 3 report results from the tests carried out to evaluate the effect of the current density, which is expected to be the main operation parameter in an electrolytic galvanostatic process. This parameter was evaluated within the range 20 to 100 mA·cm^{-2}, which is the typical range of current densities used in environmental applications. The lowest value corresponds to soft oxidation conditions in which the formation of hydroxyl radicals is not promoted [45]. Conversely, for the highest current density, this radical mediated oxidation is expected to be the primary degradation mechanism, according to results discussed in previous works [46]. Nevertheless, the presence of methanol (which is

a well-known hydroxyl radical scavenger) [47] may make this process non relevant. The main figures show the changes observed versus the applied current charge, while the onsets focus on the changes with time. Although both changes are directly related, the first is associated with the efficiency of the process, that is, with the charge used in the studied process, while the second indicates the rate of the degradation.

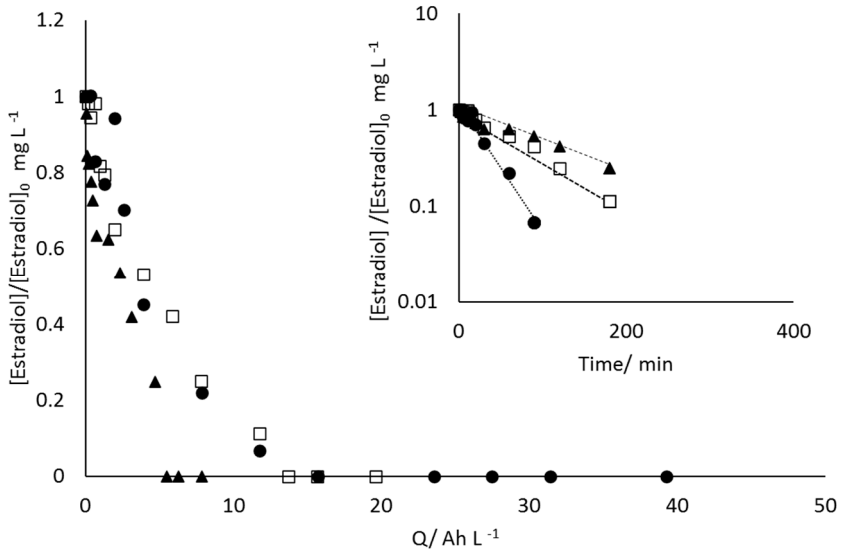


Figure 2. Changes in the concentration of 17β-estradiol during the electrolysis of synthetic urine/methanol system with BDD anodes at different current densities and at 6.77 mL·s^{-1} of flowrate. Current density: (▲) 20 mA·cm^{-2}; (□) 50 mA·cm^{-2}; (●) 100 mA·cm^{-2}.

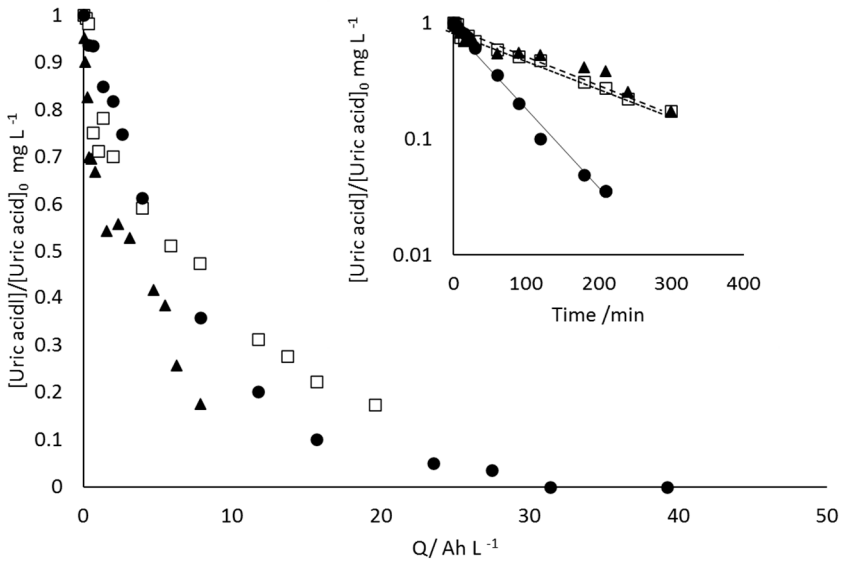


Figure 3. Changes in the concentration of uric acid during the electrolysis of synthetic urine/methanol system with BDD anodes at different current densities and at 6.77 mL·s^{-1} of flowrate. Current density: (▲) 20 mA·cm^{-2}; (□) 50 mA·cm^{-2}; (●) 100 mA·cm^{-2}.

As seen, the removals of uric acid and 17β-estradiol are observed in the three tests carried out; the higher the applied current density, the higher the rate of the degradation of uric acid and 17β-estradiol. However, this is not seen for the efficiency, which is larger at lower current densities (Figure 4). This indicates that unproductive side reactions are being promoted at larger current densities, in particular the supporting media decomposition. Anyway, it can be seen that in the worst case,

total removal of 17β-estradiol is obtained for electric charge passes as low as 15 kAh·m^{-3}, which can decrease down to even less than half when applying lower current densities. Electric charges required for the depletion of uric acid are higher and this difference in the oxidazability points to new areas of research into methods that allow the selective oxidation of the most hazardous materials from urine. Thus, the effluents of these technologies can be combined with a later treatment that uses cheaper biological treatments.

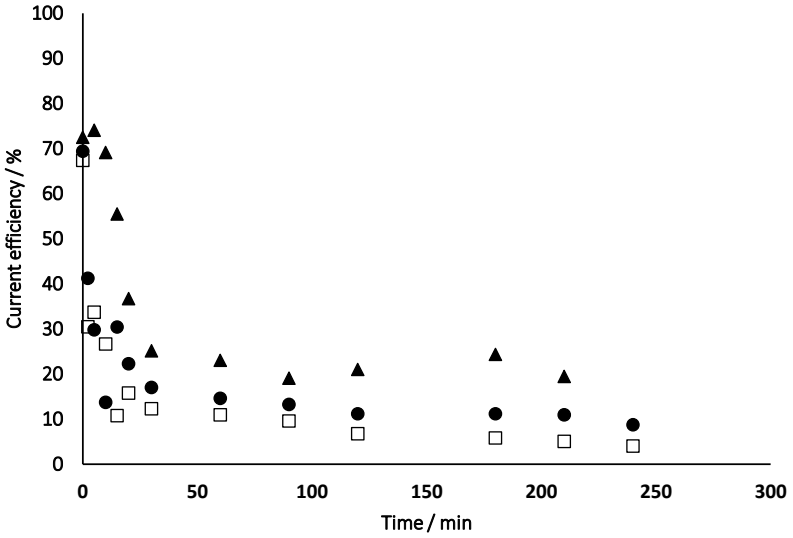


Figure 4. Changes in the current efficiency during the electrolysis of 17β-estradiol in synthetic urine/methanol system with BDD anodes at different current densities and at 6.77 mL·s^{-1} of flowrate. Current density: (▲) 20 mA·cm^{-2}; (□) 50 mA·cm^{-2}; (●) 100 mA·cm^{-2}.

The maximum concentration of intermediates produced in the three tests, measured as total chromatographic areas, depends on the current density being 3 and 6 times higher from the electrolysis performed at 50 mA·cm^{-2} and 20 mA·cm^{-2} as compared with the electrolysis carried out at 100 mA·cm^{-2}. Hence, the concentrations of intermediates decrease with the increase in the current density, indicating a more vigorous reaction with the increase in the current density, which lead to the mineralization of the intermediates once formed in the hasher oxidations conditions.

Another important parameter in the electrochemical oxidation processes is the flowrate, because it is expected to affect not only the residence time in the electrochemical cell (and hence the contact time between waste and electrodes) but also the hydrodynamic conditions, which in turn are expected to affect to mass transport limitations. Figure 4 shows the influence on the degradation of 17β-estradiol and uric acid of this parameter, with tests carried out using fluxes of 6.77 mL·s^{-1}, 11.66 mL·s^{-1} and 12.83 mL·s^{-1} at a current density of 50 mA·cm^{-2}.

As observed in Figure 5, it is evident that, despite applying different fluxes, the influence of the flux is not as significant as that of the current density during the degradation process, as shown by the similarity of the degradation in each of the three experiments, both for the uric acid and the 17β-estradiol. This means that, although the concentrations of pollutants are rather low and, thus, direct electrochemical oxidation processes on the surface of the anode can be mass transport controlled, mediated oxidations control the overall rate of the process. At this point, it is important to bear in mind that the large amount of salts contained in the synthetic urine can help to promote a large variety of oxidants, which can contribute to the efficient removal of the pollutants.

For a better understanding of the process, experimental data were fitted to first order kinetic models. In electrolytic processes, first order kinetics can be explained in terms of mass transfer-controlled processes or in terms of processes controlled by mediated oxidation in which the produced oxidants

reach a pseudo stationary, which means that the expected second order kinetic model is transformed into a pseudo-first kinetic model, as shown in Equation (3).

$$r = (k \times [\text{oxidant}]ss) \times [\text{pollutant}] = k' \times [\text{pollutant}] \quad (3)$$

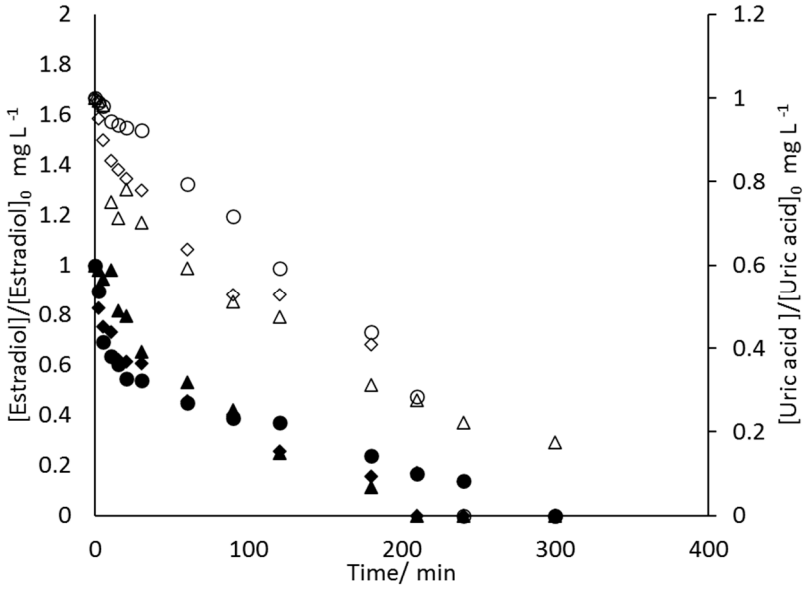


Figure 5. Changes in the concentration of 17β-estradiol (black symbols) and uric acid (white symbols) during the electrolysis of 20 mg·L^{-1} of 17β-estradiol in synthetic urine/methanol media with BDD anodes 50 mA·cm^{-2} of current density and at different flowrates: (▲, △) 6.77 mL·s^{-1}; (●, ○) 11.66 mL·s^{-1}; (♦, ◊) 12.833 mL·s^{-1}.

The almost nil influence of the flowrate observed (despite doubling its value) indicates that for this experimental system the primary mechanisms should be the second. Mass balances in the discontinuous setup used in this work are shown in Equations (4) and (5) for 17β-estradiol and uric acid, respectively, where k_1 and k_2 are the kinetic constant of the degradation of 17β-estradiol and uric acid, respectively.

$$\frac{d\,[17\beta - \text{estradiol}]}{dt} = -k_1 \times [17\beta - \text{estradiol}] \quad (4)$$

$$\frac{d\,[\text{uric acid}]}{dt} = -k_1 \times [\text{uric acid}] \quad (5)$$

Experimental data were fitted to these balances. In the case of 17β-estradiol, not one but 2 slopes were found, namely k_1 and k_1' (with an average constant named as k_{1m}). The first part corresponds to the first 20 min in which competition in the degradation of 17β-estradiol with that of intermediates is negligible because of the absence of significant concentrations of intermediates. The second corresponds to the stage in which intermediates are contained in significant concentrations and hence there is a competition between the oxidation of the different organics by the electrogenerated mediators. In the case of uric acid, only one constant is necessary to explain the full range.

Figure 6 compares the oxidazability of 17β-estradiol and uric acid by showing the effect on the ratio k_1/k_2 of the operation conditions evaluated. This ratio between kinetic constants does not provide information about the rate but about which of the two pollutants is more oxidizable at given conditions. As seen, lower current densities favour the oxidation of 17β-estradiol respect to uric acid. This higher oxidazability is more important when there are no intermediates in the reaction media (k_1) and the effect is buffered for longer times (k_{1m}). This means that, by controlling the current density, a certain selectivity can be attained during the treatment of urine polluted with this hormone, which may

become a great advantage, especially if the purpose of the application of the electrochemical technology is the reduction of the hazardousness of urine, previous to the application of a cheaper technology, such as the biological treatment.

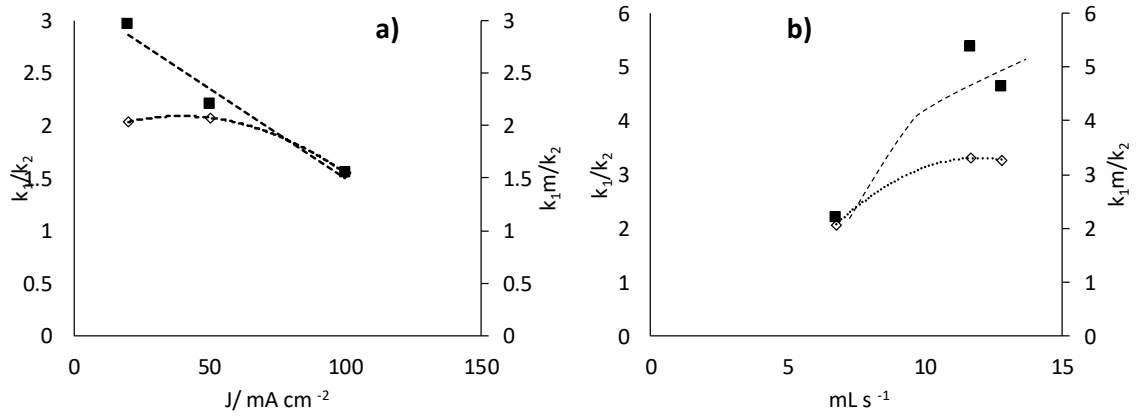


Figure 6. Comparison of the oxidazability of 17β-estradiol and uric acid by showing the trends of the ratios k_1/k_2 (■) and k_{1m}/k_2 (◊) as function of current density (**a**) and flowrate (**b**).

Regarding the influence of the flowrate on the ratio k_1/k_2, it can be seen that it is even more important than that of current density, because the degradation of the hormone at high flowrates is favoured. This is important because the conditions in which the hormone is preferentially oxidized are those in which direct electrolysis is favoured with respect to the mediated process (higher mass transport coefficient and low current density). This points out that although mediated oxidation is the primary mechanism in the degradation of both, the hormone and the uric acid, the selectivity is favoured when the pure direct electrochemical process is promoted. Such effects are more clearly seen for the initial moments, in which the competition in the oxidation with intermediates is not very important. Conversely, this effect is diluted at longer reaction times when the concentration of intermediates formed in the reaction media increases significantly.

Figure 7 shows the changes in the concentration of protons generated during the electrochemical process. As seen, this concentration increases in all experiments that are associated with the production of carboxylic acids by degradation of the complex aromatic species [48,49]. Obviously, it is more important at higher current densities because of the higher progress of the reaction and is hardly influenced by flowrate, because the electrolysis of the charge passed and, hence, the oxidation capacity is only driven by the current density.

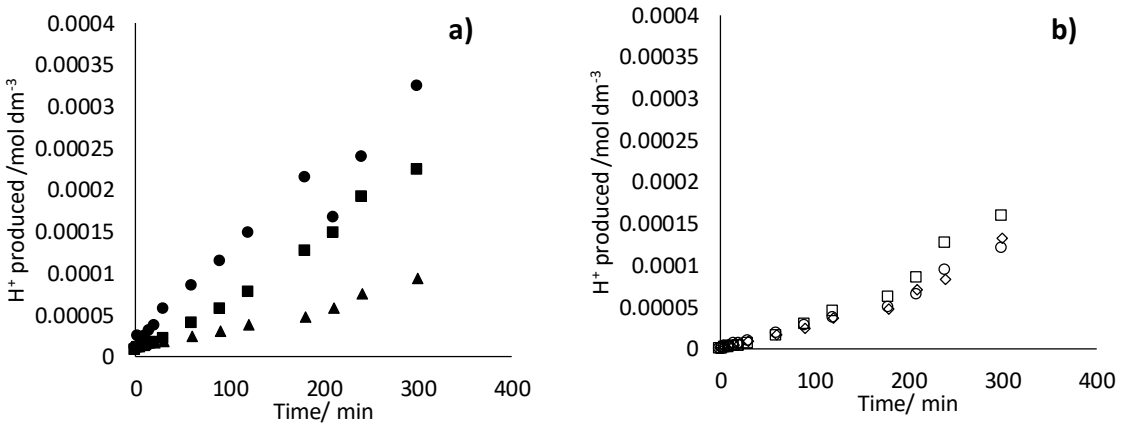


Figure 7. (**a**) Concentration of protons produced during the electrolytic tests at 6.77 mL·s^{-1} of flowrate. Current density: (▲) 20 mA·cm^{-2}; (■) 50 mA·cm^{-2}; (•) 100 mA·cm^{-2}. (**b**) Concentration of protons produced during the electrolytic tests at 50 mA·cm^{-2} of current density. Flowrate: (□) 10.166 mL·s^{-1}; (○) 11.66 mL·s^{-1}; (◊) 12.833 mL·s^{-1}.

4. Conclusions

From this work, the following conclusions can be drawn:

- 17β-estradiol can be efficiently destroyed from mixtures urine/methanol. This removal is simultaneous with the removal of uric acid and leads to the formation of other organic species that behave as intermediates. This opens the possibility of using a concentration strategy based on the adsorption of pollutants using granular activated carbon and their later desorption in methanol, at a much higher concentration. Despite methanol being a well-known radical scavenger, the electrolysis is found to be very efficient and, in the best case, current charge lower than 7 kAh·m^{-3} is enough to completely deplete the hormone from urine.
- Increases in the operation current density lead to faster but less efficient removal of the 17β-estradiol. Increases in the operation flowrate do not markedly affect the efficiency in the removal, indicating that the process is not mass transport controlled and that mediated oxidation plays a very important role.
- Degradation of 17β-estradiol and uric acid can fit first order models. However, in the case of 17β-estradiol, two zones are clearly discerned. In the first the removal is faster and it can be explained in terms of the lack of competition with the oxidation of intermediates or, alternatively/simultaneously, with the oxidation of the solubilized 17β-estradiol as it is contained in solution in the form of micelles and solubilized.
- Degradation of 17β-estradiol is favoured with respect to that of uric acid at low current densities and at high flowrates. In those conditions, direct oxidation processes on the surface of the anode are promoted. This means that these direct processes can have a higher influence on the degradability of the hazardous species and opens the possibility for the development of selective oxidation processes, with a great economic impact on the degradation of the hazardousness of hospitalary wastewater.

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