Scientific Research Publishing

American Journal of Analytical Chemistry, 2023, 14, 434-450
https://www.scirp.org/journal/ajac
ISSN Online: 2156-8278
ISSN Print: 2156-8251

Differential Pulse Voltammetric Simultaneous Determination of Paracetamol and Omnipaque on Boron Doped Diamond Electrode: Application to Natural Tomato, Carrot, Cucumber Juices and Wastewater

Koffi Konan Martin[1], Sadia Sahi Placide[1], Kouadio Brou Albert[2], Gnamba Corneil Quand-Même[3], Fofié Thiery Auguste Appia[3], Koffi Konan Sylvestre[3], Lassiné Ouattara[3]

[1]UFR Environnement, Université Jean Lorougnon Guédé, Daloa, Côte d'Ivoire
[2]UFR Sciences et Technologies, Université Alassane Ouattara, Bouaké, Côte d'Ivoire
[3]Laboratoire de constitution et de réaction de la matière, UFR SSMT, Université Félix Houphouet Boiguy, Abidjan, Côte d'Ivoire
Email: konanmartinkoffi@gmail.com

How to cite this paper: Martin, K.K., Placide, S.S., Albert, K.B., Quand-Même, G.C., Appia, F.T.A., Sylvestre, K.K. and Ouattara, L. (2023) Differential Pulse Voltammetric Simultaneous Determination of Paracetamol and Omnipaque on Boron Doped Diamond Electrode: Application to Natural Tomato, Carrot, Cucumber Juices and Wastewater. *American Journal of Analytical Chemistry*, **14**, 434-450.
https://doi.org/10.4236/ajac.2023.1410025

Received: September 26, 2023
Accepted: October 27, 2023
Published: October 30, 2023

Abstract

This article describes the use of a boron-doped diamond electrode (BDDE) as an electrochemical sensor for the simultaneous determination of omnipaque (OMP) and paracetamol (PCM) in perchloric acid medium ($HClO_4$ 0.1 M) and in complex matrices such as tomato, carrot and cucumber juices and waste water from the Treichville University Hospital. Voltammetric studies allowed us to have well-defined oxidation peaks at distinct potentials of OMP (E = 0.5 V/SCE) and PCM (E = 0.7 V/SCE). Under optimized conditions, well-defined quantities of OMP and PCM, introduced simultaneously by metered additions, gave linear responses in concentration ranges of 259.8 - 467.2 µM for OMP and 58.73 - 116.3 µM PCM. The detection limits obtained are 7.23 µM and 3.6 µM respectively for OMP and PCM with recovery rates between 85.8% ± 0.1% and 92.6% ± 0.1% for OMP and between 99.9% ± 0.1% and 101.2% ± 0.4% for the PCM. This technique has been successfully used to simultaneously detect these pharmaceuticals in these complex environments. It allows recovery of OMP and PCM respectively up to 97.5% ± 0.0% and 91.6% ± 0.3% in tomato juice; 100.0% ± 0.0% and 95.2% ± 0.2% in carrot juice; 101.4% ± 0.1% and 97.3% ± 0.3% in cucumber juice; 100.1% ± 0.9% and 100.9% ± 0.1% in wastewater. The relevance of this technique for the simultaneous detection of OMP and PCM in tomato, carrot, cucumber juices and in waste water can be studied in the context of the contamination of certain fruits and vegetables by the substances organic pharmaceuticals released

into the environment without prior treatment.

Keywords

Omnipaque, Paracétamol, Differential Pulse Voltammetry, Boron Doped Diamond Electrode

1. Introduction

Numerous pharmaceutical molecules are increasingly consumed throughout the world, particularly in Côte d'Ivoire, and are liable to contaminate environmental waters (surface water, groundwater, etc.). A review of the literature has shown that pharmaceuticals are present in various aqueous matrices such as influents and effluents from wastewater treatment plants, surface water, groundwater, marine water and drinking water [1] [2].

Among the pharmaceutical products present in water are paracetamol and omnipak, an iodinated contrast agent commonly known as iohexol.

Paracetamol (PCM) or acetaminophen ($C_8H_9NO_2$) is a widely used analgesic and antipyretic. It is well tolerated and does not have the side effects of aspirin.

It is therefore commonly used for the relief of fever, headaches and minor pain, as well as for the management of more severe pain, where lower doses than other non-steroidal anti-inflammatory drugs are permitted, minimizing overall side effects [3] [4].

Omnipaque (OMP) or iohexol ($C_{19}H_{26}I_3N_3O_9$), like most contrast agents, is not biodegradable and highly soluble in water, in neutral and acidic media [5]. Iohexol is an iodine X-ray contrast media member, a class of drugs mainly used to enhance soft tissue imaging in diagnostic tests [6]. Consumption of iodine X-ray contrasts can reach 3.5 million kilograms in one year worldwide [7].

Humans can be treated with up to 200 g of iohexol per day [8] and consume up to 4 g of paracetamol per day [9]. Humans cannot digest these pharmaceutical products in a short space of time, and most of them are eliminated in the urine and faeces.

Persistent products like OMP and PCM [5] [10] are a danger to the aquatic environment and our environment in general. Duirk and al. showed in a 2011 study that iodine contrasts were frequently detected in raw water at a concentration of 2.7 µg/L [8] and Nikoulaou and al showed so in a 2007 study the presence of trace paracetamol in drinking water [11].

Because of their preference in clinical practice, paracetamol and iohexol are increasingly present either individually or simultaneously in the aquatic environment in the form of used products, products not consumed or products released by the human body. To protect this environment, paracetamol and iohexol must be detected, quantified and degraded individually or simultaneously before being released into the aqueous environment (wastewater, groundwater,

etc.)

It is therefore essential to find techniques or implement simple, rapid, effective and inexpensive methods for the individual and simultaneous detection and quantification of these discharges of pharmaceutical products, which become bioresistant pollutants in our soil and water. These pollutants then contaminate the plants and animals in our environment, leading to a growing risk of human intoxication.

Analytical methods have been developed for the individual determination of PCM and OMP, as well as for the simultaneous determination of these analytes with other pharmaceutical and biologically active compounds. These include chromatography [12] [13] [14] [15], spectrophotometry [16] [17] [18] and electroanalytical methods [19]-[27]. However, very little work has been done with a method for the simultaneous voltammetric determination of PCM and OMP in pharmaceutical dosage forms or biological fluids.

Voltammetric methods, in particular differential pulse voltammetry (DPV), are considered an important electrochemical technique used in the development of analytical procedures for the individual and/or simultaneous determination of a wide range of compounds of pharmaceutical interest because they provide reliable, rapid, sensitive, precise, accurate and simple results [28] [29].

Boron-doped diamond electrode (BDDE) has been widely used in electroanalytical applications for pharmaceutical compounds [24] [30] [31] [32] [33] [34], because of unique properties, such as a very wide working potential window, very low and stable background current, long term stability, low sensitivity to dissolved oxygen, and an extreme electrochemical stability in both alkaline and acidic media [35]. In this work, the development of a reliable, low cost and selective method based on DPV using a cathodically pretreated boron-doped diamond electrode for the individual and simultaneous determination of PCM and OMP in pharmaceutical formulations has been proposed.

2. Experimental Method

2.1. Reagents and Solutions

The sulfuric acid (H_2SO_4, 95% - 98%) was purchased from SIGMA-ALDRICH, USA, and the perchloric acid ($HClO_4$, 60%) solution was obtained from Panreac, GERMANY. Paracetamol 500 mg and Iohexol (Omnipaque™ 300 mg I/mL) were supplied respectively by the laboratories of BAILY-CREAT (France) and GE Healthcare (France). A stock solution of paracetamol was prepared by dissolving an accurate mass of the drug in an appropriate volume of $HClO_4$. Stocks of paracetamol and omnipaque solutions were prepared by disolving a precise quantity of paracetamol or omnipaque in a certain volume of perchloric acid ($HClO_4$ 0.1 M).

The working solutions for the voltammetric investigations were prepared by dilution of stocks solutions. All solutions were protected from light and used within 24 h to avoid decomposition. 0.1 M of $HClO_4$ is used to prepare the sup-

porting electrolytes. Distilled water was used to prepare all the solutions.

2.2. Equipment and Electrodes

The voltammetric measurements were performed using an AUTOLAB PGSTAT 20 (Ecochemie) connected to a potentiostat equipped with a USB 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 cm^2. 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.

2.3. Analytical Procedures

Analytical curves in the supporting electrolyte ($HClO_4$) were constructed and used to produce a calibration curve. Simultaneous DPV measurements were carried out, for iohexol concentrations varying alone up to 262.6 µM with that of fixed PCM, PCM concentrations varying alone up to 210 µM with that of fixed OMP, PCM and OMP concentrations varying.

Prior to the experiments, the BDD electrode was electrochemically pretreated in a 0.5 mol/L H_2SO_4 solution. For this pre-treatment, an anodic pre-treatment (+2 V, 15 s) is followed by a cathodic pre-treatment (−2 V, 90 s). In this way, the BDD surface was cleaned of all impurities, then rendered predominantly hydrogenated [36].

By the metered addition method, suitable quantities of PCM and/or OMP were taken from the stock solutions and introduced into the measuring cell containing 100 ml of the carrier.

After stirring, with a magnetized bar, to homogenize the mixture obtained, DPV curves were recorded at each test.

The calibration curves for each of the species were then represented for each series of experiments.

The detection limits (LOD) and quantification limits (LOQ) of PCM and OMP were then calculated from the following equations: LOD = 3 * SD/b and LOQ = 10 * SD/b with SD the standard deviation and b the slope of the calibration curve.

3. Results and Discussion

3.1. Electrochemical Behavior of PCM and OMP

In order to determine the best conditions for studying the electrochemical behavior of PCM and OMP on the boron-doped diamond electrode (BDDE), our previous work [37] enabled us to choose the perchloric acid solution with a concentration of 0.1 M at pH = 0.217 as the support medium in which the best vol-

tammetric responses are obtained.

The electrochemical behavior of PCM and OMP on BDDE has been studied by CV (Figure 1) respectively illustrates the cyclic voltammetric profile of the electrochemical oxidation of the PCM with a concentration of 2 g/L (**curve (b)**) and of the OMP (**curve (c)**) with a concentration of 4 g/L in a 0.1 M $HClO_4$ solution.

As can be seen, PCM and OMP have only a well-defined oxidation peak at 0.8 V/SCE (**curve (b)**), 0.6 V/SCE (**curve (c)**), respectively, without the true presence of a cathode peak. It is clear that the electrochemical reactions of these compounds at the BDDE level are irreversible. These curves were recorded under the pretreatment conditions indicated above, in order to have better resolutions of the oxidation peaks of the compounds studied.

On the same Figure 1, **curve (d)** shows the simultaneous behavior of the PCM and of the OMP on the BDDE in the same support electrolyte. Two oxidation peaks are observed at very distinct potentials, that is to say 0.8 V/SCE and 0.6 V/SCE respectively as previously.

The good resolution and the good separation of these oxidation peaks clearly show that studies of detection and quantification of PCM and OMP can be carried out simultaneously in the reaction medium on the surface of our BDDE without interference.

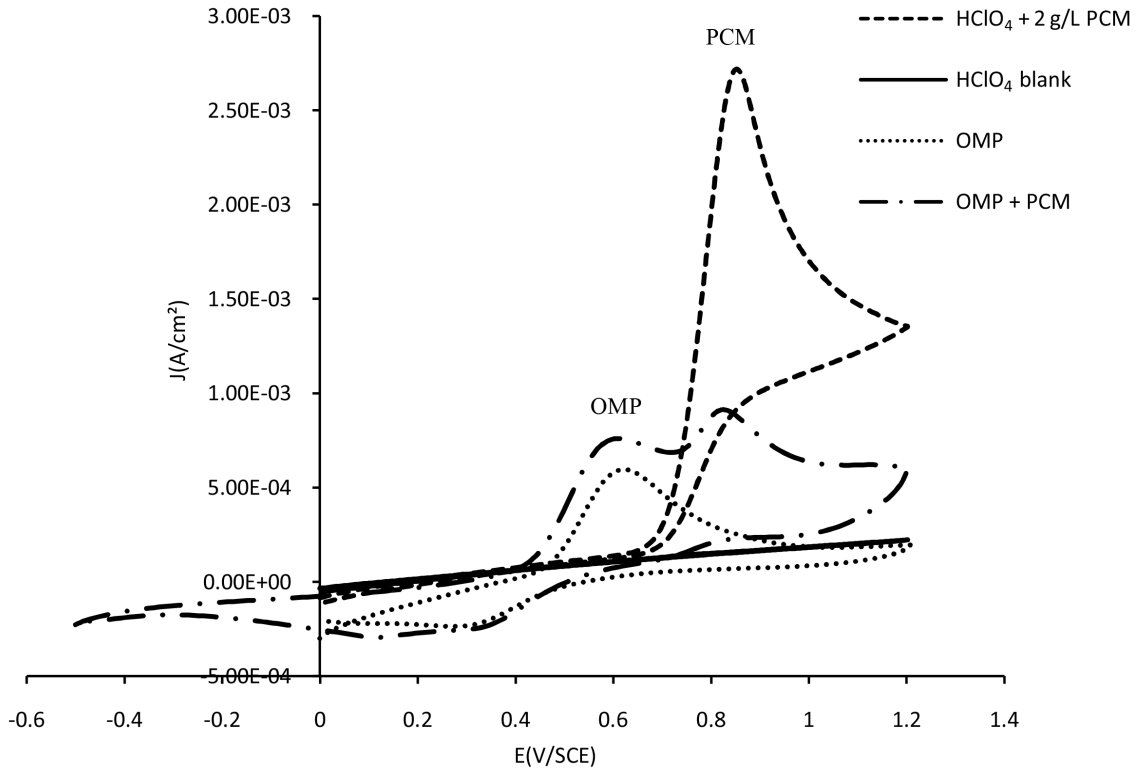


Figure 1. Cv voltammograms of BDD electrode in $HClO_4$ 0.1 M electrolytes: (a) blank ——, (b) only 2 g/L of PCM – –, (c) only 4 g/L of OMP ....., (d) 2 g/L of PCM + 4 g/L of OMP – · – ·: Working electrode: DDB (1 cm^2), Counter electrode: Pt wound, Reference electrode: SCE. Scanning rate: 50 mV/s.

3.2. Individual and Simultaneous Determination of PCM and OMP

Before recording the voltammograms with differential pulses for the individual or simultaneous determination of the PCM and of the OMP using a BDDE pretreated anodially then cathodically, the influence of the key parameters in DPV on the peak potential and the peak current were studied in the following ranges: pretreatment potential ($-2.5 \leq Ep \leq 3$ V/SCE); pretreatment time ($15 \leq tEp \leq 300$ s); modulation amplitude ($0.01 \leq AM \leq 0.5$ V/SCE); modulation time ($0.005 \leq tM \leq 0.25$ s); step potential ($0.001 \leq Ep \leq 0.02$ V/SCE). The optimized parameters obtained and used in this work are therefore: Ep = −2 V/SCE, tEp = 90 s, AM = 0.1 V/SCE, tM = 0.05 s and Ep = 0.007 V/SCE [37].

3.3. Individual Determination of PCM and OMP

Figure 2(a) shows the voltammetric response of the oxidation peaks for each of the concentrations of PCM ranging from 0 µM to 13.87 µM. Voltamograms recorded under the optimum conditions obtained show that the oxidation peaks of the PCM are all observed at the same potential (E = 0.7 V/SCE), whatever its concentrations. **Figure 2(b)** shows the intensity of the oxidation peak current of the PCM increases linearly with paracetamol concentration. The limit of detection and quantification are 0.167 µM and 0.559 µM, respectively, using the equations LOD = 3 SD/b and LOQ = 10 SD/b.

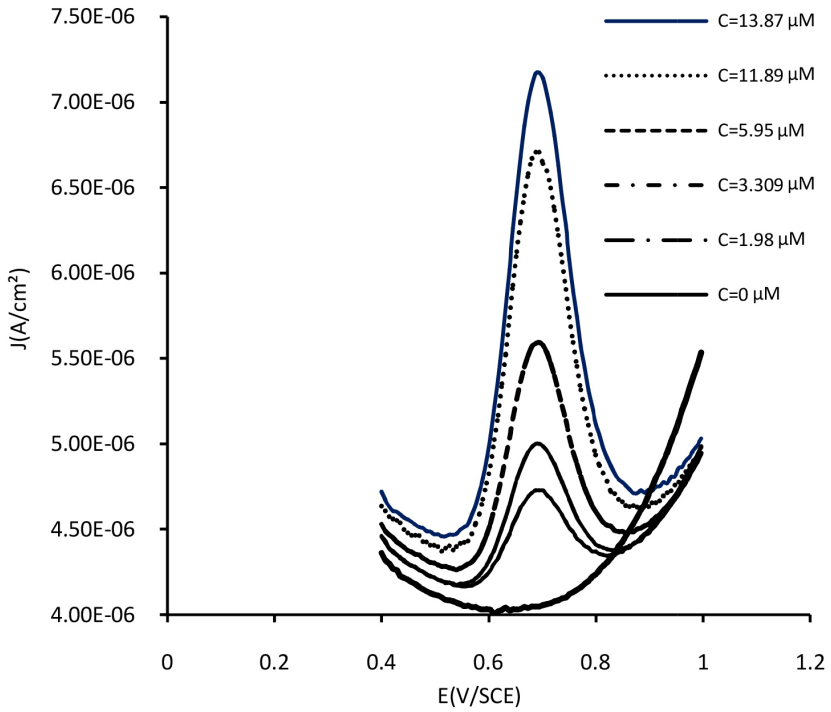
Three series of independent measurements, each with five (05) different concentrations of paracetamol, were carried out and used to determine the recovery rate, which is close to 98%. A calibration curve of $R^2 = 0.9999$ was obtained [37].

All these results show the reliability, reproducibility, sensitivity and selectivity of the method.

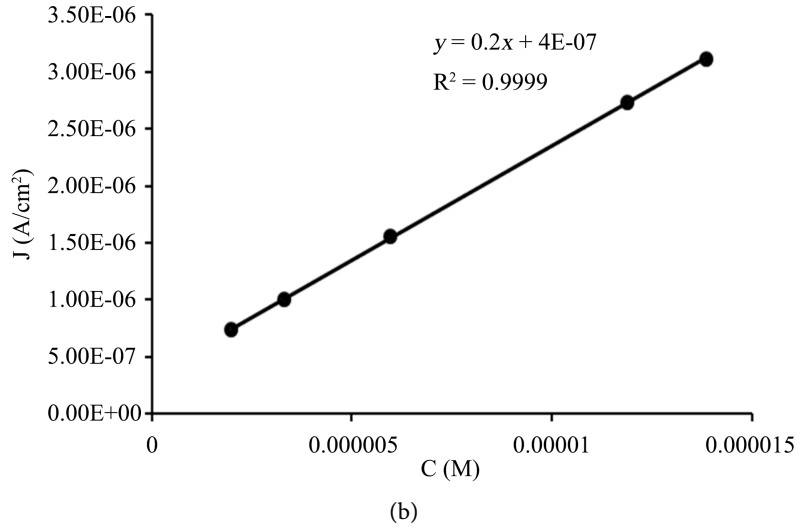
In **Figure 3(a)**, the voltamograms recorded under the same optimum conditions show that the oxidation peaks of the OMP are all observed at the same potential (E = 0.5 V/SCE) for the concentrations varying from 0 to 52.43 µM. An increase in the intensity of the oxidation peak current of the OMP with its concentration is observed in **Figure 3(b)**, giving a linear calibration curve of $R^2 = 0.9996$. Applying the same experimental conditions, the calculated limit of detection and quantification are 0.77 µM and 2.57 µM respectively with recovery rates ranging from 98.7% to 100.7%.

3.4. Simultaneous Determination of PCM and OMP

For the simultaneous determination of OMP and PCM, DPV were performed for their mixture keeping the concentration of one species constant while changing that of the other. Thus, the separate determination of the OMP in the concentration range 71.63 - 262.6 µM was carried out in solutions containing PCM at the fixed concentration of 63.91 µM, using BDDE (**Figure 4(a)**). Then, the concentration of the OMP was fixed at 115.4 µM and that of the PCM varied in the range from 62.71 to 210 µM (**Figure 4(b)**). Examination of **Figure 4(a)** makes it possible to conclude that the oxidation peak current of the OMP



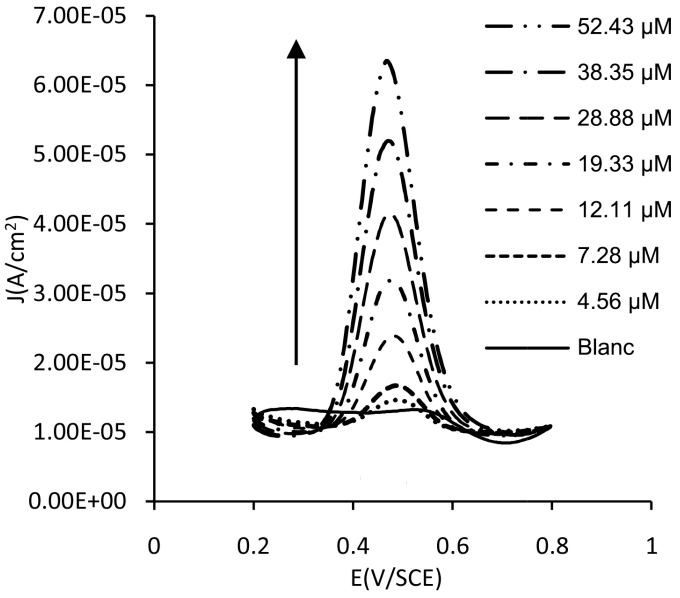
(a)



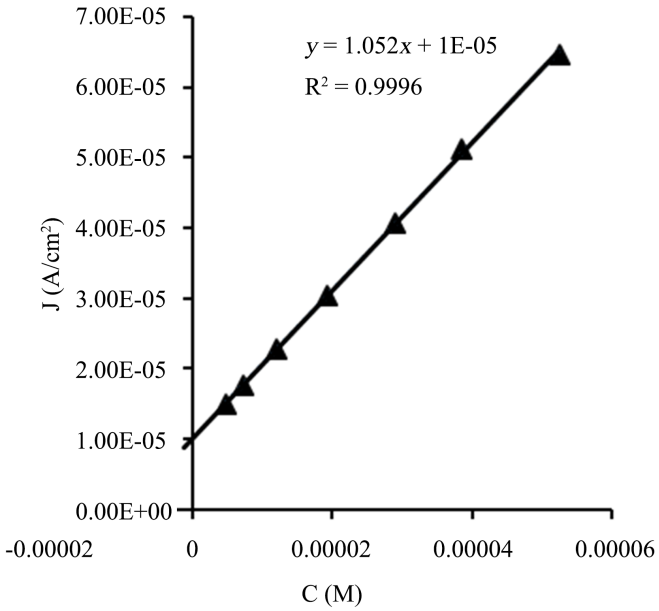
(b)

Figure 2. (a) Differential pulse voltammograms at different concentrations of paracetamol in HClO4 solution on BDD electrode by DPV; the concentration varies from 0 µM to 19.8 µM, (b) Calibration curve of method.

increases regularly as its concentration increases in the presence of a fixed concentration of PCM. Similarly, the oxidation peak current for the PCM increases regularly as its concentration increases in the presence of a fixed concentration of OMP, as shown in **Figure 4(b)**. In addition, the slope of the linear regression line for the calibration graph for each species in the mixture was almost the same as for the individual calibration graph, concluding that these two species do not interfere in the determination of the other.



(a)

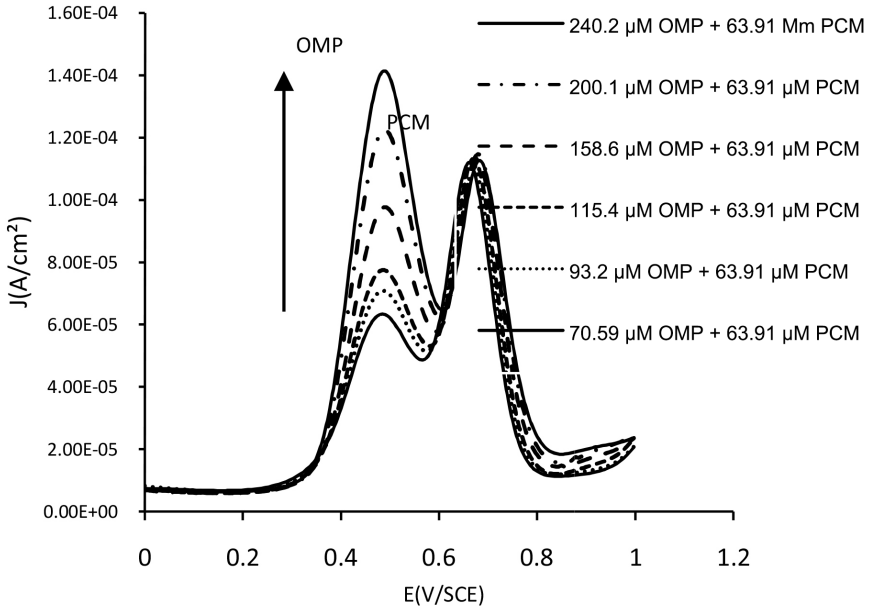


(b)

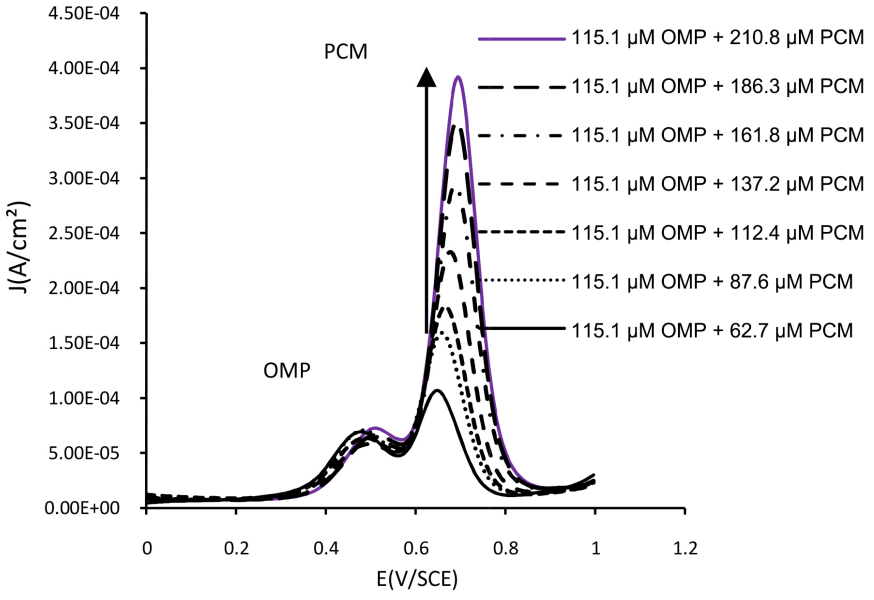
Figure 3. (a) Differential pulse voltammograms at different concentrations of omnipaque in $HClO_4$ solution on BDD electrode by DPV; the concentration varies from 0 µM to 52.43 µM, (b) Calibration curve of method.

The performance of the boron-doped diamond electrode was evaluated by varying the concentrations of OMP and PCM. Peak currents increased linearly with OMP concentrations in the range of 259.8 to 467.2 µM and PCM concentrations in the range of 58.73 to 116.3 µM with good correlation coefficients (**Figure 6(c)**).

The calibration curves for OMP and PCM (**Figure 5(b)** and **Figure 5(c)**) each show a good linear response.



(a)



(b)

Figure 4. DPV curves with different concentrations of OMP (71.63 - 262.6 µM) in the presence of a fixed concentration of 63.91 µM PCM (a); of PCM (62.71 - 210 µM) in the presence of a fixed concentration of 115.4 µM de OMP (b). Epr = −2 V/SCE, tEp = 90 s, MA = 0.1 V/SCE, tM = 0.05 s and ΔEp = 0.007 V/SCE.

The equations of these curves are respectively $J(A/cm^2) = -0.0001 + 0.9109$ $[C/(mol{\cdot}L^{-1})]$ and $J(A/cm^2) = -0.0001 + 4.547$ $[C/(mol{\cdot}L^{-1})]$, with regression coefficients $R^2 = 0.9998$ and $R^2 = 0.9993$. The calculated detection limits are 7.23 µM and 3.6 µM, respectively.

It should be noted that when comparing these results with those obtained for the separate determination of OMP and PCM, the detection limits obtained are

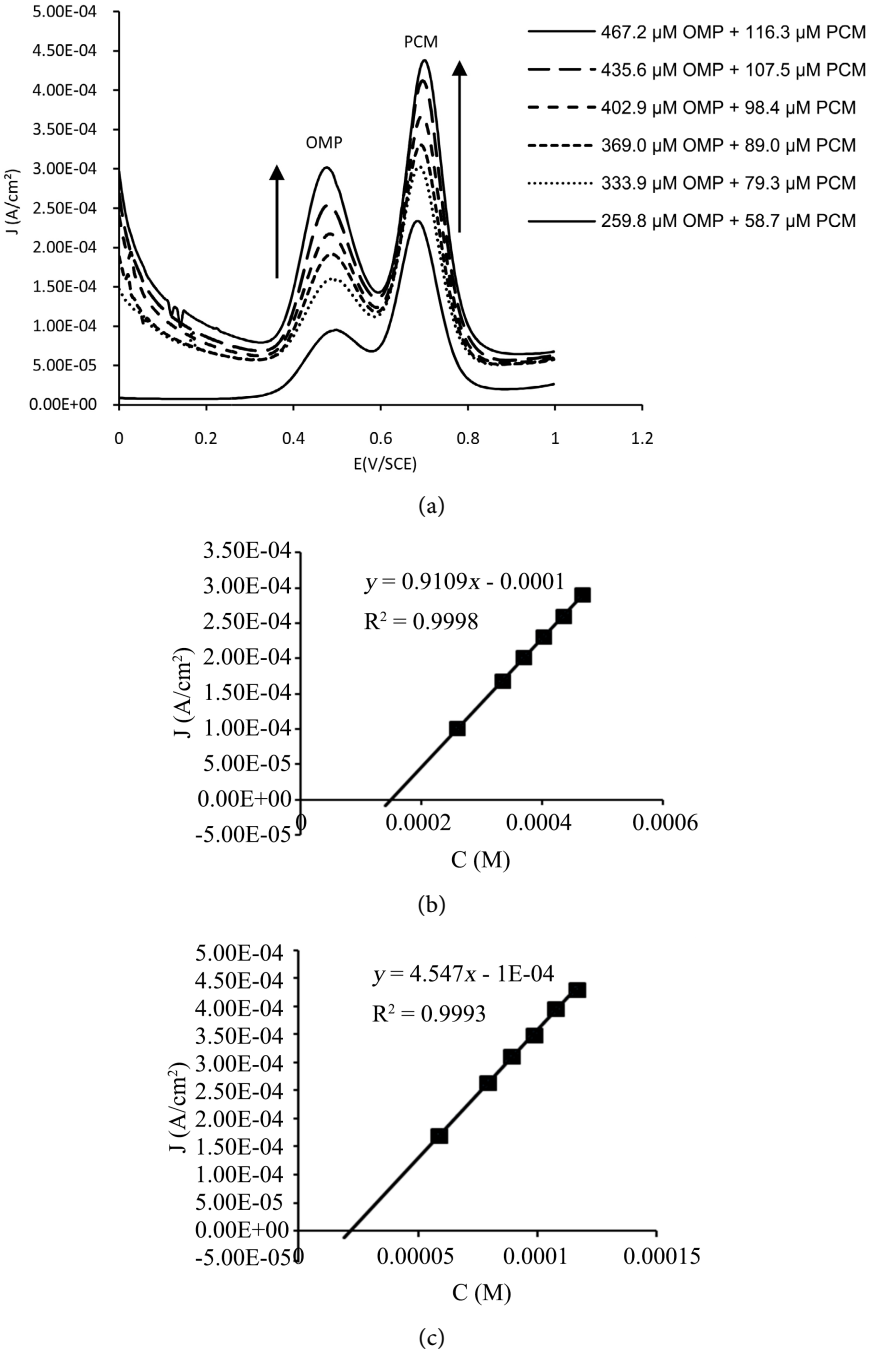


Figure 5. DPV curves with different concentrations of OMP (259.8 - 467.2 µM) and different concentrations of PCM (58.73 - 116.3 µM) (a); Calibration curves for OMP (b) and PCM (c). Epr = −2 V/SCE, tEp = 90 s, MA = 0.1 V/SCE, tM = 0.05 s and ΔEp = 0.007 V/SCE.

of the same order of magnitude. Determination of OMP and PCM in the same matrix is as effective as separate determination.

The high recovery rates of OMP and PCM (Table 1) obtained in this study demonstrate the efficacy of the method and its applicability to the simultaneous detection of these two pharmaceutical compounds in perchloric acid medium.

Table 1. Recovery rates for simultaneous detection of OMP and PCM in perchloric acid.

Drugs	Number of the sample	Added (mL)	Added (μM)	Found (μM)	Recovery rates (% ± SD)
OMP	1	12	259.8	223.17	**85.8 ± 0.3**
	2	16	333.94	296.91	**88.9 ± 0.1**
	3	18	369.04	334.06	**90.5 ± 0.2**
	4	20	402.92	366.13	**90.8 ± 0.1**
	5	22	435.65	399.36	**91.6 ± 0.1**
	6	24	467.27	433.09	**92.6 ± 0.4**
PCM	1	0.5	58.79	59.09	**100.5 ± 0.5**
	2	0.7	79.34	80	**100.8 ± 0.4**
	3	0.8	89.08	90.18	**101.2 ± 0.4**
	4	0.9	98.47	98.49	**100.0 ± 0.4**
	5	1	107.55	108.77	**101.1 ± 0.1**
	6	1.1	116.32	116.31	**99.9 ± 0.1**

3.5. Interference Studies

The selectivity of the proposed method was evaluated by the addition of any interfering agents (frequently present in the pharmaceutical formulations analyzed), such as chlorine, magnesium, sulfate, potassium and sodium ions with variable contractions in solution containing a fixed concentration of PCM and OMP. The selectivity of this method was also tested in the presence of ceftriaxone, an organic pharmaceutical compound.

The corresponding oxidation peak currents were compared with those obtained in the absence of each interferer. Analysis of the responses obtained led to the conclusion that these elements do not significantly interfere (<5%) in the simultaneous determination the PCM and the OMP under the proposed working conditions.

3.6. Comparison Method

Voltammetric studies for the individual determination of PCM [38] [39] [40] or OMP [41] by DPV have given low limits of detection and quantification, and other studies have introduced techniques for the simultaneous determination of PCM and one or two other pharmaceutical organic substances with also low limits of detection and quantification. However, the simultaneous determination of PCM and OMP in $HClO_4$ 0.1 M medium has been the subject of very little or no work, while consulting the literature. In this work, the technique used to determine the PCM and the OMP simultaneously is selective, sensitive and precise in view of the results obtained.

3.7. Application to the Simultaneous Detection of OMP and PCM in Complex Media

To assess the applicability of the proposed method, OMP and PCM were detected simultaneously in complex media such as wastewater, tomato, cucumber and carrot juice. These complex media were obtained by diluting 1 mL of wastewater or juice in 0.1 M perchloric acid to obtain 100 mL of solution for each series of voltammetric measurements.

The analysis technique developed with these optimized DPV parameters was applied to the simultaneous detection of OMP and PCM in these complex media.

Well-defined quantities of OMP and PCM were introduced by simultaneous dosed additions to the same carrier media. The different voltammogram responses (Figure 6) obtained were used to calculate the overlap rates of the added quantities with the equations of the calibration curves obtained with each of the pharmaceutical substances (Table 2).

Table 2. Recovery rates for simultaneous detection of OMP and PCM in perchloric acid, tomato, carrot, cucumber juice and wastewater.

Electrolye support	OMP				PCM			
	Added mL	Added µM	Found µM	Recover rate ± SD	Added mL	Added µM	Found µM	Recover rate ± SD
Perchloric acid	12	259.8	223.1	**85.8 ± 0.1**	0.5	58.8	59.1	**100.5 ± 0.5**
	16	333.9	269.9	**88.9 ± 0.2**	0.7	79.3	80	**100.8 ± 0.4**
	18	369	334	**90.5 ± 0.1**	0.8	89.1	90.1	**101.2 ± 0.4**
	22	435.6	399.3	**91.6 ± 0.1**	1	107.5	108.7	**101.1 ± 0.1**
Tomato	8	179.9	175.4	**97.5 ± 0.0**	0.3	36.6	-	-
	12	259.8	201.3	**77.5 ± 0.1**	0.5	58.8	53.8	**91.6 ± 0.3**
	18	369	279.3	**75.7 ± 0.0**	0.8	89.1	72.6	**81.4 ± 0.3**
	22	435.6	310.6	**71.3 ± 0.1**	1	107.5	86.2	**80.1 ± 0.1**
Carrot	8	179.9	179.9	**100.0 ± 0.0**	0.3	36.6	-	-
	12	259.8	214.1	**82.4 ± 0.1**	0.5	58.8	56	**95.2 ± 0.2**
	18	369	298.1	**80.7 ± 0.2**	0.8	89.1	74.5	**83.6 ± 0.2**
	22	435.6	364.2	**83.6 ± 0.3**	1	107.5	84.7	**78.7 ± 0.1**
Concumber	8	179.9	182.4	**101.4 ± 0.1**	0.3	36.6	-	-
	12	259.8	252.8	**97.3 ± 0.2**	0.5	58.8	57.2	**97.3 ± 0.3**
	18	369	262.2	**71.8 ± 0.1**	0.8	89.1	80.9	**90.8 ± 0.8**
	22	435.6	308.7	**70.8 ± 0.1**	1	107.5	86.3	**80.2 ± 0.1**
Eau usée	8	179.9	-	-	0.3	36.6	-	-
	12	259.8	260	**100.1 ± 0.9**	0.5	58.8	59.3	**100.9 ± 0.1**
	18	369	327.4	**88.7 ± 0.8**	0.8	89.1	81.4	**91.4 ± 0.2**
	22	435.6	373.9	**85.8 ± 0.2**	1	107.5	96.9	**90.1 ± 0.2**

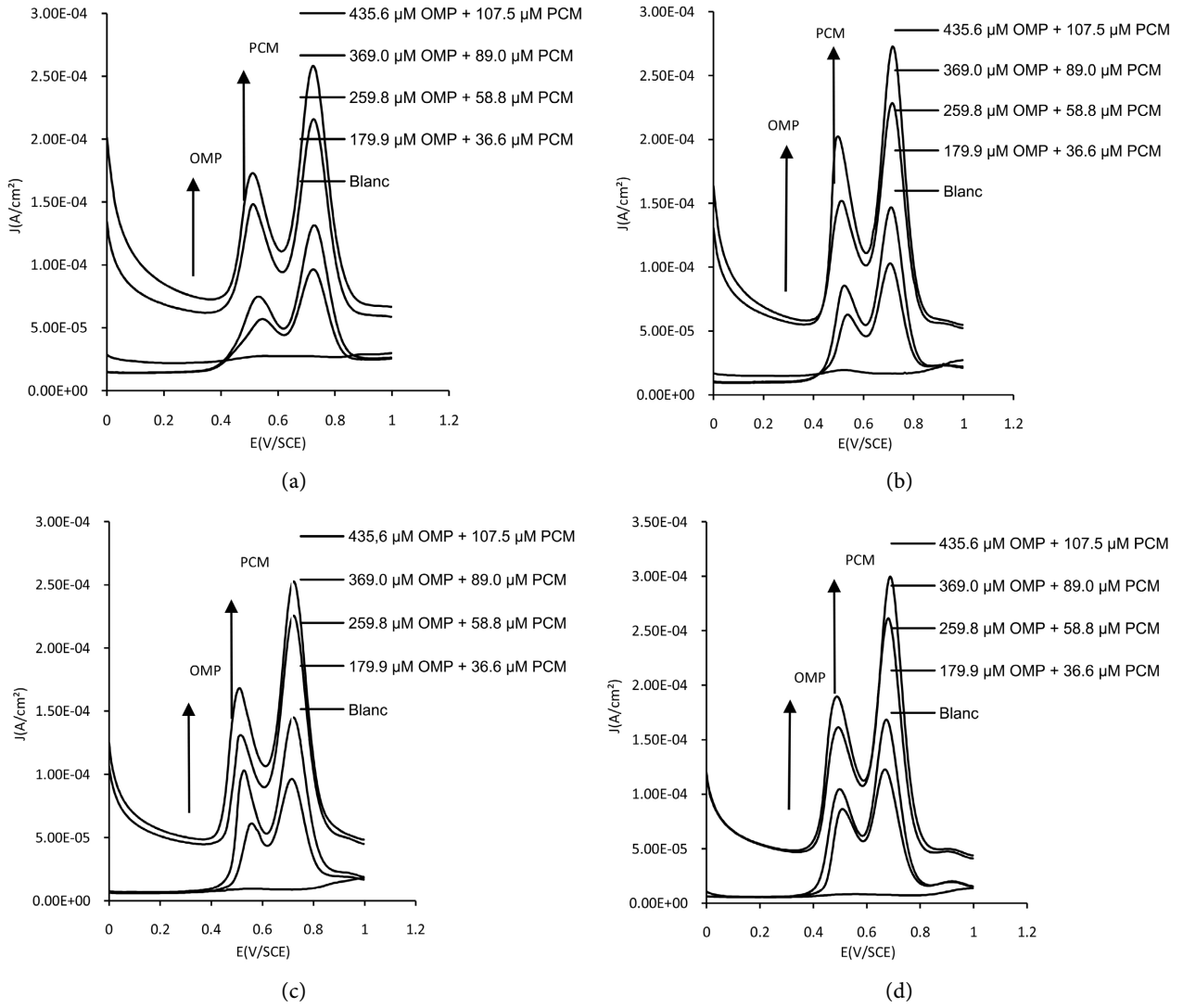


Figure 6. DPV for a mixture of varying concentrations of OMP (0 - 35.65 µM) and PCM (0 - 107.57 µM) in (A) tomato, (B) carrot, (C) cucumber juice or (D) wastewater medium; Epr = −2 V/SCE, tEp = 90 s, MA = 0.1 V/SCE, tM = 0.05 s and ΔEp = 0.007 V/SCE.

The voltammograms presented on Figure 6 show an increase in the current density of the OMP and PCM oxidation peaks in the same order of magnitude with their concentrations. Moreover, in each electrolyte, the potential of the oxidation peaks related to OMP is 0.5 V/SCE and that related to PCM is 0.7 V/SCE as in the case of their individual study in 0.1 M $HClO_4$ medium.

The reproducibility and repeatability of the measurements were also demonstrated during these series of experiments.

Good linear dependencies between the recorded current densities and the concentrations of OMP and PCM in tomato, carrot, cucumber juice, and wastewater were obtained.

The calculated recovery rates are shown in Table 2. They vary from 71.3% ± 0.1% to 101.2% ± 0.4% from one complex medium to another. These fairly high values show that OMP and PCM can be clearly detected simultaneously in com-

plex media of tomato juice, carrot juice, cucumber juice and wastewater without interfering with each other, hence the reliability of the method employed.

4. Conclusions

To our knowledge, this is one of the first reports on the simultaneous determination of OMP and PCM by a cyclic or differential voltammetric technique using BDDE. This work demonstrates that BDDE, which has excellent electrochemical properties, is suitable for the simultaneous voltammetric determination of OMP and PCM.

The results obtained allow us to conclude that DPV can be used with many advantages for the quantitative determination of these drugs, alone or in combination, as they are commonly found in pharmaceutical formulations.

This DPV technique, operated with optimized parameters, enabled the simultaneous detection of OMP and PCM in 0.1 M $HClO_4$ solution with very low limits and fairly high recoveries. The same analytical procedure was used to simultaneously detect OMP and PCM in fresh natural juices from tomatoes, carrots and cucumbers, and in wastewater from Treichville University Hospital. The voltammograms recorded show the same characteristics as those obtained in 0.1 M $HClO_4$. The high recovery rates determined, ranging from 71.3% ± 0.1% to 101.4% ± 0.1% in the various complex media, show that the method developed is effective. Thus, the use of BDDE in the DPV technique for the simultaneous detection of OMP and PCM appears to have significant potential due to its application in various natural matrices.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Schlüsener, M., Löffler, D. and Ternes, T. (2008) List of the Relevant PPs. Projet Européen KNAPPE, Deliverable D11, European Commission, 6th Framework Program, 63.

[2] Sadezky, A., Löffler, D. and Ternes, T. (2008) Proposal of an Environmental Indicator and Classification System of Pharmaceutical Product Residues for Environmental Management. Projet Européen KNAPPE, Deliverable D12, European Commission, 6th Framework Program, 92.

[3] Goyal, R.N. and Singh, S.P. (2006) Voltammetric Determination of Paracetamol at C60-Modified Glassy Carbon Electrode. *Electrochimica Acta*, **51**, 3008-3012. https://doi.org/10.1016/j.electacta.2005.08.036

[4] Dongre, V.G., Shah, S.B., Bayes, G.S., Phadke, M. and Jadhav, V.K. (2009) Simultaneous Determination of Etodolac and Acetaminophen in Tablet Dosage Form by RP-LC. *Chromatographia*, **69**, 1019-1023. https://doi.org/10.1365/s10337-009-0974-6

[5] Lv, X.D., Cui, Y.H., Xue, W.J., Yang, S.Q., Li, J.Y. and Liu, Z.Q. (2019) Comparison of Inert and Noninert Cathode in Cathode/Fe3þ/Peroxymonosulfate Processes on

Iohexol Degradation. *Chemosphere*, **223**, 494-503. https://doi.org/10.1016/j.chemosphere.2019.02.079

[6] Jeong, J., Jung, J., Cooper, W.J. and Song, W. (2010) Degradation Mechanisms and Kinetic Studies for the Treatment of X-Ray Contrast Media Compounds by Advanced Oxidation/Reduction Processes. *Water Research*, **44**, 4391-4398. https://doi.org/10.1016/j.watres.2010.05.054

[7] Tian, F.X., Xu, B., Lin, Y.L., Hu, C.Y., Zhang, T.Y. and Gao, N.Y. (2014) Photodegradation Kinetics of Iopamidol by UV Irradiation and Enhanced Formation of Iodinated Disinfection By-Products in Sequential Oxidation Processes., *Water Research*, **58**, 198-208. https://doi.org/10.1016/j.watres.2014.03.069

[8] Duirk, S.E., Lindell, C., Cornelison, C.C., Kormos, J., Ternes, T.A., Attene-Ramos, M., Osiol, J., Wagner, E.D., Plewa, M.J. and Richardson, S.D. (2011) Formation of Toxic Iodinated Disinfection By-Products from Compounds Used in Medical Imaging. *Environmental Science & Technology*, **45**, 6845-6854. https://doi.org/10.1021/es200983f

[9] Paracetamol. https://www.drugs.com/paracetamol.html

[10] Oulton, R.L., Kohn, T. and Cwiertny, D.M. (2010) Pharmaceuticals and Personal Care Products in Effluent Matrices: A Survey of Transformation and Removal during Wastewater Treatment and Implications for Wastewater Management. *Journal of Environmental Monitoring*, **12**, 1956-1978. https://doi.org/10.1039/c0em00068j

[11] Nikolaou, A., Meric, S. and Fatta, D. (2007) Occurrence Patterns of Pharmaceuticals in Water and Wastewater Environments. *Analytical and Bioanalytical Chemistry*, **387**, 1225-1234. https://doi.org/10.1007/s00216-006-1035-8

[12] Saracino, M.A., Petio, C., Vitali, M., Franchini, L. and Raggi, M.A. (2009) Determination of Orphenadrine Plasma Levels Using HPLC with Diode Array Detection and a Novel Solid-Phase Extraction Procedure in Psychiatric Patients. *Journal of Pharmaceutical and Biomedical Analysis*, **50**, 501-506. https://doi.org/10.1016/j.jpba.2009.05.010

[13] Wang, A., Sun, J., Feng, H., Gao, S. and He, Z. (2008) Simultaneous Determination of Paracetamol and Caffeine in Human Plasma by LC-ESI-MS. *Chromatographia*, **67**, 281-285. https://doi.org/10.1365/s10337-007-0493-2

[14] Arayane, M.S., Sultana, N. and Siddiqui, F.A. (2009) Simultaneous Determination of Paracetamol and Orphenadrine Citrate in Dosage Formulations and in Human Serum by RP-HPLC. *Journal of the Chinese Chemical Society*, **56**, 169-174. https://doi.org/10.1002/jccs.200900024

[15] Darwish, K., Salama, I., Mostafa, S. and El-Sadek, M. (2012) Validated Stability-Indicating Reversed-Phase-HPLC Method for Simultaneous Determination of Orphenadrine Citrate, Caffeine and Aspirin. *Chemical and Pharmaceutical Bulletin*, **60**, 1426-1436. https://doi.org/10.1248/cpb.c12-00596

[16] Walash, M.I., Belal, F.F., Eid, M.I. and Mohamed, S.A.A. (2011) Spectrophotometric Determination of Tizanidine and Orphenadrine via Ion Pair Complex Formation Using Eosin Y. *Chemistry Central Journal*, **5**, Article No. 60. https://doi.org/10.1186/1752-153X-5-60

[17] Dinc, E. and Onur, F. (1998) Application of a New Spectrophotometric Method for the Analysis of a Ternary Mixture Containing Metamizol, Paracetamol and Caffeine in Tablets. *Analytica Chimica Acta*, **359**, 93-106. https://doi.org/10.1016/S0003-2670(97)00615-6

[18] Khoshayand, M.R., Abdollahi, H., Shariatpanahi, M., Saadatfard, A. and Mohammadi, A. (2008) Simultaneous Spectrophotometric Determination of Paracetamol,

Ibuprofen and Caffeine in Pharmaceuticals by Chemometric Methods. *Spectrochimica Acta Part A*, **70**, 491-499. https://doi.org/10.1016/j.saa.2007.07.033

[19] Li, S.J., Deng, D.-H., Pang, H., Liu, L., Xing, Y. and Liu, S.-R. (2012) Preparation of Electrochemically Reduced Graphene Oxide-Modified Electrode and Its Application for Determination of *p*-Aminophenol. *Journal of Solid State Electrochemistry*, **16**, 2883-2889. https://doi.org/10.7312/li--16274-017

[20] Kachoosangi, R.T., Wildgoose, G.G. and Compton, R.G. (2008) Sensitive Adsorptive Stripping Voltammetric Determination of Paracetamol at Multiwalled Carbon Nanotube Modified Basal Plane Pyrolytic Graphite Electrode. *Analytica Chimica Acta*, **618**, 54-60. https://doi.org/10.1016/j.aca.2008.04.053

[21] Svorc, L., Tomcik, P., Svtkov, J., Rievaj, M. and Bustin, D. (2012) Simultaneous Square-Wave Voltammetric Determination of Paracetamol, Caffeine and Orphenadrine in Pharmaceutical Formulations Using a Cathodically Pretreated Boron-Doped Diamond Electrode. *Food Chemistry*, **135**, 1198-1204. https://doi.org/10.1016/j.foodchem.2012.05.052

[22] Frag, E.Y.Z., Ali, T.A., Mohamed, G.G. and Awad, Y.H.H. (2012) Construction of Different Types of Ion-Selective Electrodescharacteristic Performances and Validation for Directpotentiometric Determination of Orphenadrine Citrate. *International Journal of Electrochemical Science*, **7**, 4443-4464. https://doi.org/10.1016/S1452-3981(23)19552-6

[23] Nebsen, M., Abd El-Rahman, M.K., El-Kosasy, A.M., Salem, M.Y. and El-Bardicy, M.G. (2011) Miniaturized Membrane Sensors for the Determination of Orphenadrine Citrate Portug. *Electrochimica Acta*, **29**, 165-176. https://doi.org/10.4152/pea.201103165

[24] Lourenao, B.C., Medeiros, R.A., Rocha-Filho, R.C., Mazo, L.H. and Fatibello-Filho, O. (2009) Simultaneous Voltammetric Determination of Paracetamol and Caffeine in Pharmaceutical Formulations Using a Boron-Doped Diamond Electrode. *Talanta*, **78**, 748-752. https://doi.org/10.1016/j.talanta.2008.12.040

[25] Sanghavi, B.J. and Srivastava, A.K. (2010) Simultaneous Voltammetric Determination of Acetaminophen, Aspirin and Caffeine Using an *In-Situ* Surfactant-Modified Multiwalled Carbon Nanotube Paste Electrode. *Electrochimica Acta*, **55**, 8638-8648. https://doi.org/10.1016/j.electacta.2010.07.093

[26] Ghorbani-Bidkorbeh, F., Shahrokhian, S., Mohammadi, A. and Dinarvand, R. (2010) Simultaneous Voltammetric Determination of Tramadol and Acetaminophen Using Carbon Nanoparticles Modified Glassy Carbon Electrode. *Electrochimica Acta*, **55**, 2752-2759. https://doi.org/10.1016/j.electacta.2009.12.052

[27] Silva, W.C., Pereira, P.F., Marra, M.C., Gimenes, D.T., Cunha, R.R., da Silva, R.A.B., Munoz, R.A.A. and Richter, E.M. (2012) A Simple Strategy for Simultaneous Determination of Paracetamol and Caffeine Using Flow Injection Analysis with Multiple Pulse Amperometric Detection. *Electroanalysis*, **23**, 2764-2770. https://doi.org/10.1002/elan.201100512

[28] Scholz, F. (2002) Electroanalytical Methods-Guide to Experiments and Applications. Springer, New York.

[29] Kalayci, S., Ünal, U. and Somer, G. (2020) Determination of Vitamin B12 Using Differential Pulse Polarography. *American Journal of Analytical Chemistry*, **11**, 187-196. https://doi.org/10.4236/ajac.2020.115014

[30] Peckov, K., Musilov, J. and Barek, J. (2009) Boron-Doped Diamond Film Electrodes—New Tool for Voltammetric Determination of Organic Substances. *Critical Reviews in Analytical Chemistry*, **39**, 148-172.

https://doi.org/10.1080/10408340903011812

[31] Sartori, E.R., Medeiros, R.A., Rocha-Filho, R.C. and Fatibello-Filho, O. (2009) Square-Wave Voltammetric Determination of Acetylsalicylic Acid in Pharmaceutical Formulations Using a Boron-Doped Diamond Electrode without the Need of Previous Alkaline Hydrolysis Step. *Journal of the Brazilian Chemical Society*, **20**, 360-366. https://doi.org/10.1590/S0103-50532009000200022

[32] Batista, E.F., Sartori, E.R., Medeiros, R.A., RochaFilho, R.C. and Fatibello-Filho, O. (2010) Differential Pulse Voltammetric Determination of Sildenafil Citrate (Viagra®) in Pharmaceutical Formulations Using a Boron-Doped Diamond Electrode. *Analytical Letters*, **43**, 1046-1054. https://doi.org/10.1080/00032710903491153

[33] Sartori, E.R., Medeiros, R.A., Rocha-Filho, R.C. and Fatibello-Filho, O. (2010) Square-Wave Voltammetric Determination of Propranolol and Atenolol in Pharmaceuticals Using a Boron-Doped Diamond Electrode. *Talanta*, **81**, 1418-1424. https://doi.org/10.1016/j.talanta.2010.02.046

[34] Ardila, J.A., Sartori, E.R., Rocha-Filho, R.C. and Fatibello-Filho, O. (2013) Square-Wave Voltammetric Determination of Bezafibrate in Pharmaceutical Formulations Using a Cathodically Pretreated Boron-Doped Diamond Electrode. *Talanta*, **103**, 201-206. https://doi.org/10.1016/j.talanta.2012.10.033

[35] Gil, J.S., Yanez, E.C. and Frontana-Uribe, B.A. (2022) Recent Advances on Boron Doped Diamond (BDD) Electrode as Cathode in Organic and Inorganic Preparative Electrotransformations. *Current Opinion in Electrochemistry*, **34**, Article ID: 101004. https://doi.org/10.1016/j.coelec.2022.101004

[36] Salazar-Banda, G.R. andrade, L.S., Nascente, P.A.P., Pizani, P.S., Rocha-Filho, R.C. and Avaca, L.A. (2006) The Changing Electrochemical Behaviour of Boron-Doped Diamond Surfaces with Time after Cathodic Pre-Treatments, *Electrochimica Acta*, **51**, 4612-4619. https://doi.org/10.1016/j.electacta.2005.12.039

[37] Koffi, K.M. and Ouattara, L. (2019) Electroanalytical Investigation on Paracetamol on Boron-Doped Diamond Electrode by Voltammetry. *American Journal of Analytical Chemistry*, **10**, 562-578. https://doi.org/10.4236/ajac.2019.1011039

[38] Zheng, M., Gao, F., Wang, Q., Cai, X., Jiang, S., Huang, L. and Fei, G. (2013) Electrocatalytical Oxidation and Sensitive Determination of Acetaminophen on Glassy Carbon Electrode Modified with Graphene-Chitosan Composite. *Materials Science and Engineering C*, **33**, 1514-1520. https://doi.org/10.1016/j.msec.2012.12.055

[39] Tanuja, S.B., Swamy, B.E.K. and Pai, K.V. (2017) Electrochemical Determination of Paracetamol in Presence of Folic Acid at Nevirapine Modified Carbon Paste Electrode: A Cyclic Voltammetric Study. *Journal of Electroanalytical Chemistry*, **798**, 17-23. https://doi.org/10.1016/j.jelechem.2017.05.025

[40] Koffi, K.M. and Ouattara, L. (2019) Differential Pulse Voltammetric Determination of Paracetamol on a Boron-Doped Diamond Electrode: Application to Natural Tomato and Carrot Juices. *Revue Ivoirienne des Sciences et Technologie*, **34**, 44-66.

[41] Koffi, K.S., Foffié, T.A.A., Kouadio, K.E., Kimou, K.J., Kone, S. and Ouattara, L. (2021) Cyclic and Differential Pulse Voltammetry Investigations of an Iodine Contrast Product Using Microelectrode of BDD. *Mediterranean Journal of Chemistry*, **11**, 244-254.