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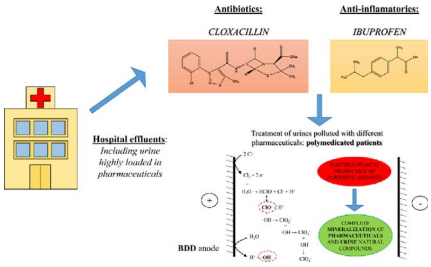
# Removal of pharmaceuticals from the urine of polymedicated patients: A first approach

Salvador Cotillas[a], Engracia Lacasa[a], Cristina Sáez[b], Pablo Cañizares[b], Manuel A. Rodrigo[b,*]

[a] Department of Chemical Engineering, School of Industrial Engineering, University of Castilla-La Mancha, Avenida de España S/N, 02071 Albacete, Spain
[b] Department of Chemical Engineering, Faculty of Chemical Sciences and Technologies, University of Castilla-La Mancha, Avenida Camilo José Cela 12, 13005 Ciudad Real, Spain

## GRAPHICAL ABSTRACT

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## ABSTRACT

The electrolysis with diamond anodes of synthetic urines containing different concentrations of ibuprofen and cloxacillin is evaluated in this work, with the aim of determining if this technology is effective in the mineralization of both species in urine matrix and the main characteristics of the competitive oxidation among these two products and the natural organic compounds contained in urine (uric acid, creatinine and urea). Results point out that electrolytic technology can mineralize all organic contained in the urine very efficiently and that oxidation of the two pharmaceuticals is faster than that of the natural products contained in urine, opening the possibility of a selective treatment of the urine up to the point in which it can be merged safely with domestic wastewater without generating a negative impact on environment. Occurrence of perchlorate is the main drawback of this technology, although its impact is not believed to be as serious as the impact of the pharmaceuticals on environment.

## 1. Introduction

Over the last two decades, a great number of works dealing with the applications of diamond coatings on the electrolysis of wastewater have been published [1]. They have pointed out the outstanding performance of this material as anode, clearly reflected on a very high oxidation efficiency and the absence of refractory species. These characteristics have been explained in terms of the combination of different oxidation mechanisms, which involved not only hydroxyl radicals oxidation but also other mediated oxidation pathways throughout oxidants formed from salts contained in the waste (peroxosulfates, peroxophosphates, peroxocarbonates, etc.). Most of these species can be activated chemically, electrochemically and/or by irradiation of UV light or ultrasounds resulting in a very powerful cocktail of oxidants [2].

Use of this technology for the treatment of small amounts of especially difficult-to-treat wastes is becoming a relevant application, as it is also the disinfection of swimming pools or spas, in which many

* Corresponding author.
*E-mail addresses:* manuel.rodrigo@uclm.es (S. Cotillas), manuel.rodrigo@uclm.es (M.A. Rodrigo).

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companies are currently focusing on their business model. Treatment of soil flushing or washing fluids is also an important potential application [3]. Production of oxidants seems also to be a good possibility, although it is still under commercial evaluation [4]. It is also intended to use this technology in disinfection of human supplies for small populations, although the strict regulation about the quality of this type of water makes necessary to carry out more work in order to optimize this application [5].

In the recent years, a new concern has appeared which may lead to a new application of diamond electrolytic technology: the treatment of hospital wastewaters before being merged with the domestic wastewater in the municipal sewers. A success in this treatment is a challenge, because it may help to prevent the appearance of pharmaceutical persistent organic pollutants (POPs) in the environment. In addition, it will also contribute to eliminate pathogens more efficiently, in particular those associated to resistances to antibiotics, which are needed to be prevented from environment, if the efficiency of these medicines is aimed to be maintained in the near future. In hospital wastewaters, and more particularly in urine, both pharmaceuticals and pathogens are more concentrated and hence their treatment is much more efficient. This is because most AOPs, including electrolysis with diamond, follows first order kinetics, which are known to lead to more efficient treatments as the raw wastes are more contaminated [6].

Degradation of organics contained in urine has been faced scarcely in the literature with different aims (disinfection, reclaiming, etc.) [7,8] and even nowadays there are some works that aim to obtain energy from urine using microbial fuel cells [9–12]. In this context, treatment by electrolysis with diamond anodes of raw synthetic urines was faced in previous works, one of them of our group [13]. This work demonstrated the technological viability of the process and it pointed out the higher mineralization efficiency of this technology as compared to the electrolysis with other electrodes such as MMO (mixed metal oxides) coatings [14]. However, not all the results produced good news and, unfortunately, they also indicated the formation of chlorates and perchlorates as the main technological drawback. These results are in agreement with those obtained in research works focused on the degradation of pharmaceuticals from synthetic and industrial wastes [15–20].

This paper focuses again on synthetic urine, but now we want to concentrate on a different and really important problem: the treatment of the urine excreted by polymedicated patients. As the real urine is a very complex matrix, which changing ratios between pollutants, we are focusing again on the same synthetic medium, well characterized in the previous works. The main novelty of this manuscript is the evaluation of the competing oxidation of two pharmaceuticals in a matrix containing also urea, uric acid and creatinine. It is true that urine of polymedicated patients does not only contain the surplus raw pharmaceutical species but it also contains metabolites. However, we consider this work as a first step in our way to obtain a technological process capable of treating urines of hospital patients before being discharged into municipal sewers, giving change to pathogens and hazardous emerging pollutants to disperse into the environment producing very dangerous effects such as the appearing of new superbacteria. Results will also help to face the important problem of oxidation competition between the different organics.

## 2. Materials and methods

### 2.1. Experimental procedure

Electrolysis experiments were carried out in a single compartment electrochemical cell working under batch-operation mode [21]. Circular boron doped diamond (BDD) plates (purchased from WaterDiam in France, formerly Adamant Technologies) with a geometric area of 78 $cm^2$ were used as electrodes, and the inter-electrode gap between both electrodes was 9 mm. The same BDD electrode was used as anode for all the tests carried out with a boron content of 500 mg $dm^{-3}$. A Delta Electronika ES030-10 power supply (0–30 V, 0–10 A) provided the electric current. Details are given elsewhere [13]. All experiments were carried out under galvanostatic conditions and the current densities applied were 100 and 1000 A $m^{-2}$. The synthetic urine was stored in a glass tank (1 $dm^3$). Its formulation was also proposed in a previous work [13] and it contained 3333.34 mg $dm^{-3}$ of urea, 166.67 mg $dm^{-3}$ of creatinine and 50.00 mg $dm^{-3}$ of uric acid. This composition is typically found in hospital effluents where the concentration of urine organic compounds is diluted with water from domestic activities in these facilities. In this case, it was enriched with ibuprofen (IBP) and cloxacillin (CLX) in two different mass ratios: synthetic urine 1 ($su_1$), with 10.00 mg $dm^{-3}$ of CLX and 1.00 mg $dm^{-3}$ of IBP, and synthetic urine 2 ($su_2$), with 1.00 mg $dm^{-3}$ of CLX and 10.00 mg $dm^{-3}$ of IBP. These low concentrations of organics have been selected taking into account that patients cannot completely metabolize pharmaceuticals.

### 2.2. Analysis

High performance liquid chromatography was used to determine the concentration of different organics using an Agilent 1200 series coupled a DAD detector. A ZORBAX Eclipse Plus C18 analytical column was used and its temperature was maintained at 25 °C. The mobile phase consisted of 2% acetonitrile/98% aqueous solution with 0.1% of formic acid, applying a flow rate of 1.0 $cm^3$ $min^{-1}$, an injection volume of 10 μL and a DAD detection wavelength of 292 nm to determine uric acid (retention time: 0.78 min). In the case of pharmaceuticals determination, the mobile phase consisted of 64% phosphate buffer ($KH_2PO_4$ 0.025 M)/27% acetonitrile/9% methanol for the detection of cloxacillin. The flow rate was 0.6 $cm^3$ $min^{-1}$, the injection volume was 20 μL and the DAD detection wavelength was 225 nm (retention time: 5.70 min). On the other hand, the mobile phase for the determination of ibuprofen consisted of 60% acetonitrile/40% aqueous solution with 0.1% of formic acid. A flow rate of 0.8 $cm^3$ $min^{-1}$ and a DAD detection of 200 nm were used. The injection volume was 20 μL (retention time: 4.70 min).

The urea concentration was determined by a spectrophotometric method using the Cary Series UV–Vis Spectrophotometer (Agilent Technologies). This method is based on the yellow-green color produced when p-dimethylaminobenzaldehyde is added to urea in dilute hydrochloric acid solution [22].

Ions (nitrite, nitrate, ammonium, chlorate and perchlorate) concentrations were measured by ion chromatography using a Metrohm 930 Compact IC Flex coupled to a conductivity detector. A Metrosep A Supp 7 column was used to determine anions, using a mobile phase consisting of 85:15 v/v 3.6 mM $Na_2CO_3$/acetone with a flow rate of 0.8 $cm^3$ $min^{-1}$. In addition, a Metrosep A Supp 4 column was used to analyze cations, using a mobile phase consisting of 1.7 mM $HNO_3$ and 1.7 mM 2,6-pyridinedicarboxylic acid with a flow rate of 0.9 $cm^3$ $min^{-1}$. The temperature of the oven was 45 and 30 °C for the determination of anions and cations, respectively. The volume injection was 20 μL. The same system of cations determination was used for the quantification of creatinine concentration.

TOC concentration was monitored using a Multi N/C 3100 Analytik Jena analyzer. Hypochlorite ion was analyzed by titration with 0.001 M $As_2O_3$ in 2 M NaOH [23,24]. Oxidants were determined iodometrically according to Kolthoff & Carr [25]. The pH and conductivity were measured using a CRISON pH25 + and CRISON CM35 +, respectively.

The intermediates generated from the organic products were extracted with ethyl acetate within a ratio pollutant/solvent of 0.6 w/w. Then, both phases were stirred using a vortex mixer during 5 min and after that, samples were centrifuged during 15 min at 4000 rpm [26]. The organic phase was analyzed by GC–MS using a Thermo Scientific DSQ II Series Single Quadrupole GC–MS with a NIST05-MS library. The column was a polar TR-WAXMS (30 m × 0.25 mm × 0.25 μm). The