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# Anodic oxidation of ketoprofen on boron-doped diamond (BDD) electrodes. Role of operative parameters

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ABSTRACT

Electrochemical oxidation is a promising technology to treatment of bio-refractory compounds. Anodic oxidation of Ketoprofen, a representative endocrine disrupting chemical, was carried out using boron-doped diamond (BDD) electrodes at galvanostatic mode. A design of experiments procedure has been carried out in order to optimize the process and study the interaction between the studied variables: pH, current ($I$), supporting electrolyte concentration, $Na_2SO_4$, and solution flow rate ($Q_v$). The influence of current was the greatest in studied variables, the second one was the salt concentration and the third one was the flow rate. The fourth one, pH, does not present significant influence inside the region of the central composite orthogonal and rotatable design. ANOVA test reported significant for four of the fourteen involved variables. An optimum ketoprofen degradation, $X_K$, of 100% was found at pH 3.99, $Q_v = 1.42\ cm^3\ min^{-1}$, current density equal to $235\ mA\ cm^{-2}$ and a supporting electrolyte concentration equal to $0.5\ mol\ L^{-1}$.



## 1. Introduction

Pharmaceuticals compounds (PCs) have emerged as a novel class of pollutants because of their potential adverse impacts on human health and the environment even at trace levels. Of special concerns are those that have been found to be resistant in water and wastewater treatment processes [1–3]. In these concerns nonsteroidal anti-inflammatory drugs (NSAID) are paid more attention to environmental scientists due to their large consumption in terms of thousands of tons annually for therapeutic purposes; as anti-inflammatory, analgesic or antipyretic.

Ketoprofen (2-(3-benzoylphenyl)-propanoic acid), chemical formula $C_{16}H_{14}O_3$ molecular formula (see Fig. 1) and CAS number 22071-15-4 is a type of NSAID extensively used as non-prescription drug, which has been frequently detected in wastewater treatment plant (WWTP) effluent, surface water, groundwater, and drinking water [4,5]. After intake of ketoprofen in humans, it is primarily metabolized by acyl glucuronidation and subsequently excreted in the urine for more than 80% of the given doses [6]. Once glucuronide conjugates reached wastewater treatment plants (WWTPs), they can be cleaved by enzymatic processes releasing ketoprofen. Several studies have demonstrated that biodegradation of ketoprofen in WWTP was limited. The removal efficiencies of ketoprofen in WWTPs were reported by several authors, ranging from 37% to almost 100% [7,8]. Results obtained by Quintana et al. [9] using activated sludge in aerobic conditions indicated that ketoprofen (in a concentration of $20\ mg\ L^{-1}$) was partially mineralized as a sole source of carbon and energy by microorganisms in WWTPs. Other authors suggested direct phototransformation and biodegradation as the main elimination processes of ketoprofen in the environment [5,10]. In any case, ketoprofen is not completely removed in most of sewage treatment plants and it is detected in both sewage sludge and effluent from WWTPs [11].

These facts have stimulated recent research for different processes for removing these types of compounds, namely advanced oxidation processes (AOP) [12–14] and electrochemical advanced oxidation processes (EAOP) [15–17]. The degradation of ibuprofen solution at pH 3.0 has been comparatively studied by different EAOPs like electro-Fenton, UVA photoelectro-Fenton and solar photoelectro-Fenton at constant current density [18]. Paracetamol solutions at pH 3.0 have been efficiently mineralized by environmentally clean electrochemical methods such as electro-Fenton and photoelectro-Fenton processes [19,20]. The mineralization of clofibric acid solutions by indirect electro-Fenton was carried out by Sirés et al. [21]. On the other hand, the direct anodic oxidation of 17-β-estradiol on boron-doped diamond anodes using cathodes of Pt has been carried out by Murugananthan et al. [22]. However, research studies based on the design of experiments to analyse the influence of the different variables were not found.

In this context, anodic oxidation (AO) is an interesting EAOP based on chemical reaction with electrogenerated species from water discharge at the anode such as physically adsorbed "active

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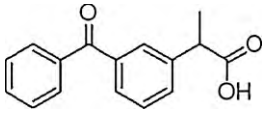

**Fig. 1.** Molecular formula of Ketoprofen.

oxygen" (physisorbed hydroxyl radical (•OH)) or chemisorbed "active oxygen" (oxygen in the form of a higher metal oxide (MO)). The proposed model assumes that the initial reaction in the anode (denoted as M) corresponds to the oxidation of water molecules leading to the formation of physisorbed hydroxyl radicals (M(•OH)):

$$M + H_2O \rightarrow M(^{\bullet}OH) + H^+ + e^- \quad (1)$$

Both the electrochemical and chemical reactivity of heterogeneous M(•OH) are dependent on the nature of the electrode material. Usually, the surface of active anodes interacts strongly with •OH radicals and then, a socalled higher oxide (MO) may be formed following reaction (2). This may occur when higher oxidation states are available for a metal oxide anode.

$$M(^{\bullet}OH) \rightarrow MO + H^+ + e^- \quad (2)$$

For the case of boron-doped diamond (BDD) electrodes, these new materials have received great attention, because they possess several technologically important characteristics including an inert surface with low adsorption properties, remarkable corrosion stability even in strongly acidic media and extremely high $O_2$ evolution overvoltage [23,24]. This material is considered the best "non-active" anode, the material interacts so weakly with •OH radicals that allows the direct reaction of organics with M(•OH) to give fully oxidized reaction products such as $CO_2$ as follows:

$$\alpha M(^{\bullet}OH) + R \rightarrow \alpha M + mCO_2 + nH_2O + xH^+ + ye^- \quad (3)$$

where R is an organic compound with $m$ carbon atoms and without any heteroatom, which needs $\alpha = (2m + n)$ oxygen atoms to be totally mineralized to $CO_2$. The latter reaction also competes with the side reactions of M(•OH) such as direct oxidation to $O_2$ from reaction (4) or indirect consumption through dimerization to hydrogen peroxide by reaction (5):

$$2M(^{\bullet}OH) \rightarrow 2M + O_2 + 2H^+ + 2e^- \quad (4)$$

$$2M(^{\bullet}OH) \rightarrow 2M + H_2O_2 \quad (5)$$

These reactive oxygen species such as heterogeneous (•OH), $H_2O_2$, and $O_2$ are generated, although physisorbed (•OH) is the strongest oxidant of organics. This species, however, has so short lifetime that only acts while direct current is supplied to the anode.

When BDD is used, other oxidizing species like peroxodisulphate (if $Na_2SO_4$ is used as supporting electrolyte, as in this investigation) can also be competitively formed with reactive oxygen species (see Eq. (6)):

$$2SO_4^{2-} \rightarrow S_2O_8^{2-} + 2e^- \quad (6)$$

In this context, EAOP in general, and AO in particular, have attracted wide attention as one of the environmental-friendly technologies in wastewater treatment. Other advantages of AO include high efficiency in organic degradation, simple structure and easy control [25]. AO of various refractory pollutants have been extensively studied, such as phenol [26], nitrophenols [27], dyes [28,29] and surfactants [23].

In this work, we present the results obtained from the BDD-AO of ketoprofen. The design of experiments was used to study the effect of pH (in the range 3–11), current intensity ($J$ = 0–320 mA cm$^{-2}$), supporting electrolyte concentration (SEC), $Na_2SO_4$ in the range 0.05–0.50 mol L$^{-1}$, and solution flow rate ($Q_v$) between 1.42 and 8.34 cm$^3$ min$^{-1}$. Response Surface Methodology (RSM) technique was used to optimize ketoprofen degradation ($X_K$, %), after AO treatment (against four input process variables). So, the objective of the present study is to find out the optimum values of the process.

## 2. Materials and methods

### 2.1. Chemicals

Ketoprofen was provided by Sigma–Aldrich Spain of the highest purity available (>98%). Ketoprofen stock solution ($1.96 \times 10^{-4}$ mol L$^{-1}$) was prepared with high purity water obtained from a Millipore Milli-Q® system. All reagents and solvents were of analytical reagent grade and were purchased from Panreac (Spain). The solution pHs were adjusted with sodium hydroxide and orthophosphoric acid (0.01/0.01 mol L$^{-1}$) buffer solution. The supporting electrolyte used in this investigation, $Na_2SO_4$, was provided by Panreac in analytical purity grade.

### 2.2. Electrolytic cell and power supply

Electrochemical experiments were carried out using an electrochemical module based on Adamant®-Electrodes (Adamant Technologies, CSEM SA, Switzerland). This module consists in a single compartment two-electrode cell in conjunction with a controlled DC Power Supply FA-665 (Promax, Ltd., Spain). The electrodes consist in a boron-doped diamond (BDD) coating deposit (3 μm, 100–150 mΩ cm) on a silicon plate (p-silicon, 100 mΩ cm, 2 mm thick). The electrode surface area was 12.5 cm$^2$ with a gap of 0.1 cm. This implies a reactor volume of 1.25 cm$^3$. This reactor was equipped with a water inlet and outlet. Two adaptable copper current feeding electrodes allow efficient electrical connections with 4 mm diameter connectors. The Adamant®-Electrodes are connected with the current feeding electrode using an Adamant®-Silver paste.

### 2.3. Degradation experiments

Electro-oxidation experiments were conducted at galvanostatic mode. The initial concentration of ketoprofen for all experiments was $1.96 \times 10^{-4}$ mol L$^{-1}$. A thermo-regulated water bath was used to maintain a constant temperature (25 ± 0.1 °C). The cell potential was remained constant during the galvanostatic electrolysis, indicates that electrode activity is not affected. Fig. 2 shows a general scheme of the experimental installation used in this work. Experimental installation can vary the flow rate between 0 and 10 cm$^3$ min$^{-1}$ and the current density between 0 and 320 mA cm$^{-2}$.

### 2.4. Analytical methods

Ketoprofen concentration present in each sample was determined by HPLC in a Waters Chromatograph equipped with a 996 Photodiode Array Detector and a Waters Nova-Pak C18 Column (5 μm 150 mm × 3.9 mm). It displayed a well defined peak for ketoprofen at a retention time ($t_r$) of 4.1 min at 261 nm. For these analyses, samples of 50 μL were injected into the chromatograph and a 60:40 (v/v) methanol/water ($10^{-2}$ M orthophosphoric acid) mixture was passed at a flow rate of 1 mL min$^{-1}$ as mobile phase.

Total Organic Carbon content (TOC) was determined by using a Lange TOC® cuvette test (Hach Lange Ltd., Spain), using a shaker TOC-X5, where the open digestion cuvette is inserted during 5 min. The range of concentrations selected was 3–30 mg L$^{-1}$. For COD determination the Lange COD® cuvette test method was used. The range of concentrations selected was 15–150 mg $O_2$ L$^{-1}$. For both

**Table 1**
Variables design. Operating levels.

| pH | | | $Q_v$ ($cm^3\ min^{-1}$) | | | $I$ (A) | | | SEC ($mol\ L^{-1}$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Low level (−1) | High level (+1) | Center point | Low level (−1) | High level (+1) | Center point | Low level (−1) | High level (+1) | Center point | Low level (−1) | High level (+1) | Center point |
| 5 | 9 | 7 | 3.15 | 6.61 | 4.88 | 1 | 3 | 2 | 0.163 | 0.388 | 0.275 |

analyses a thermostat Lange LT 200 and a Hach Lange Xion Σ-500 photometer were used.

### 2.5. Mathematical and statistical procedures

Section 3.1 was statistically analysed by using StatGraphics® Plus for Windows 5.1. A factorial central composite orthogonal and rotatable design (CCORD) was used with 12 replicates of central point, so the total number of experiments was 36.

## 3. Results and discussion

### 3.1. Design of experiments. Response surface methodology

The one factor at a time approach is the traditional way to study the influence of several operation variables (factors) on a parameter (response). However, this classical method involves a large number of experiments and some important conclusions on the interaction among factors can be missed. An efficient way to solve this problem is the design of experiments (DOE). It offers a better alternative to study the effect of variables and their responses with minimum number of experiments [30]. DOE is a common methodology in order to improve industrial and economical production processes [31–33]. Therefore, this methodology can be a useful tool to examine the influence of operative parameters on AO of different pollutants, and to determine the optimum conditions using response surface methodology (RSM).

Using RSM, the aggregate mix proportions can be arrived with minimum number of experiments without the need for studying all possible combination experiments. StatGraphichs® software provides a useful and powerful mathematical and statistical tool in order to develop the experimental planning and to analyse the results, searching for conclusions. In this methodology, the data obtained must be analysed in a statistically manner, using regression, in order to determine if there exist a relationship between the factors and the response variables investigated. The test factors were coded according to Eq. (7)

$$x_i = \frac{X_i - X_i^X}{\Delta X_i} \tag{7}$$

where, $x_i$ is the coded value of the $i$th independent variable, $X_i$ is the natural value of the $i$th independent variable, $X_i^X$ is the natural value of the $i$th independent variable at the center point, and $\Delta X_i$ is the value of step change. Each response $Y$ can be represented by a mathematical equation that correlates the response surface.

$$Y = b_0 + \sum_{j=1} b_j x_j + \sum_{i,j=1} b_{ij} x_i x_j + \sum_{j=1} b_{jj} x_j^2 \tag{8}$$

where $Y$ is the predicted response, $b_0$ is the offset term, $b_j$ is the linear effect, $b_{ij}$ is the first-order interaction effect and $b_{jj}$ is the squared effect and $k$ is the number of independent variables.

For this work, central composite orthogonal and rotatable design (CCORD) was selected, which is one of the most popular classes of second-order design. It involves the use of a two-level factorial design with $2^k$ points combined with $2k$ axial points and $n$ center runs, $k$ being the number of factors. $N$, total number of experiments with $k$ factor is obtained according to Eq. (9).

$$N = 2^k + 2k + n \tag{9}$$

$n$ is considered to be 12 and the axial distance is 2 in order to guarantee an orthogonal and rotatable design. Table 1 shows the variables design with their high (+1), low (−1) and center point values. On the other hand, Table 2 shows the experimental planning in DOE, and obtained response in each experiment we have carried out (removal of ketoprofen in percentage, $X_K$, %).

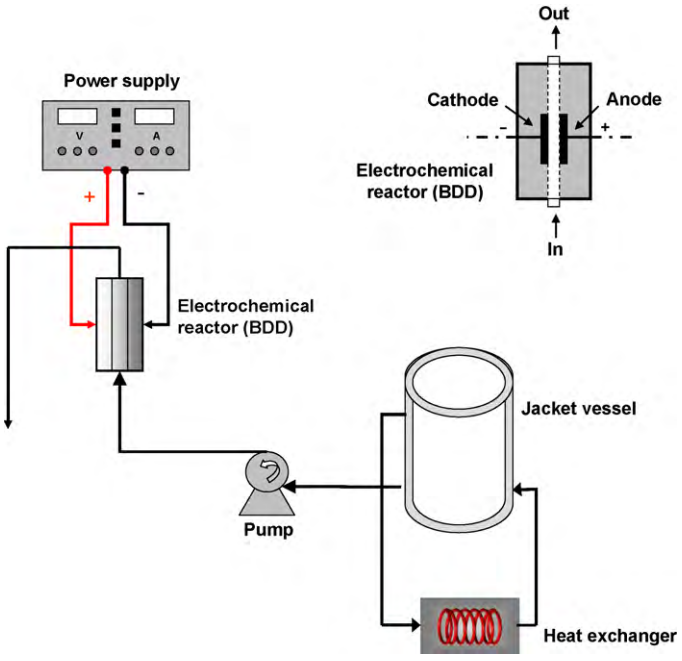


**Fig. 2.** Sketch of the electrochemical installation.

### 3.2. ANOVA test

In a first approach, we should refer the ANOVA analysis that shows us the significance of the different operative parameters. According to the RSM, 14 factors are considered and four of them have a $p$-value below 0.05 (limit of significance) (see Table 3), so they are statistically significant. This means that the model used to represent the behaviour of the interactive factors is consistent. Also, the mean absolute error (MAE) is obtained and resulted be equal to 3.9.

Non-linear polynomial regression is carried out taking into account Eq. (8). In this sense, this regression is the following expression (Eq. (10)):

$$\begin{aligned} X_K = {} & 68.56 + 0.292A - 6.48B + 13.26C + 9.68D - 0.485A^2 \\ & + 0.175AB - 0.0625AC - 0.663AD + 1.41B^2 - 1.35BC \\ & - 0.05BD - 6.48C^2 - 1.94CD + 0.427D^2 \end{aligned} \tag{10}$$

where the values of $A$ (pH), $B$ (flow rate, $Q_v$), $C$ (current, $I$) and $D$ ($Na_2SO_4$, SEC) should be coded according to Eq. (7). The values of ketoprofen removal, $X_K$, are given in %. The correlation factor $r^2$ is equal to 0.90 and the "adjusted correlation factor" $R^2$ (this

**Table 2**
Experimental planning in DOE and obtained response in each experiment.

| Run | Real pH | Real $Q_v$ ($cm^3\ min^{-1}$) | Real $I$ (A) | Real SEC ($mol\ L^{-1}$) | $X_K$ (%) |
|---|---|---|---|---|---|
| 1 | 9 | 6.61 | 1 | 0.163 | 39 |
| 2 | 9 | 3.15 | 1 | 0.388 | 75 |
| 3 | 5 | 3.15 | 1 | 0.163 | 50 |
| 4 | 9 | 3.15 | 3 | 0.163 | 75 |
| 5 | 5 | 6.61 | 1 | 0.388 | 67 |
| 6 | 7 | 4.88 | 2 | 0.050 | 50 |
| 7 | 7 | 1.42 | 2 | 0.275 | 86 |
| 8 | 9 | 3.15 | 3 | 0.388 | 87 |
| 9 | 7 | 4.88 | 0 | 0.275 | 0 |
| 10 | 5 | 3.15 | 3 | 0.388 | 95 |
| 11 | 5 | 6.61 | 3 | 0.163 | 60 |
| 12 | 7 | 4.88 | 2 | 0.275 | 69 |
| 13 | 9 | 6.61 | 3 | 0.163 | 60 |
| 14 | 7 | 4.88 | 2 | 0.275 | 73 |
| 15 | 5 | 6.61 | 1 | 0.163 | 35 |
| 16 | 7 | 4.88 | 2 | 0.275 | 71 |
| 17 | 7 | 4.88 | 2 | 0.275 | 74 |
| 18 | 7 | 4.88 | 2 | 0.500 | 85 |
| 19 | 11 | 4.88 | 2 | 0.275 | 65 |
| 20 | 7 | 4.88 | 2 | 0.275 | 71 |
| 21 | 9 | 3.15 | 1 | 0.163 | 47 |
| 22 | 9 | 6.61 | 1 | 0.388 | 59 |
| 23 | 7 | 4.88 | 2 | 0.275 | 69 |
| 24 | 5 | 3.15 | 1 | 0.388 | 68 |
| 25 | 7 | 4.88 | 2 | 0.275 | 68 |
| 26 | 7 | 4.88 | 2 | 0.275 | 69 |
| 27 | 5 | 3.15 | 3 | 0.163 | 72 |
| 28 | 7 | 8.34 | 2 | 0.275 | 57 |
| 29 | 7 | 4.88 | 4 | 0.275 | 80 |
| 30 | 7 | 4.88 | 2 | 0.275 | 66 |
| 31 | 5 | 6.61 | 3 | 0.388 | 72 |
| 32 | 7 | 4.88 | 2 | 0.275 | 70 |
| 33 | 7 | 4.88 | 2 | 0.275 | 58 |
| 34 | 7 | 4.88 | 2 | 0.275 | 64 |
| 35 | 3 | 4.88 | 2 | 0.275 | 63 |
| 36 | 9 | 6.61 | 3 | 0.388 | 78 |

includes the effect of number of degrees of freedom) is equal to 0.84. This regression leads to an optimum $X_K$ (100%) at pH equal to 3.99, operating with a flow rate of 1.42 $cm^3\ min^{-1}$ (retention time equal to 0.88 min), with a current density of 235 $mA\ cm^{-2}$ and a salt concentration of 0.5 $mol\ L^{-1}$.

ANOVA test also gives us the value of Durbin–Watson statistic, which has a value equal to 1.77, with a $p$-value of 0.30. As this $p$-value is higher than 0.05, there are no evidence of correlation in the residuals series. This means the random order of experiments has been effective in order to avoid any systematic error.

**Table 3**
ANOVA results.

| Factor | Sum of squares | Degrees of freedom | $F$-ratio | $p$-Values |
|---|---|---|---|---|
| $A$: coded pH | 2.04 | 1 | 0.04 | 0.83 |
| $B$: coded $Q_v$ | 1008 | 1 | 21.67 | 0.00 |
| $C$: coded $I$ | 4218 | 1 | 90.62 | 0.00 |
| $D$: coded SEC | 2250 | 1 | 48.34 | 0.00 |
| AA | 7.54 | 1 | 0.16 | 0.69 |
| AB | 0.49 | 1 | 0.01 | 0.92 |
| AC | 0.06 | 1 | 0.00 | 0.97 |
| AD | 7.02 | 1 | 0.15 | 0.70 |
| BB | 64.03 | 1 | 1.38 | 0.25 |
| BC | 29.16 | 1 | 0.63 | 0.44 |
| BD | 0.04 | 1 | 0.00 | 0.97 |
| CC | 1346 | 1 | 28.91 | 0.00 |
| CD | 60.06 | 1 | 1.29 | 0.27 |
| DD | 5.84 | 1 | 0.13 | 0.73 |
| Total error | 997.6 | 21 | | |

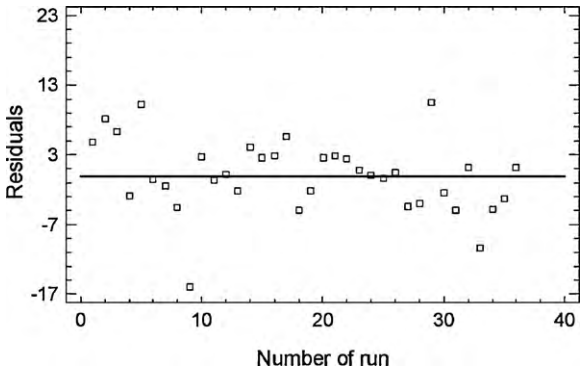


**Fig. 3.** Residuals vs. run number.

For each experiment, the difference between experimental $X_K$ and calculated $X_K$ (according to Eq. (10)) is represented in Fig. 3 vs. the specific run number. As no correlation can be appreciated (residuals are located in a random order to both the sides of the 0 axis), the randomization of the design is fully working and no accumulation of experimental error is observed.

### 3.3. Significant variables

Modelization is made on the basis of 14 factors which correspond to Eq. (10). A graphical expression of the ANOVA test results may be the Pareto graphic (Fig. 4). Bars represent the standardized effects of each involved factor, considering them as the pH, current ($I$), supporting electrolyte concentration (SEC), the flow rate ($Q_v$) and combinations of all them. Filled bars are a graphical representation of negative-affecting factors, such as flow rate, the squared of current and pH, the combination of $I$–SEC, $Q_v$–$I$, pH–SEC, pH–$I$ and $Q_v$–SEC. That means that these factors appear in the expression (10) behind a negative sign. On the other hand, unfilled bars represent positive-affecting factors, such as $I$, SEC, pH, the squared of $Q_v$ and SEC, and the combination of pH–$Q_v$, pH–$I$. The vertical rule stands near to 2 and has to do with the signification level of ANOVA test, which is equal to 95% of confidence. Factors above this rule (as $B$, $C$, $D$ and CC) are inside the significance region, while the rest of them are not statistically significant. The Pareto graphic also gives us an idea of how factors influence on the final response $X_K$. Positive bars indicate that by varying the variable $X_K$ increases. Negative bars indicate the contrary. As it can be shown, as rate flow level raises $X_K$ decreases and as current and salt concentration raises $X_K$ increases.

### 3.4. Main variables

The evaluation of the CCORD model leads also to the study of the main effects of the involved variables. This can be observed

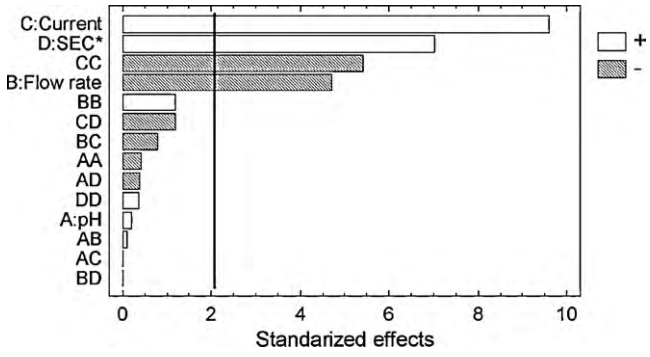


**Fig. 4.** Pareto graphic: standardized effects.

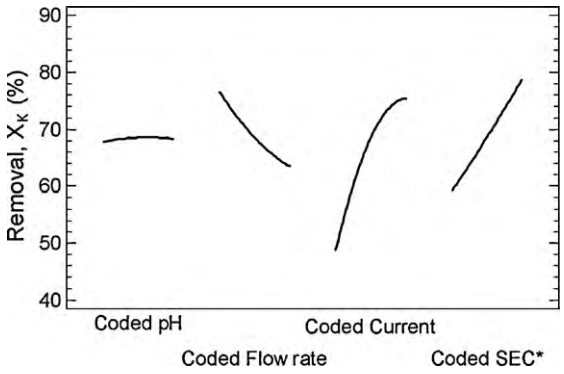


**Fig. 5.** Main effects of flow rate, pH, dosage of $SO_4Na_2$ and current.

in Fig. 5. Four curves are drawn representing the effect of varying each variable while the other ones keep constant. Current tends to present an optimum in the end part of the curve (region of +1), SEC presents a linear positive-affecting tendency, while $Q_v$ presents a linear negative-tendency. The fourth one, pH, does not present significant influence. This will be clearly appreciated in the response surface and in the optimum point. As can be seen the influence of current was the greatest in studied variables, the second one was the supporting electrolyte concentration and the third one was the flow rate.

### 3.5. Operating parameters interaction

Fig. 6 shows the interaction between each two of the four variables studied. Each pair of curves represents the evolution of $X_K$ by varying one variable in the extremes of the CCORD model, that is, with its pair variable equal to 1 (upper value) and equal to −1 (low value). Parallel lines mean there is no interaction between them, crossing lines indicate the contrary. The level of interaction of one variable on the other is represented between these two situations As the curves, for the pairs of variables AB, AC, BC and BD, present a parallel behaviour, it may be assumed that there is not interaction, and the modification of one of the variables does not affect to the other one. When the pairs AD and CD are observed in Fig. 6, the fact that interaction appears between these variables is evident. As the curves do not present a parallel behaviour, it may be assumed that there is interaction, and the modification of one of the variables affects to the other one. The crossing occurs outside the region of the CCORD model.

### 3.6. Response surfaces and contour plots

The surface graphic is the most important graphical representation in the RSM (see Figs. 7 and 8). It plots Eq. (10) and allows to evaluate from a qualitative point of view how is the behaviour

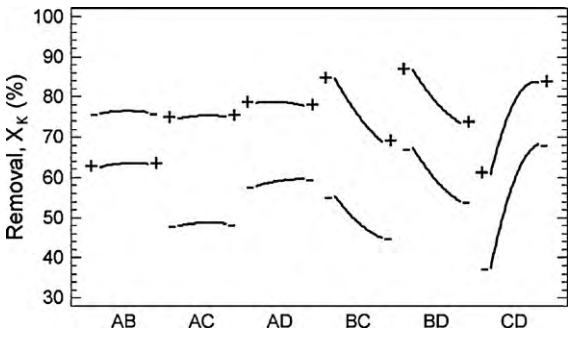


**Fig. 6.** Interaction graphic for flow rate, pH, dosage of $SO_4Na_2$ and current.

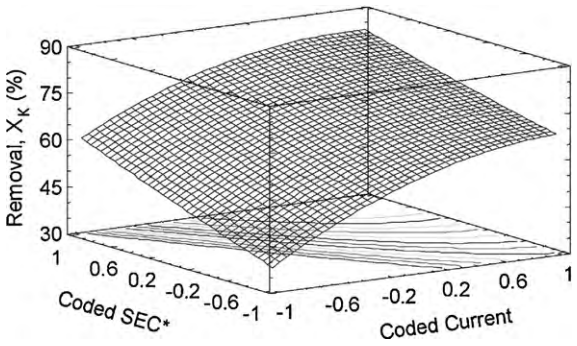


**Fig. 7.** Response surface: current–SEC.

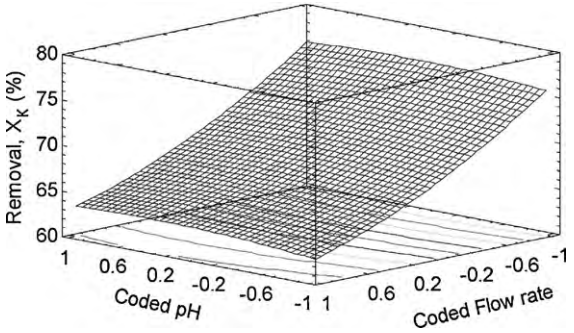


**Fig. 8.** Response surface: pH–$Q_v$.

of the whole studied system. As it can be appreciated in Fig. 7, the response is a quite convex surface and a maximum is apparent in the final region of coded $I$ (+1) of the studied region. Numerical coordinates of this point are −1.5 for pH, −1.99 for $Q_v$, +0.90 for $I$ and +2 for SEC. This is outside drawn region, so the contour plot does not include it.

On the other hand, in Fig. 8, the response is a quite plain surface as there is no interaction between variables inside the studied region. The strong influence of $Q_v$ is represented by the inclined plane where the slope is primarily due to the variation of $Q_v$, while pH affects this level only slightly.

The contour plot, which is drawn in Fig. 9, is more clearly in order to identify the maximum point. Quantitatively, a statistical analysis of the model yields to an optimum in the point −1.5 for pH, −1.99 for $Q_v$, +0.90 for $I$ and +2 for SEC, which is equivalent to pH 3.99, $Q_v = 1.42\ cm^3\ min^{-1}$ (retention time equal to 0.88 min), 2.937 A (equivalent to a current intensity, $J$, equal to $235\ mA\ cm^{-2}$) and a SEC equal to $0.5\ mol\ L^{-1}$ of salt. As three of the four factors are inside the significant region of the model (that is, three of them

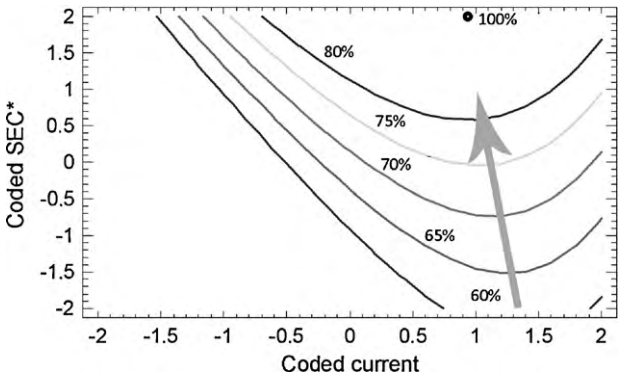


**Fig. 9.** Contour plot of the response surface: current–SEC.

**Table 4**
Experimental results for ketoprofen anodic oxidation in optimum conditions.

| $[Ketoprofen]_o$ (mg $L^{-1}$) | $X_K$ (%) | $COD_o$ (mg $L^{-1}$) | $X_{COD}$ (%) |
|---|---|---|---|
| 50 | 100 | 116 | 38 |

are statistically significant as their *p*-values are under 0.05), this optimum may be considered as statistically different from other near points. Maximum value of $X_K$ (equal to 100% of degradation) is predicted by the model in these conditions.

### 3.7. Experimental confirmation of the theoretical maximum

An experiment was carried out in optimal conditions (pH 3.99, $Q_v = 1.42\ cm^3\ min^{-1}$, $J = 235\ mA\ cm^{-2}$ and SEC = 0.5 mol $L^{-1}$), in order to determine the reached removals of ketoprofen ($X_K$) and chemical oxygen demand ($X_{COD}$). Table 4 shows the obtained results for the experiment carried out in these optimal conditions. As can be seen, in these conditions, the reductions of ketoprofen and COD result to be equal to 100% and 38%, respectively.

### 3.8. Physical meaning to the results of the DOE

As can be seen in Fig. 5, the influence of current was the greatest in studied variables. This may be explained by Eq. (1). The hydroxyl radical generation is due to the current. However, current tends to present an optimum in the end part of the curve (region of +1). From the results of the DOE, we can conclude that above a certain value of current density ($J = 235\ mA\ cm^{-2}$) the radical production does not increase with current. Radical production reaches a saturation value, and an increase in current intensity is negative.

The second more important variable studied was the supporting electrolyte concentration. The influence of this parameter was positive in all the range. There is not an optimum value for this parameter. This can be justified taking into account two factors. An increase in the concentration of salt favours, on the one hand, the conduction of current in solution, and on the other, radical formation of oxidizing species like peroxodisulphate (see Eq. (6)).

The obtained result for the flow rate was expected if we consider that this parameter is inversely proportional to the residence time of molecules into reactor. The pH does not present significant influence, although there is an optimal value. This pH value should be adequate to support both, the reaction of the anode (favoured at basic pH) and the cathode reaction (favoured at acid pH). Furthermore, in the optimal conditions (pH 3.99) the drug remains protonated being more reactive to hydroxyl radicals.

## 4. Conclusions

Boron-doped diamond anodic oxidation of ketoprofen in aqueous solution was studied. DOE was used to study the effect of pH (in the range 3–11), current intensity ($J = 0–320\ mA\ cm^{-2}$), supporting electrolyte concentration ($Na_2SO_4$) in the range 0.05–0.5 mol $L^{-1}$, and solution flow rate ($Q_v$) between 1.42 and 8.34 $cm^3\ min^{-1}$. Response Surface Methodology technique was used to optimize ketoprofen degradation ($X_K$, %). So, the objective of the present study was to study the influence of operative parameters and to find out the optimum experimental conditions for this oxidation technology.

An orthogonal, rotatable factorial central composite design of experiments was carried out. It showed that the influence of current intensity was the greatest in studied variables, the second one was the supporting electrolyte concentration and the third one the flow rate. The influence of pH was very soft. Anova test reported significance for four variables (current, SEC, flow rate and the squared of current) of the 14 involved. An optimum oxidation point was found at pH 3.99, $Q_v = 1.42\ cm^3\ min^{-1}$, $J = 235\ mA\ cm^{-2}$ using a SEC = 0.5 mol $L^{-1}$.

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