DIFFERENTIAL PULSE VOLTAMMETRIC DETERMINATION OF PARACETAMOL ON A BORON-DOPED DIAMOND ELECTRODE: APPLICATION TO NATURAL TOMATO AND CARROT JUICES

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ABSTRACT

This work deals with the analysis of the paracetamol in tomato and carrot juices. Such purpose, a differential pulse voltammetry was used. The measurements were performed on a boron-doped diamond electrode and the adjusted parameters such MA; tM; Ep; tEp and ∆E were investigated in aqueous HClO₄ 0.1M. It results from this work that paracetamol was detected in simulated wastewater with good accuracy with a recovery rate of 98.25 ± 0.91 with a detection limit of 0.16 µM. This technique has been successfully used to detect the paracetamol in tomato and carrot juices where the paracetamol recovery rate are between 94.56 ± 0.05 and 103.24±1.18 for tomato juice and between 97.05 ± 0.45 and 109.41 ± 0.42 for the carrot juice. The suitability of this technique to determine the low quantity of paracetamol in tomato and carrot juice can be investigated to detect antibiotic in further work.

Keywords: paracetamol, differential pulse voltammetry, boron-doped diamond electrode, simulated wastewater.

RÉSUMÉ

Détermination du paracétamol par voltammetrie à impulsion différentielle sur une électrode de diamant dopée au bore : application aux jus naturels de tomate et de carotte

Ce travail traite de l’analyse du paracétamol dans les jus de tomates et de carottes par voltamétrie à impulsion différentielle. Les mesures ont été effectuées sur une électrode de diamant dopé au bore et les paramètres tels que MA ; tM ; Ep ; tEp et ∆E ont été optimisés dans une solution aqueusee de HClO₄ 0,1M. Dans ce travail, le paracétamol a été détecté dans les eaux usées simulées...
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avec une bonne précision soit un taux de recouvrement de 98.25 ± 0.91 et une limite de détection de 0.16 µM. Cette technique a été utilisée avec succès pour détecter le paracétamol dans du jus de tomate avec des taux de recouvrement compris entre 94.56 ± 0.05 et 103.24 ± 1.18 et entre 97.05 ± 0.45 et 109.41 ± 0.42 dans du jus de carotte. La pertinence de cette technique pour déterminer la faible quantité de paracétamol dans le jus de tomate et de carotte peut être étudiée pour détecter un antibiotique dans des travaux ultérieurs.

Mots-clés : paracétamol, impulsion différentielle, électrode de diamant dopé au bore, eaux usées simulées.

I - INTRODUCTION

Pharmaceutical substances are molecules used to induce a biological favorable effect to health in the animal or human organism. Their important use is at the origin of a generalized contamination of the aquatic environment by a broad spectrum of molecules. They have healing, preventive properties or administered for established diagnosis. These pharmaceutical substances are classified according to the effect for which they are designed (antibiotics, analgesics, etc.), to their chemical structure and to their mode of action [1]. They are generally considered like emerging pollutants and are often classified in a category that is called "micropolllutants" because the concentrations found in aquatic environments are of the order of nanogram or microgram per liter [1]. Part of the active ingredients contained in the drugs is metabolized by the organisms (human beings and animals) and the rest, as well as the metabolites, are finally released into the environment in different ways, such as direct excretion by humans and animals [2], via wastewater (more or less treated) [3]; the runoff water from fields after the application of livestock manure and more or less stabilized urban sludge [4, 6]. These pharmaceutical substances, through these contaminated waters, can be found in market gardening products such as tomatoes, carrots, cucumbers, etc. Among these emerging micropolllutants, paracetamol, which is the subject of our study, holds our attention because of its high level of use for humans health. Paracetamol (N-acetyl-p-aminophenol) is an effective and important analgesic and antipyretic agent used widely to relieve pain related to arthralgia, neuralgia, headache and cancer [7]. In general, paracetamol seems to be safe and appears to have no toxic effects on human's health when taken in normal therapeutic doses. However, large doses and chronic use of paracetamol or concomitant use with alcohol or other drugs can cause skin rashes, liver disorders, nephrotoxicity and inflammation of the pancreas. In this case, the precise determination and control of the paracetamol becomes vital [8]. Moreover, the presence of trace paracetamol in drinking water is of great interest since little is known about
potential chronic health effects associated with long term ingestion of these compounds through drinking water [9]. A number of methods are available to determine paracetamol in various types of samples [10]. These methods include capillary electrophoresis (CE) [11], high performance liquid chromatography (HPLC) [12], etc. Unfortunately, these techniques are expensive and need costly maintenance. In recent development, electrochemical sensors have been proven as an inexpensive and simple analytical method with remarkable detection sensitivity, reproducibility and easy to miniaturize rather than other instrumental analysis methods [13]. They have been found to have a wide range of application in clinical, industrial, environmental and agricultural analysis [14]. In this area, several electrodes, such as gold electrodes [15], glassy carbon electrodes [16], modified glassy carbon electrodes [17] and modified carbon paste electrodes [18] have been used for the paracetamol determination. For seeking of stable electrodes for the determination of paracetamol, our focus was made on boron doped electrodes. This type of electrode has already shown that it can be used to oxidize paracetamol [18].

The use of boron-doped diamond (BDD) as an electrode substrate is now well established, mainly due to its properties such as a wide potential window in aqueous solutions, low background currents, long term stability, and low sensitivity to dissolved oxygen [18]. These properties make BDD particularly suitable for electrochemical studies of analytes with a high oxidation potential [19]. The properties of BDD are commonly affected by morphologic factors and defects in the film, presence of impurities (sp² carbon), crystallographic orientation, surface termination (hydrogen or oxygen), and electrochemical pre-treatments of its surface [20]. Suffredini and al. [21], have shown that cathodic pre-treatment of the BDD electrode increased dramatically the electroanalytical detection limit of chlorophenols. BDD has also successfully been used for the determination of acetylsalicylic acid (ASA) in its pharmaceutical formulations [22], as well as the determination of aspartame and cyclamate in dietary products, individually [23] or simultaneously [24]. In this paper, we describe the use of a cathodically pre-treated BDD electrode for the selective and sensitive determination of paracetamol in natural tomato and carrot juice by differential pulse voltammetry (DPV).

II - MATERIALS AND METHOD
II-1. Equipment and electrodes

The voltammetric measurements were performed using an AUTOLAB PGSTAT 20 (Ecochemie) connected to a potentiostat equipped with a USB

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electrochemical interface. This system is connected to a three-electrode single compartment glass cell and a computer for data storage and processing. A GPES 4 software was employed to get the voltammograms. The glass electrochemical cell consisted of saturated calomel electrode (SCE) and platinum wire as reference and counter electrode respectively. BDD electrode was used as working electrode. The surface of the BDD in contact with the electrolyte is 1 cm². All the pH values were measured with pH meter. All the potentials reported in this paper were given against (SCE) electrode at an ambient temperature of 25°C.

II-2. Reagents and materials

Paracetamol was supplied by laboratoire BAILY-CREAT (France). A stock solution of 1.32*10⁻² mol/L (2g/L) of paracetamol was prepared by dissolving an accurate mass of the drug in an appropriate volume of HClO₄ and KClO₄. The working solutions for the voltammetric investigations were prepared by dilution of the stock solution. All solutions were protected from light and used within 24h to avoid decomposition. 0.1M of HClO₄ and 0.1M of KClO₄ were used to prepare the supporting electrolytes. Distilled water was used to prepare all the solutions.

II-3. Calibration graph for quantitative determination

The stock solution of paracetamol was diluted in HClO₄ 0.1M to obtain different paracetamol concentrations. In the experimental section, a linear calibration curve for DPV analysis was constructed in the paracetamol concentration range from 0 µmol/L to 13.87 µmol/L. The repeatability, accuracy and precision were checked.

II-4. For voltammetry investigations

Two tablets (500 mg) of PCM were ground into a fine powder. An adequate amount of this powder, corresponding to the 13.2 mmol L stock solution, was weighed and transferred into a 500 mL calibration flask. The volume was adjusted with 0.1 M HClO₄ or KClO₄. The contents of the flask were stirred for 30 minutes to ensure complete dissolution and then diluted with the same electrolyte. The tomato juice and carrot stocks used in our study were obtained after several steps. First, the tomatoes and carrots bought on the market were rinsed with distilled water. Then, they were milled in a blender with an appropriate amount of 0.1M HClO₄ and filtered several times. Finally, 1 ml of this filtrate was dissolved in a volumetric flask containing 0.1M HClO₄ so as to have the stock of 100 ml of tomato or carrot juice. CV and DPV were used to study the electrochemical behavior or quantification of PCM. The analytical
curves were obtained by adding small volumes of PCM stock solution to the carrier electrolyte of HClO$_4$, of KClO$_4$, of tomato juice or carrot juice. DP voltamograms were obtained after each dosing. Prior to the experiments, the BDD electrode was electrochemically pretreated in a solution of 0.5 mol.L$^{-1}$ H$_2$SO$_4$. For that pretreatment, an anodic pretreatment (+2V, 15 s) is followed by a cathodic one (-2V, 90 s). Doing so, the BDD surface was first cleaned of all impurities and then made primarily hydrogen [21]. The choice of the pretreatment potential and the procedure are discussed in elsewhere [21].

III - RESULTS AND DISCUSSION

III-1. Physical Characterization of the Boron Doped Diamond (BDD) Electrode

*Figure 1* shows the scanning electron microscopic image of the boron doped diamond electrode.

![Figure 1](image_url)

*Figure 1* : *Scanning electron micrograph of boron doped diamond*

That image indicates that BDD presents a polycrystalline structure. The morphological grains sizes are ranging between 0.3 and 0.6 µm. The grains are heavily twinned. At the bottom of the diamond grains, a relative dark space was observed especially at grains boundary which can be related probably to graphitic carbon (Csp$^3$) formed during the BDD preparation.

III-2. Electrochemical characterization of BDD electrode

The Characterization of the boron-doped diamond electrode was carried out in ferri/ ferrocyanide of potassium medium ([Fe(CN)$_6$]$^{3-}$/[Fe(CN)$_6$]$^{4-}$).
III-2-1. Influence of Fe(CN)$_6^{3-/4-}$ concentration, of potential scan rate and of pH

The study of redox reactions makes it possible to determine the kinetics of these species with a working electrode. The aqueous solution used is the solution of potassium ferri-ferrocyanide in the presence of potassium perchlorate (0.1M KClO$_4$) chosen as the supporting electrolytes. The ferri-ferrocyanide couple causes a mono electron transfer to the electrode without adsorption of the electroactive species. Three series of measurements were carried out in the supporting electrolyte (0.1M KClO$_4$): the first consisted in varying the concentration of the ferri-ferrocyanide couple (Figure 2), the second concerned the influence of the potential scan rate on the voltammograms (Figure 3) and the third allowed to observe the effect of the pH of the medium (Figure 4). Figure 2A shows the influence of the concentration of potassium ferri-ferrocyanide on the boron-doped diamond electrode.

![Figure 2](image)

**Figure 2**: (A) Voltammetric curves as a function of the concentration of the ferri-ferrocyanide potassium pair; (B) Curves of anodic and cathodic peak currents constructed as a function of ferri / ferrocyanide concentration. Support electrolytes: KClO$_4$ 0.1M; ET: DDB, ER: ECS, CE: rolled platinum, $T = 25^\circ$C, $v = 100$ mV/s

There is an increase in peak current densities with concentration. In this figure, the anodic and cathodic peaks observed correspond to the oxidation and reduction of the ferrocyanide and ferricyanide respectively. The peaks observed are typical of such a redox couple on good electronic conductors [25]. The treatment of the voltammograms of figure 2A led to the plots of the anodic and cathodic peak currents as a function of the concentration of the ferri-ferrocyanide potassium couple (Figure 2B). The obtained straight lines ($R^2 = 0.999$) passing through the origin of the axes suggest that oxidation and
reduction of redox species are responsible for the appearance of these peaks. This shows that the DDB electrode used in this work has quasi-metallic properties [25]. For an equimolar concentration of 50 mM of the selected redox couple, voltammograms were made at 25; 50; 75; 100; 125; 150; 200 mV/s in the same medium. **Figure 3A** shows the voltammograms obtained on DDB. The observed anodic and cathodic peaks correspond respectively to oxidation and reduction of the redox couple. In this figure, the current densities of the anodic and cathodic peaks increase with the potential scan rate. These peak current densities were determined and plotted against the square root of the potential scan rate (**Figure 3B**). They are proportional to the square root of the scanning speed. The same observations have been made in previous laboratory work [25, 26]. The linearity between the peak current densities and the square root of the potential scan rate indicates that the oxidation-reduction kinetics at the electrode is diffusion-controlled.

**Figure 3**: (A) Voltammetric curves as a function of sweep rate in the 50 mM potassium ferri-ferrocyanide pair, (B) Anodic and cathodic peak current curves constructed as a function of the square root of the sweep rate in potential; Support electrolytes: KClO₄ 0.1M; ET: DDB, ER: ECS, CE: rolled platinum, T = 25°C

The difference between the anodic and cathodic peak potentials is greater than 60 mV characteristic of a fast and reversible system. However, the ratio (is close to 1) between the anodic and cathodic peak current density would indicate that the process at the BDD electrode is quasi-reversible with homogeneous kinetics. In this study, the influence of the pH on the response of ferri/ferrocyanide on BDD has been investigated. In fact, it has been pointed out in literature that when the pH increases, the surface charge transfer can be degraded in case the electrode has oxygenated terminations [27]. That charge could be due to the deprotonation of some oxygenated groups which induces an electrostatic repulsion with this redox couples.

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In the case where the electrode is perfectly hydrogenated, the $\Delta E_p$ remains identical. *Figure 4* presents voltammograms recorded in $\text{KClO}_4$ 0.1M containing the $\text{Fe(CN)}_6^{3-/4-}$ couple at various pH values varying in the range 2.82 to 11.79. There is an almost perfect superposition of the voltammograms obtained with a $\Delta E_p$ almost constant around 0.37V. This could indicate the absence or very low proportion of oxygenated groups on the surface of the electrode. So, regardless of the pH of the electrolyte, the surface of the BDD electrode used in this work is perfectly hydrogenated and therefore favorable for charge transfer with the $\text{Fe(CN)}_6^{3-/4-}$ couple. All these investigations show that the boron-doped diamond electrode is a good electronic conductor with excellent quasi-metallic properties. The proportionality observed between the current and the concentration of the redox couple studied indicates that the DDB electrode can be used as an electrochemical sensor for the detection and quantification of certain pharmaceutical organic compounds in solution.

**III-2-2. Electrochemical Oxidation of paracetamol on the BDD electrode**

**III-2-2-a. Influence of the supporting electrolyte**

The voltammetric investigation of the paracetamol containing HClO$_4$ or KClO$_4$ was performed. *Figure 5* illustrates the CV voltammograms in the absence and in the presence of 13.2mM of paracetamol either in HClO$_4$ or in KClO$_4$ solution.
Figure 5: CV voltammograms of BDD electrode in HClO$_4$ 0.1M and KClO$_4$ 0.1M electrolytes blank and containing 2g/L of paracetamol.

Working electrode: BDD (1 cm$^2$), Counter electrode: Pt wound, Reference electrode: SCE. Scanning rate: 50mV/s

No peak is observed in the absence of paracetamol in the two electrolytes. However, an anodic peak is observed at the potential of 0.86V in the presence of 13.2mM of paracetamol in each of the electrolytes used. That anodic peak could be related to the oxidation of the paracetamol. Figure 1 also shows that for the same quantity of PCM in the electrolyte, the current intensity recorded in HClO$_4$ is higher than that recorded in KClO$_4$. Moreover, no current peak was observed in the backwards of the potential scanning indicating that the PCM oxidation process is irreversible on the BDD electrode. PCM has been made more active to be oxidized in its protonated form. From such a finding, HClO$_4$ have been chosen for further investigation in this work.

III-2-2-b. Influence of PCM concentration

Figure 6A shows the voltammetric curves recorded on the boron-doped diamond electrode in the potential window of 0 to 1.2 V/ECS in 0.1 M HClO$_4$ containing different concentrations of PCM. This figure shows that the anodic current peak increases with the concentration of PCM. In addition, the potential of this oxidation peak shifts toward positive values as the concentration of PCM increases. This result indicates that the PCM oxidation process is irreversible on the BDD electrode even for all concentration investigated. On Figure 6B, the plot of the PCM oxidation peak current density versus the PCM concentration leads to a straight line with a slope of 0.0005 A.L/g with $R^2 = 0.9989$. This result shows that the increase of the oxidation peak current density is directly related to the oxidation of the PCM. The PCM oxidation occurs through a direct electron transfer process between BDD and the organics since it happened in the potential window of water stability on the BDD electrode.
Figure 6: Cyclic voltammograms for different concentrations of paracetamol in 0.1M HClO₄ solution. Working electrode: BDD (1 cm²), Counter electrode: Pt wound, Reference electrode: SCE. Scanning rate: 50mV/s

III-2-2-c. Influence of the potential Scan Rates

The electrochemical oxidation process related to the oxidation of PCM by tackling the influence of the potential scan rate was carried out using CV techniques. The CV voltammogram of paracetamol exhibited also only one anodic peak, with no peak on the reverse scan (Figure 7A), indicating the totally irreversible nature of the electrode reaction. In addition, for an irreversible oxidation process, the peak potential (E_p) shifts to less positive values as the potential scan rates increase. That results shows also that the paracetamol oxidation process is irreversible [28].

Figure 7: Cyclic voltammograms in a 0.1 M HClO₄ solution containing 2 g / L PCM at different scans (A), evolution as a function of the square root of the scanning speed of the anodic peak currents (B) and evolution as a function of the logarithm of the scanning speed of the anodic peak currents (C); Working electrode: BDD (S = 1 cm²), against electrode: Pt wound, Reference: SCE. Scan rate = 50 mV.s⁻¹, T = 25 ° C
The oxidation peak current density was plotted against the square root of the potential scan rates and the result is illustrated in Figure 7B. That figure shows a straight line \( (J_a = 0.0065 \sqrt{v} + 0.001) \) with a correlation coefficient of 0.9964 (closed to 1). Moreover, the logarithm of the oxidation peak current density against the logarithm of the potential scan rates leads to Figure 7C. This figure shows a straight line \( (\ln J_a = 0.3488 \ln v - 0.5005) \) with a slope of 0.3488 which is closed to theoretical value 0.5. All those findings indicated that the PCM oxidation process is predominantly diffusion-controlled [28].

**III-2-2-d. Influence of the pH**

The effect of the pH on the oxidation of paracetamol was studied in 0.1M HClO\(_4\) in the pH range from 0.217 to 11.18 by cyclic voltammetry. Figure 8 shows the recorded voltammograms. The shape of the oxidation peak changes from narrow to a broad peak when the pH of the solution passes from acidic pH to the alkaline pH. As the pH increases, the oxidation peak changes to an oxidation wave. That wave is very pronounced in the very alkaline medium (pH=11.18). This result is probably explained by a very strong electrostatic repulsion effect between the surface of the electrode material and the species in solution, in particular the PCM molecules. The well resolved oxidation peak observed in a very strong acid medium (pH = 0.217) could be explained by hydrogen terminated BDD surface induced by this pH which allow electrons and protons exchanges at the electrode/electrolyte interface. The peak potential of the oxidation peak shifted toward positive values as the pH increases (Figure 8). These can be explained by changes in protonation of the acid-base functions in the paracetamol molecules (Scheme 1). In other word, proton takes part in the electrochemical reactions of paracetamol [28].

![Figure 8](image)

Figure 8: Cyclic voltammograms at different pH of 0.1M HClO\(_4\) solution containing 2g/L PCM; AND: BDD (1 cm\(^2\)), CE: Pt wound, ER: SCE. \( V = 100\text{mV/s} \).
From this study and that performed on graphite electrodes, two protons were transferred in the reaction. The paracetamol oxidation could be a two-electron and two-proton process as given below in Scheme 1 [29].

![Scheme 1](image_url)

The CV technique allowed to observe that the PCM oxidation process is irreversible on BDD electrode with a higher and well resolved oxidation peak in acidic medium compared to the alkaline medium. The oxidation peak current density of the PCM varies linearly against its concentrations and the square root of its potential scan rates indicates the irreversible nature of the reaction that takes place on the BDD surface. However, this technique did not allow us to determine very small quantities of pharmaceuticals in aqueous solution with the BDD electrode. In this case, the differential pulse voltammetry technique, a more sensitive technique, is used in this study to develop a voltammetric technique to determine and quantify the drug in its pharmaceutical formulation. For such a technique, it is better to investigate the optimized conditions for which it can be properly used.

### III-3. Optimization of DPV parameters

The pretreatment potential (Ep), the pretreatment time (tEp), the modulation amplitude (MA), the modulation time (tM) and the potential step (ΔE) are parameters that influence the quality, the height and the potential of the peaks, which is why they were optimized. During the adjustment of the above parameters, each parameter was changed, while the others were kept constant for a concentration of $1.32 \times 10^{-2}$ mol L$^{-1}$ of PCM in 0.1M HClO$_4$. The obtained results are shown in Figure 9. Bearing in mind that the analytical performance of BDD electrodes depends on their surface termination (eg, hydrogen or oxygen terminated) [30], the effect of different electrochemical pretreatments of the BDD electrode on its Analytical response in 2g/L PCM containing 0.1M HClO$_4$ was studied. Thus, the BDD electrode was anodically (+ 2V, 15 s) or cathodically (-2V; 15 s) pretreated in a 0.5 mol L$^{-1}$ H$_2$SO$_4$ solution. The analytical response of this electrode was monitored and recorded in the potential range varying between -3V and + 2V (Figure 9A). As can be seen in
**Figure 9A**, the cathodic pretreatment leads to a better peak current density (better repeatability was also found), compared to the anodic pretreatment indicating that the cathodically pretreatment of the electrode leads to a higher electrochemical activity for the oxidation of PCM on the electrode, as it is observed in several other analytes \[31\]. The influence of the duration (15 to 300 s) of the cathodic pretreatment of the BDD electrode on its analytical signal was also studied. Greater peak current amplitude was achieved for 90s pretreatment. Thus, all of the following analytical determinations of PCM were performed with the cathodically pretreated BDD electrode (Ep = -2V, tEp = 90 s, **Figure 9B**), which provided a predominantly hydrogen-terminated surface of the electrode. This pretreatment, performed daily before starting the voltammetric measurements, was always preceded by an anodic pretreatment (+2V, 15 s) to clean the BDD surface from contaminant oxidant. This pretreatment coupling the anodically and cathodically technique led to excellent repeatability in the determination of PCM on BDD. The effect of the modulation amplitude (MA) on the PCM oxidation peak current was also studied. The MA investigated varies between 10 and 500 mV. In this investigation, the potential was fixed (**Figure 9C**). In the MA studied range, the symmetrical voltammogram relative to its peak, without distortion and whose peak current density is the highest was obtained with a modulation amplitude of 100 mV. The influence of the modulation time (Mt) on the PCM oxidation current peak density has been studied in the range 5 ms to 250 ms (**Figure 9D**). It has been found that the analytic signal of the PCM oxidation current peak density decreased with Mt. The best results have been obtained for a modulation time of 50 ms. In addition, the influence of the potential step (ΔE) was studied in the interval between 1 mV and 20 mV (**Figure 9E**). The PCM oxidation peak current increases with the increase of ΔE, however, the potential step greater than 7 mV caused a distortion in peak shape. Finally, ΔE = 7 mV was chosen in this work as the optimal value.
Figure 9: The effect of optimization of the parameters of $1.32 \times 10^{-2}$ mol L$^{-1}$ Jma obtained at BDD electrode in HClO$_4$ 0.1M, pH 0.217; (A) pretreatment potential, (B) pretreatment time, (C) modulation amplitude (MA), (D) modulation time (Mt) and (E) step potential ($\Delta$E).

The pretreatment potential of -2V, the pretreatment time of 90s, the modulation amplitude of 100 mV, the modulation time of 50 ms and the potential step of 7 mV have been found to be the optimal values of the cited variables.

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III-4. Detection and quantification of paracetamol by DPV method

In order to validate this analytical method for the determination of PCM for pharmaceutical and environmental purposes, PCM signals at different concentrations were recorded on the BDD electrode in perchloric acid medium (0.1M HClO₄).

**Figure 10**: (A) Differential pulse voltammograms at different concentrations of paracetamol in HClO₄ solution on BDD electrode by DPV; the concentration varies from 0µM to 19.8µM, (B) Calibration curve of method and (C) curve of the experimental concentration of PCM versus the theoretical concentration of PCM.

**Figure 10A** shows the voltammetric response of the oxidation peaks for each PCM concentration ranging from 0µM to 13.87µM. The voltammograms recorded under the optimal conditions Ep = -2V, tEp = 90s, MA = 0.1V, tM = 0.05s and ∆Ep = 0.007V shows that the PCM oxidation peaks are all observed at the same potential (E = 0.7V) regardless of its concentrations. It appears from **Figure 10B** that the intensity of the PCM oxidation peak current increases linearly with the concentration of paracetamol. The limit of detection and quantification are respectively 0.167µM and 0.559µM using the equations LOD = 3 S_D/b and LOQ=10S_D/b for their determination; S_D is the standard deviation and b the slope of the straight line in **Figure 10B** [32]. Three sets of independent measurements have been made. Five (05) different concentrations of the paracetamol (Cth) were used to determine the recovery rate. The results obtained are assigned in table 1. With the calibration curve obtained, the experimental concentration was calculated for each of the five (05) concentrations of the paracetamol used. The plot of the experimental concentration as a function of the theoretical concentration of paracetamol (figure 10C) gives a straight line whose equation is: C_exp = 0.9999 C_théo - 0.0000002 with R² = 0.9999. This line has a correlation coefficient which is substantially equal to 1 indicating a proportionality between the experimental
concentration and the theoretical concentration, and also the reliability of the
differential pulse voltammetric analysis method.

**Table 1** : *Recovery rate of the method*

<table>
<thead>
<tr>
<th>Number of the sample</th>
<th>Concentration introduced (µM)</th>
<th>Concentration found (µM)</th>
<th>Recovery rate ± SD</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>1.98</td>
<td>1.707</td>
<td>86.25 ± 0.92</td>
</tr>
<tr>
<td>2</td>
<td>3.309</td>
<td>3.02</td>
<td>91.27 ± 0.51</td>
</tr>
<tr>
<td>3</td>
<td>5.95</td>
<td>5.78</td>
<td>97.17 ± 0.72</td>
</tr>
<tr>
<td>4</td>
<td>11.89</td>
<td>11.68</td>
<td>98.25 ± 0.91</td>
</tr>
<tr>
<td>5</td>
<td>13.87</td>
<td>13.56</td>
<td>97.80 ± 0.14</td>
</tr>
</tbody>
</table>

This results show a high recovery rate of the PCM by this method. That indicates that this method is suitable for the PCM determination analytically in its pharmaceutical formulation.

**III-5. Comparison with other methods**

The differential pulse voltammetric determination of paracetamol in this study is compared with other methods described in literature (*Table 2*). It can be seen that the boron-doped diamond electrochemical sensor provides reasonable analytical performance with a low detection limit (0.16 µM). This table shows that a much better detection limit value is obtained with the BDD than with several modified electrodes [33 - 37] except the Graphene/GCE [38]. Thus, the electroanalytical technique developed in this work is suitable for the detection and quantification of some trace organic pharmaceutical compounds present in wastewater.

**Table 2** : *Comparison of the efficiency of some voltammetric methods in the determination of paracetamol*

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Method</th>
<th>Linear range (µM)</th>
<th>Detection Limit (LOD, µM)</th>
<th>Reference</th>
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<td>GR-CS</td>
<td>DPV</td>
<td>1-100</td>
<td>0.3</td>
<td>33</td>
</tr>
<tr>
<td>CPE-CS</td>
<td>CV</td>
<td>0.2-200</td>
<td>0.508</td>
<td>34</td>
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<td>DPV</td>
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<td>0.77</td>
<td>35</td>
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<tr>
<td>GI/GCE</td>
<td>DPV</td>
<td>10-500</td>
<td>2.7</td>
<td>36</td>
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<tr>
<td>Graphene/GCE</td>
<td>SWV</td>
<td>0.1-20</td>
<td>0.032</td>
<td>37</td>
</tr>
<tr>
<td>BDD</td>
<td>DPV</td>
<td>1.98-13.87</td>
<td>0.16</td>
<td>This work</td>
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</tbody>
</table>

Abbreviations: GCE: glassy carbon electrode; DPV: differential pulse voltammetry; SWV: square-wave voltammetry; PGA : poly (glutamic acid); PAY: poly (acid yellow 9) ; Nafion/TiO₂–graphene/GCE: Nafion/TiO₂–graphene modified glassy carbon electrode ; PAYnano-TiO₂/GCE: poly (acid yellow 9)/nano-TiO₂ modified glassy carbon electrode ; C60/GCE: C60-modified glassy carbon electrode ; PANI-MWCNTs/GCE: a polyaniline–multi-walled carbon nanotubes (PANI–MWCNTs) composite modified electrode.
III-6. Interference study

The influence of some inorganic ions existing in physiological and environmental media has been studied on the detection of PCM. The interfering compounds selected are potassium nitrate \((K^+ , NO_3^-)\), potassium chloride \((K^+ , Cl^-)\), potassium sulfate \((2K^+, SO_4^{2-})\) and potassium hydrogen phosphate \((2K^+, HPO_4^{2-})\). Thus, to each 100mL solution of PCM of \((0.25g/L)\) in the \(0.1M\) HClO\(_4\) was successively added 0.5 ;1 ;1.5 ;2 ;2.5 ;5 and 10mL of each interfering compound of concentration 25g/L. From the recorded differential pulse voltammograms, the PCM oxidation peak current densities were deduced for each concentration of the interfering species. The interference \((X, \text{in} \%)\) of each compound on the PCM signal is calculated by the formula \(X = \left[\left(\frac{J'}{J}\right) \times 100\right] - 100\) where \(J'\) is the interfering signal of the PCM or the signal of the PCM in the presence of the interfering compound in solution, and \(J\) is the PCM signal in the absent of the interfering species. The results are gathered in the Table 3.

\[\text{Table 3 : Influence of the concentration of the interfering compounds on PCM oxidation peak current}\]

<table>
<thead>
<tr>
<th>Interfering compounds</th>
<th>Concentration in g/L of the interfering added</th>
<th>% change in peak current density in DPV (with (J_{PCM} = 100%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>((K^+ , NO_3^-))</td>
<td>\begin{align*} 0.124 \; 0.248 \; 0.369 \; 0.490 \; 0.610 \; 1.19 \; 2.27 \end{align*}</td>
<td>\begin{align*} -1.38 \; +3.13 \; -0.29 \; +0.50 \; -4.04 \; +0.12 \; +0.37 \end{align*}</td>
</tr>
<tr>
<td>((K^+ , Cl^-))</td>
<td>\begin{align*} 0.124 \; 0.248 \; 0.369 \; 0.490 \; 0.610 \; 1.19 \; 2.27 \end{align*}</td>
<td>\begin{align*} -2.42 \; -2.17 \; -4.68 \; +5.06 \; +4.06 \; +0.97 \; +4.99 \end{align*}</td>
</tr>
<tr>
<td>((2K^+, SO_4^{2-}))</td>
<td>\begin{align*} 0.124 \; 0.248 \; 0.369 \; 0.490 \; 0.610 \; 1.19 \; 2.27 \end{align*}</td>
<td>\begin{align*} -3.02 \; -0.71 \; +1.77 \; +0.577 \; +3.88 \; +3.75 \; +0.46 \end{align*}</td>
</tr>
<tr>
<td>((2K^+, HPO_4^{2-}))</td>
<td>\begin{align*} 0.124 \; 0.248 \; 0.369 \; 0.490 \; 0.610 \; 1.19 \; 2.27 \end{align*}</td>
<td>\begin{align*} -0.77 \; -4.74 \; -5.26 \; -5.07 \; -5.45 \; -5.04 \; -4.03 \end{align*}</td>
</tr>
</tbody>
</table>
These results show that the ions such as K$^+$, Cl$^-$, SO$_4^{2-}$, NO$_3^-$ and HPO$_4^{2-}$, which are 100 times more concentrated than paracetamol produce a negligible effect on its oxidation peak current in 0.1M HClO$_4$. The relative error recorded on the PCM signal is about ±5 %, which is the acceptable tolerance limit of the concentration of the interfering compounds or substances added. It can be considered that there has been no interference of the above-mentioned ions on the oxidation of PCM in the acidic medium. Such result indicated that this technique can be employed to determine the pharmaceuticals in highly loaded media with inorganic ions.

III-7. Application to Detection of the paracetamol in tomato and carrot juice

**Figure 11**: (A) Differential pulse voltammograms recorded on the BDD electrode in natural tomato juice and in the presence of various PCM concentrations. (B) Calibration plots of the current densities recorded versus PCM concentrations

**Figure 12**: (A) Differential pulse voltammograms recorded on the BDD electrode in natural carrot juice and in the presence of various PCM concentrations. (B) Calibration plots of the current densities recorded versus PCM concentrations

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The proposed method was applied to detect PCM in natural tomato and carrot juices under the optimized conditions described above. The freshly filtered, adequately diluted tomato and carrot juice were each enriched with certain PCM concentrations and added directly to the cell. The DPV technique was used to detect the PCM on the boron-doped diamond electrode. The voltammetric curves recorded in the tomato juice and the carrot juice are shown in the Figures 11A and 12A respectively. The oxidation peak of PCM in these two natural juices has the same potential as that recorded in perchloric acid (0.1M HClO₄), but the electroanalytical parameters recorded in terms of limit of detection and quantification are slightly lower than those have been recorded in the support electrolyte. This phenomenon is probably due to an intense background current corresponding of the juice, which can be linked to other electroactive components of the tomato and carrot matrix such as ascorbic acid (vitamin C) and sucrose [57]. Good linear dependencies between the recorded current densities and the PCM concentration in the tomato juice (R = 0,999, figure 10B) and the carrot juice (R = 0,9983, Figure 11B) were obtained. The reproducibility of the proposed methodology was observed on the basis of three (03) different measurements in the same fresh tomato and carrot juice containing the same concentration of PCM (5,2*10⁻⁵ mol/L) with coefficients of variation of 1,19 and 0,38 % respectively.

**Table 4 : Recovery rate of PCM quantities added to electrolytes of 0.1M HClO₄, tomato juice or carrot juice**

<table>
<thead>
<tr>
<th>supporting Electrolyte</th>
<th>PCM added mL</th>
<th>PCM found (mg)</th>
<th>recover rate±SD (%)</th>
<th>peak potential(V)</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>perchloric acid</td>
<td>0,4</td>
<td>7,96</td>
<td>7,95</td>
<td>99,83 ± 0,21</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>0,6</td>
<td>11,92</td>
<td>12</td>
<td>100,3 ± 0,53</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>19,8</td>
<td>20</td>
<td>100,9 ± 0,05</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>1,5</td>
<td>29,55</td>
<td>29,2</td>
<td>98,91 ± 0,92</td>
<td></td>
</tr>
<tr>
<td>tomato juice</td>
<td>0,4</td>
<td>7,96</td>
<td>8,03</td>
<td>100,77±1,19</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>0,6</td>
<td>11,92</td>
<td>12,31</td>
<td>103,24 ± 1,18</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>19,8</td>
<td>19,84</td>
<td>102,52 ± 0,10</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>1,5</td>
<td>29,55</td>
<td>28,83</td>
<td>97,54 ± 0,08</td>
<td></td>
</tr>
<tr>
<td>carrot juice</td>
<td>0,4</td>
<td>7,96</td>
<td>8,17</td>
<td>102,57 ± 0,38</td>
<td>0,7</td>
</tr>
<tr>
<td></td>
<td>0,6</td>
<td>11,92</td>
<td>13,05</td>
<td>109,41 ± 0,42</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>19,8</td>
<td>20,09</td>
<td>101,46 ± 0,008</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1,5</td>
<td>29,55</td>
<td>29,73</td>
<td>100,61 ± 0,09</td>
<td></td>
</tr>
</tbody>
</table>

The recovery rate obtained for the detection of PCM in these juices is presented in the table. These values indicate that the proposed method is well suited for PCM electroanalysis in tomato and carrot juices.

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IV - CONCLUSION

The BDD electrode showed interesting electroanalytical performances for the oxidation of PCM on its surface. It allowed to obtain very good results in the investigations carried out by cyclic and differential voltammetric techniques. The DPV technique, exploited with optimized parameters, enabled the detection of PCM in 0.1M HClO₄ solution with a detection limit of 0.16 μM and a recovery rate of 98.25 ± 0.91%. The same analytical procedure was applied to detect PCM in fresh natural tomato and carrot juices. The recorded voltammograms have the same characteristics as those obtained in 0.1M HClO₄. The determined recovery rates ranging between 94.56 ± 0.05 % and 103.24 ± 1.18 % in the tomato juice and between 97.05 ± 0.45 % and 109.41 ± 0.42 % in the carrot juice, show that the method developed is efficient. Thus, the use of BDD in conjunction with the DPV technique to detect PCM appears to have significant potential because of its application in various natural matrices.

ACKNOWLEDGEMENT

We are thankful to the Swiss National Funds for its financial support. They funded the project (IZ01Z0_146919) which durability helped this work to be undertaken.

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