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Original scientific paper

Voltammetric quantification of the anesthetic drug propofol (2,6-diisopropylphenol) in pharmaceutical formulations on a boron-doped diamond electrode

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Abstract: In this paper, the detailed electrochemistry of propofol (PRO), which is one of the intravenous agents commonly used for sedative-hypnotic purposes, was examined. In cyclic voltammetry, the agent showed one irreversible and diffusion-controlled oxidation peak, resulting in the formation of a couple with a reduction and re-oxidation wave at less positive potentials. The effect of electrode pretreatment procedures on the electrochemical response of PRO was investigated using square wave voltammetry (SWV) and the optimum procedure was used to improve the signal response in subsequent studies. Quantification of PRO was realized based on the first oxidation peak using SWV. After optimization of all variables, the linear working range of PRO was found to be between 2.5 μg mL^{-1} (1.4×10^{-5} mol L^{-1}) and 160.0 μg mL^{-1} (1.1×10^{-3} mol L^{-1}, n = 15) with a detection limit 0.71 μg mL^{-1} (3.9×10^{-6} mol L^{-1}). No noteworthy interference effect was detected. Furthermore, the developed method was used for quantification of PRO in pharmaceutical samples.

Keywords: propofol; boron-doped diamond electrode; voltammetry; pharmaceutical formulation.

INTRODUCTION

The use of anesthetics agents for creating reversible unconsciousness was a huge breakthrough in medical procedures. Among these agents, intravenous ones are often used for sedative-hypnotic purposes in surgical operations due to their safety and rapid effectiveness. The propofol (PRO, 2,6-diisopropylphenol) agent

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in this group is one of the most preferred anesthetic agents in the western world due to advantages such as low drug interactions and relative benign side effects[1] (Fig. 1). Because of its high lipophilic character, it penetrates and distributes on the central nervous system, quickly. This allows more effective control over the onset of sedation and the thereafter recovery processes.

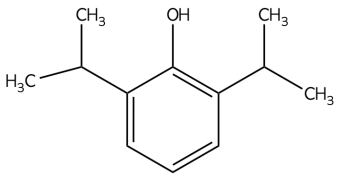


Fig. 1. Chemical structure of propofol.

The sedative and hypnotic activity of PRO is related to its concentration in plasma. So, the therapeutic concentration in plasma should be in the range of 0.5-1.5 μg mL^{-1} for sedation and 2-5 μg mL^{-1} for anesthesia.[2] On the other hand, it is a well-known fact that PRO is used for drug abuse as well as anesthetic purposes.[3] As a result of its misuse, death cases have been reported in different parts of the world, especially among healthcare professionals, such as doctors and nurses.[4] Therefore, a simple, fast, and sensitive analytical approach is required for the determination of PRO in pharmaceutical formulations. To date, many studies have been conducted for the determination of PRO in biological fluids, such as blood and urine. These studies included the use of various analytical methodologies, such as spectrophotometric,[5] high-performance liquid chromatography (HPLC),[6–9] gas chromatography–mass spectrometry (GC–MS),[10,11] liquid chromatography–mass spectrometry (LC–MS)[12–19] and capillary electrophoresis.[20] However, there are a limited number of studies in the scientific literature on the electrochemical analysis of PRO. In one of the non-quantitative studies, the researchers investigated the performance of differently produced pencil graphite electrodes (PGE) against electrode fouling in PRO monitoring.[21] In another study of the same research group, electrode cleaning procedures were developed to eliminate the fouling effect caused by propofol oxidation on rotating disk boron-doped diamond (BDD)/silica substrate material and PGE. Due to the low-adsorption capability of the BDD electrode, they used for quantitative analysis of PRO only at the PGE electrode following these cleaning procedures. After optimizing the experimental parameters, they reached a detection limit of 0.82 μM on PGE.[22] In an other electrochemical study, the performance of a bare GC electrode as substrate material was evaluated by using different electrochemical techniques. In this study, the obtained sensitivity levels based on both the reduction and oxidation peak of PRO were found as 5.5 and 3.2 μM, respectively.[23] In addition, Thiagarajan *et al.* reached a sensitivity of 0.08 μM thanks to anodized screen-printed carbon electrode (SPCE) formed as a result of pretreat-

ing the SPCE in the H_2SO_4 solution.[24] In addition, it the study in the literature reporting the electrochemical behavior of PRO in organic film-coated glassy carbon (GC) electrode should be highlighted.[25] However, this procedure has the difficulty of forming a uniform organic film on the electrode.

Electrochemical methods differ from other analytical methods in their speed, ease of application, reliability and simplicity. In addition, they offer considerable sensitivity and selectivity depending on the type of working electrode and the technique used.[26] Undoubtedly, another outstanding feature is that they clarify the redox behavior of the related species.[27] It is a known fact that the type of electrode used in the analysis performed by these methods, the pretreatment procedures, and the modification steps applied to the electrode play great roles in the electrochemical behavior of the analyte.[28–30]

A boron-doped diamond (BDD) electrode is a carbonaceous electrode material that offers distinctive features, such as wide working window (both in the cathodic and anodic direction), low ground current, low signal noise ratio, operation in corrosive environments and giving reproducible responses to electrochemical analysis.[31–34] Moreover, electroactive species that cannot be examined with conventional metal and other carbon electrodes can be analyzed with the wide working window of this electrode material.[35] However, a BDD electrode allows limited modification with modifying agents compared to electrode materials such as glassy carbon. The main reason for this is the low adsorption of both the analyte and the modifying agent to the surface of the BDD electrode material.[36]

As for the electrochemical pretreatment step, it is one of the most widely used techniques to increase the sensitivity of the BDD electrode. This procedure applies a certain potential to the BDD electrode in the anodic or cathodic direction for a certain period of time. These pretreatment steps applied to the electrode could be performed anodically or cathodically, anodically followed by cathodically or *vice versa*. Many electrochemical approaches based on BDD electrodes have increased the electrode sensitivity using such steps.[37–39]

In a recent paper, the performance of a BDD electrode together with PGE has been investigated in the effectiveness of electrode cleaning strategies in long-term PRO monitoring.[22] However, the quantitative analytical aspect of this study is based on PGE. As far as is known, no approach has been found in the literature for quantitative purposes in PRO analysis using the BDD electrode. In this article, a simple approach to the subject was implemented for quantitative analysis of PRO with just a simple pretreatment step on an unmodified BDD electrode. Its practical applicability was applied to commercial pharmaceutical dosages.

EXPERIMENTAL

Chemicals

PRO standard (Reagent Plus®, ≥99.82 %, liquid) was purchased from ChemScene LLC (USA) and used as received. A stock standard solution of 1 mg mL^{-1} of PRO was prepared by dissolving in methanol and storing in a volumetric flask in a refrigerator at 4–6 °C in order to avoid degradation when not in use. Analytical-grade reagents and purified water from a Millipore Milli-Q system (Millipore, resistivity ≥18.2 MΩ cm) were used for the preparation of Britton–Robinson (BR, 0.1 mol L^{-1}, pH 2–9), phosphate buffer (0.1 mol L^{-1}, pH 2.5 and 7.4), acetate buffer (0.1 mol L^{-1}, pH 4.7), $HClO_4$ (0.1 mol L^{-1}) and H_2SO_4 (0.1 mol L^{-1}) solutions. The working and calibration solutions of PRO were prepared from the stock solution before use with appropriate diluting with the selected supporting electrolyte. All analysis and voltammetric measurements were realized under laboratory conditions.

Apparatus and measurements

Electrochemical measurements were performed with an μAutolab Type III (Metrohm Autolab B.V., Utrecht, The Netherlands) controlled with GPES software (version 4.9). All square wave voltammograms were smoothed using a Savicky and Golay algorithm and baseline-corrected by the moving average algorithm filtering technique (peak width of 0.01 V). A conventional three-electrode setup in the electrochemical cell was used, consisting of a BDD working electrode (diameter of 3 mm, boron doping level of 1000 ppm, Windsor Scientific Ltd., Slough, UK), an Ag/AgCl/3 mol L^{-1} NaCl reference electrode (BAS, Model RE-1, USA) and a Pt counter electrode (BAS, MW-4130, USA). All potentials mentioned in the paper are refered to Ag/AgCl/3 mol L^{-1} NaCl reference electrode unless othervise stated. The pH was measured at 25 °C using a model WTW inoLab720 pH meter equipped with a combined glass electrode (Xylem, New York, USA).

At the beginning of each experiment day, an anodic pretreatment procedure was performed by applying a potential of 1.8 V to the BDD electrode in 0.5 mol L^{-1} H_2SO_4 solution for 180 s. After this process, a potential of –1.8 V was applied to the BDD electrode for the same period and in the same solution. As a result of these steps, the BDD electrode surface acquired a oxygen and hydrogen-terminated property.

First, the cyclic voltammetry (CV) technique was used to elucidate the electrochemical behavior of PRO and determine the reaction kinetics on the BDD electrode in the selected supporting electrolyte. Then, optimizations of the experimental parameters, such as supporting electrolyte and square wave voltammetric parameters, were conducted in order to improve the selectivity and sensitivity of the PRO analysis.

The quantitative analysis of PRO with the square wave voltammetry (SWV) technique was first started by immersing three electrodes into voltammetric cells containing PRO in the $HClO_4$ solution. After this step, anodic scanning was performed from 0 to 1.6 V. The quantitative analysis of PRO was carried out using an optimized 50 Hz frequency, 40 mV pulse amplitude, and 12 mV step potential values of the SWV technique.

Preparation of samples

The pharmaceutical formulations (Propofol-®Lipuro, labeled 10 mg mL^{-1} per ampoule) were obtained from a local hospital. A defined volume (10 μL) of this ampoule solution was transferred to 10 mL electrochemical cells containing 0.1 mol of L^{-1} $HClO_4$ solution. The PRO content in pharmaceutical formulation was determined by adding standard PRO concentrations to the drug sample.

RESULTS AND DISCUSSION

Electrochemical behavior of PRO on BDD electrode

The electrochemical behavior of PRO on the BDD electrode surface was examined by CV method. Three consecutive CVs for 100 μg mL^{-1} PRO between –0.7 and 1.7 V potentials were recorded in 0.1 mol L^{-1} $HClO_4$ solution at a potential scanning rate of 100 mV s^{-1}. As can be seen in Fig. 2A, upon first scanning in the oxidative direction, PRO exhibited one well-defined anodic peak, P_A, with a maximum at about 1.28 V. In the reverse scan, a reduction peak, P'_C, was obtained at about –0.27 V, which was accompanied by the appearance of a small additional anodic peak, P'_A, at a less positive potential than the main oxidation peak, P_A, during the second and subsequent scans. It should be noted that the peaks P'_C/P'_A did not appear in the CV curves if the potential was started at 0.0 V and ended at 1.7 V. As the number of scans increased, the peak height of P_A decreased, while the intensity of P'_C/P'_A increased very slightly. From these observations, it could be infered that P_A was an irreversible and P'_C/P'_A were a pair of redox peaks, which could be attributed to the products formed in the main electrooxidation step.

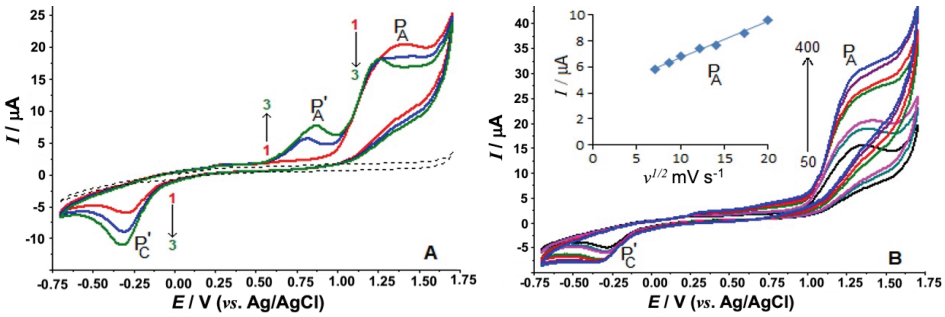


Fig. 2. The repetitive cyclic voltammograms at scan rate of 100 mV s^{-1} (A), and the cyclic voltammograms at different scan rates, 50, 75, 100, 150, 200, 300 and 400 mV s^{-1} (B), of 100 μg mL^{-1} propofol in 0.1 mol L^{-1} $HClO_4$ solution at the BDD; A: dashed lines represent background current; B: inset depicts the plot of peak current *vs.* square root of scan rate.

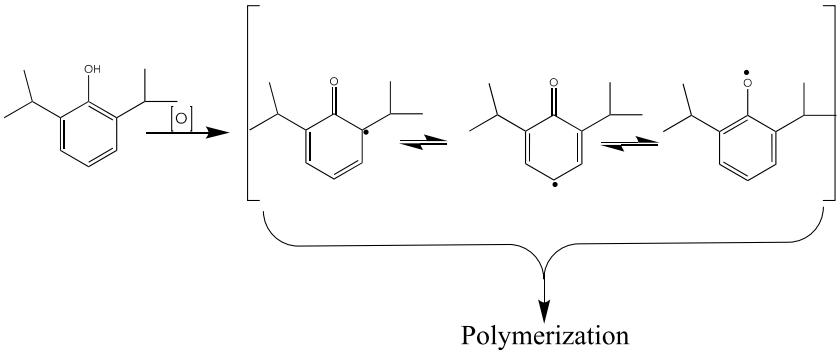
To determine the kinetics of the BDD electrode, the effect of the potential scan rates (v) on the anodic peak current response for 100 μg mL^{-1} PRO was examined by the CV technique 0.1 mol L^{-1} $HClO_4$ solution at 50–400 mV s^{-1} scan rates (Fig. 2B). The relationship between the square root scan rate ($v^{1/2}$) and anodic peak current (i_{pA}) of PRO was found to be linear according to the equation, $i_{pA} = (0.279\pm0.011)v^{1/2} + (3.92\pm0.188)$, $r = 0.994$. A similar linear correlation was found between log i_{pA} and log v, as shown in Eq. (1):

$$\log i_{pA} = (0.230\pm0.09)\log v + (0.370\pm0.019),\ r = 0.992 \quad (1)$$

These results could be evaluated as clear evidence that the kinetics of a BDD electrode are mainly diffusion controlled in the oxidation of PRO.

In order to ascertain the electron number (n) involved in the PRO oxidation process at a BDD electrode, the n value was determined from the CV voltammograms using the equation $\alpha n = 47.7/(E\text{p}–E\text{p}/2)$. In this study, the value of $E_\text{p}–E_\text{p}/2$ was 151 mV, thus the value of αn was calculated as 0.32. Generally, α (charge transfer coefficient) is assumed to be 0.5 in a totally irreversible electrode process. Hence, the n value was found to be 0.64 (≈1).

Although it is difficult to predict the general oxidation mechanism of PRO occurring on a BDD electrode surface, it is known that the mechanism that causes fouling on the electrode surface occurs through radical intermediate species polymerized similarly to the electrochemical oxidation of other phenolic compounds[21] and remain adsorbed at the electrode surface. Scheme 1 shows that electrochemical oxidation of PRO on the BDD electrode occurs first by the formation of phenoxy radicals and then by polymer formation.



Scheme 1. Possible redox mechanism of PRO at the BDD electrode in 0.1 mol L^{-1} $HClO_4$ solution.

Influence of the electrode pretreatment procedure

Before the voltammetric analysis of PRO, preliminary studies showed that the unpretreated BDD electrode could not be effective against passivation problems, especially at high PRO concentrations. This undesired situation caused the unpretreated BDD electrode to produce unsatisfactory results in terms of sensitivity and reproducibility. To overcome this and optimize the pretreatment procedures on the BDD electrode, the effectiveness of three different pretreatment procedures were investigated for 30 μg mL^{-1} PRO in $HClO_4$ solution by SWV. First, the performance of an anodic pretreated BDD electrode in voltammetric studies was examined. Secondly, the performance of a cathodic pretreated BDD electrode was investigated. Finally, anodic and cathodic pretreatment steps were applied sequentially to the BDD electrode and their performances in voltam-

metric analysis were recorded (Fig. 3). More sensitive and reproducible results were obtained in the analysis of PRO when the final pretreatment procedure was applied to the BDD electrode. For this reason, this procedure was chosen as the optimum pretreatment procedure and applied to the electrode at the beginning of each experiment day.

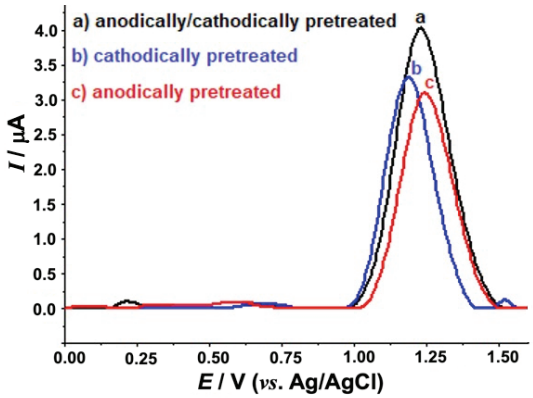


Fig. 3. SW voltammograms of 30 μg mL^{-1} propofol in 0.1 mol L^{-1} $HClO_4$ solution on BDD electrode after different electrochemical pretreatments. SWV parameters: frequency, 50 Hz; step potential, 8 mV; pulse amplitude, 30 mV.

Effect of pH

The effect of pH on oxidation peak currents and potentials of PRO was investigated by SWV on the BDD electrode using different supporting electrolytes at various pH values in order to obtain the best voltammetric response for analytical purposes., The baseline corrected SW voltammograms are depicted in Fig. 4A within the pH range 2.0–9.0 in BR buffer (0.1 mol L^{-1}) on 30 μg mL^{-1} PRO solution, within the potential range from 0 to 1.6 V.

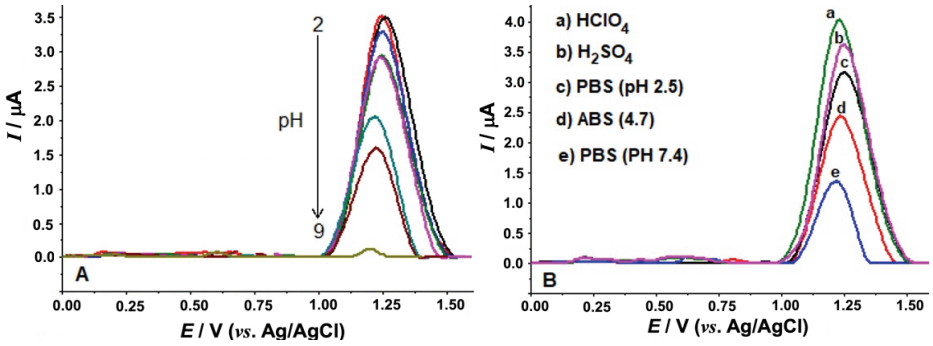


Fig. 4. SW voltammograms of 30 μg mL^{-1} propofol in BR buffer pH 2.0–9.0 (A), and in various supporting electrolytes at different pH values (B) on a BDD electrode. Other operating conditions were as indicated in Fig. 3.

Furthermore, it could be seen in Fig. 4A that PRO has one oxidation peak within the pH range 2.0–9.0 studied in the working potential range. In addition, it is clearly seen that with increasing solution pH, the potential of the oxidation peak becomes nearly pH-independent (from 1.25 to 1.22 V), indicating that no proton transfer steps occur before the rate-determining electron transfer step at these pH values. The SW voltammograms in various supporting electrolytes are depicted in Fig. 4B. Using 0.1 mol L^{-1} $HClO_4$, H_2SO_4, phosphate buffer (pH 2.5 and 7.4) and acetate buffer (pH 4.7), the oxidation peak potentials of PRO became nearly pH independent.

The evolution of peak currents with pH shows that this parameter reached the highest values in 0.1 mol L^{-1} $HClO_4$. Thus, ongoing studies will be performed in this solution.

Effect of SWV parameters

Another important factor affecting the sensitivity of PRO is optimization of the pulse parameters, such as frequency (f), pulse amplitude (ΔE_{sw}), and step potential (ΔE_s). This optimization step was realized by changing one of the pulse parameters while keeping the other two parameters constant and by recording the obtained signal. First, the f variable was examined in the range of 25–125 Hz, while ΔE_{sw} and ΔE_{ss} parameters were kept constant at 30 and 8 mV, respectively. So, the best sensitivity and peak shape for this pulse variable was recorded at 50 Hz. Next, the ΔE_{sw} value was changed between 30 and 60 mV, while the ΔE_{ss} and f values were kept constant at 8 mV and 50 Hz, respectively. The same optimization process was carried out by keeping f and ΔE_{sw} constant and examining the values of ΔE_{ss} between 6 and 12 mV. As a result, the best SWV instrumental parameters on the BDD electrode for 7.5 μg mL^{-1} PRO in 0.1 mol L^{-1} $HClO_4$ solution (not shown) were obtained at values f, 50 Hz; ΔE_s, 10 mV; ΔE_{sw}, 40 mV.

Analytical performance evaluation

The applicability of the developed SWV method based of the BDD electrode was tested under the optimized experimental and instrumental conditions. The increase in the anodic currents obtained as a function of the added PRO standards in the range from 2.5 (1.4×10^{-5}) to 160.0 μg mL^{-1} (1.1×10^{-3} mol L^{-1}) in 0.1 mol L^{-1} $HClO_4$ solution is shown in Fig. 5. The highly linear relationship between the SW voltammograms procured in response to these successively added PRO concentrations is given in Eq. (2):

$$i_p = (0.173\pm0.07\ C + (0.045\pm0.002)\ (r = 0.999, n = 15) \quad (2)$$

where i_p is the peak current, C the concentration, r the correlation coefficient, and n the number of experiments.

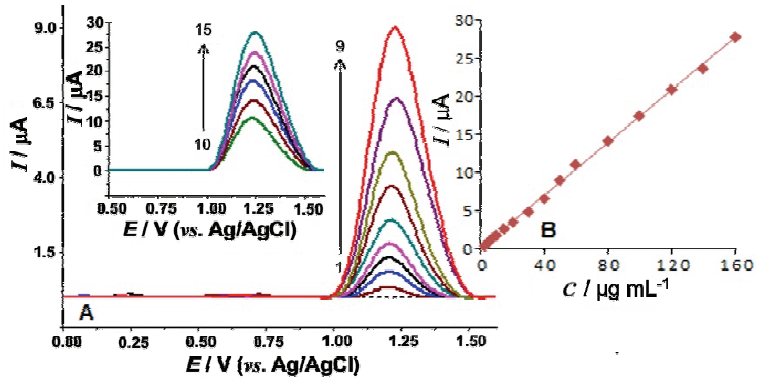


Fig. 5. SW voltammograms for propofol levels of (1–15) 2.5, 5.0, 7.5, 10, 15, 20, 30, 40, 50, 60, 80, 100, 120, 140 and 160 μg mL^{-1} in 0.1 mol L^{-1} $HClO_4$ solution (A); B: the corresponding calibration plot for the quantitation of propofol. SWV parameters: frequency, 50 Hz; step potential, 10 mV; pulse amplitude, 40 mV.

The developed methodology reached 0.71 μg mL^{-1} (3.98×10^{-6} mol L^{-1}) *LOD*, and 2.36 μg mL^{-1} (1.32×10^{-5} mol L^{-1}) *LOQ* levels with a simple pretreatment step applied to the electrode.

The *LOD* value was calculated according to the 3*s*/*m* formula where *s* and *m* are the standard deviation of ten consecutive measurements of the lowest concentration in the calibration range and the slope of the corresponding calibration curve, respectively. This *LOD* value proves that the sensitivity of the method is good enough and could be applied to real samples.

As for the comparison of the method with other techniques, Table I gives the performance of the BDD electrode with a limited number of other carbon-based electrochemical studies in the literature. The presented methods in Table I reached similar sensitivity levels except for the SPCE-based electrode.

TABLE I. Comparison of published electroanalytical methods for PRO detection; working electrodes: BDD, boron-doped diamond electrode; PGE, pencil graphite electrode; GCE, glassy carbon electrode; SPCE, screen printed carbon electrode; PVC/GCE, PVC membrane coated glassy carbon electrode; techniques**:** CV, cyclic voltammetry; DPV, differential pulse voltammetry; CSV, cathodic stripping voltammetry; CA, chronoamperometry; SWV, square-wave voltammetry

WE	Technique	E_p / V	Linear range, μM	*LOD* / μM	Analyzed sample	Reference
BDD, PGE	CV, DPV	0.4, 0.7	-	2.38-8.1	Serum	[22]
GCE	CV, CSV	0.70	0-30	5.5	–	[23]
SPCE	CV	0.56	0.09-0.9	0.08	Lab. samples	[24]
PVC/GCE	CA	-	0-56.6	0.03	–	[25]
BDD	SWV	1.25	14-1100	3.9	Pharm. formulation	This work

Furthermore, the proposed methodology has the level of sensitivity that could sense the level of PRO in plasma (between 1–60 μM) and the speed

required to analyze PRO in forensic cases. It is also very advantageous in terms of the stability of the electrode response in comparison with other electrodes. Moreover, another aspect that distinguishes the proposed method from the few electrochemical methods performed is that the PRO determination is realized at high positive potentials.

To test the precision the method, at a concentration of 2.5 μg mL^{-1} PRO, the intra-day (ten replicate) and inter-days (three days) reproducibility was examined under the same conditions and the relative standard deviation (*RSD*) values were calculated as 8.03 and 9.13 %, respectively. These values indicated that the BDD electrode produces sufficiently reproducible results in PRO measurements.

Effect of interfering compounds

Prior to the analyses of real samples, the selectivity of the proposed SWV protocol was also investigated in the presence of some species, such as lactose, sucrose, fructose, glucose, ascorbic acid, dopamine, uric acid and ions such as Ti^{4+}, Fe^{3+}, Zn^{2+}, Mg^{2+}, Ca^{2+}, K^{+}, Na^{+}, NO_3^{-}, Cl^{-}, SO_4^{2-} and some agents present in pharmaceutical formulations, such as starch, talc, cornstarch and magnesium stearate. The interfering effect on the PRO signal was examined at 1:1, 1:10 and 1:100 (PRO: interference species) molar ratios in supporting electrolyte containing 2.5 μg mL^{-1} PRO. The signal obtained from the mixture of PRO and the interfering species was compared with the signals obtained from the solution containing only PRO. The maximum concentration of a foreign substance that affected the PRO signal less than 7 % was described as the tolerance limit. Metal ions had no significant effect on the quantitative determination of PRO. This behavior could be explained by the emergence of metal ion signals in negative potentials but PRO signals in positive potential. The effects of interfering species such as starch, talc, cornstarch and magnesium stearate on the oxidation signal of PRO showed a negligible effect, even at over 100 times concentration. Species such as lactose, sucrose, fructose and glucose did not show a significant interfering effect for the quantitative determination of PRO even at 100 times the PRO concentration. However, it was not possible to analyze PRO together with dopamine and uric acid when their concentration was 10 times the concentration of PRO or ascorbic acid at concentrations 20 times higher than that of PRO. In order to analyze these compounds together, either a pre-separation method, such as chromatography or a chemometric method should be used. To conclude, the proposed voltammetric protocol is sufficiently selective and can perform PRO analysis in complex matrices.

Analytical application

The accuracy and practical usability of the proposed electroanalytical methodology was tested in commercially pharmaceutical formulations by using the multiple standard addition method. The sample preparation procedures are

described in the relevant section in detail. At this stage, it should be stressed that the sample was used directly without any dilution, pre-separation, filtering, or evaporation steps. Different volumes of standard PRO stock solution were transferred to the electrochemical cell containing the drug sample. As a result of these successive transfers, the final concentrations of PRO in the cell were adjusted to be 5, 7.5, 10, 15, 20, 30, 40 and 50 μg mL^{-1}. The overlapping voltammograms obtained from the drug sample after each added concentration are shown in Fig. 6. The appearing peak at approximately 1.23 V belonging to PRO oxidation increased linearly with increasing concentration of the added standards. Each Propofol-®Lipuro, ampoule was calculated to contain an average of 9.52 mg mL^{-1} PRO (*RSD* of 5.05 %) when evaluated based on these successive additions. This result also complies with the manufacturer's declaration claiming to contain 10 mg mL^{-1} per ampoule. As for testing the validity of the proposed method, this stage was assessed by the calibration curve and recovery method. The recovery values obtained by the SWV procedure are presented in Table II. These results proved that PRO analyzes can be performed safely without significant interference from commercial drug samples.

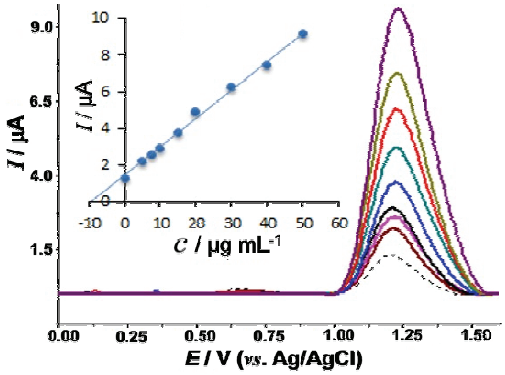


Fig. 6. SW voltammograms of the diluted drug sample (dashed line) and after standard additions of 5.0, 7.5, 10, 15, 20, 30, 40 and 50 μg mL^{-1} propofol (1–8) in 0.1 mol L^{-1} $HClO_4$ solution. Inset depicts the result of analysis by the standard addition method for the oxidation peak. Other operating conditions as indicated in Fig. 5.

TABLE II. Recovery values of pharmaceutical formulations samples spiked with standard solutions of propofol using the developed voltammetric method

c / μg mL^{-1}			Recovery ± *RSD*, %
Added[a]	Expected[a]	Found[a,b]	
0	–	9.52	–
5.0	14.52	15.20	104.7±6.07
7.5	17.02	16.37	96.2±5.43
10.0	19.52	18.64	95.5±5.13

[a]Concentration in the measured solution; [b]average of three replicate measurements

CONCLUSIONS

Within the scope of this article, the useability of a bare BDD electrode for the quantitative analysis of PRO was demonstrated. The electrochemical

behavior and electrode kinetics of PRO were revealed based on this electrode. As a result of the pretreatment procedures on the electrode, the change of PRO signals was examined and the optimum procedure was determined. To obtain the best voltammetric response, chemical variables, such as supporting electrolyte and pH, and puls variables, such as frequency, pulse amplitude, and step potential, were also optimized. Linearity was achieved between 2.5 and 160.0 μg mL^{-1} (1.4×10^{-5}–1.1×10^{-3} mol L^{-1}) under these optimized conditions while the *LOD* was calculated as 0.71 μg mL^{-1} (3.9×10^{-6} mol L^{-1}). The application of the method has been successfully demonstrated in the commercial drug formulation. The methodology proposed here is a good alternative to existing methods with its practical use, speed, and sensitivity.

И З В О Д

ВОЛТАММЕТРИЈСКА КВАНТИФИКАЦИЈА АНЕСТЕТИКА ПРОПОФОЛА (2,6-ДИИЗОПРОПИЛФЕНОЛ) У ФАРМАЦЕУТСКИМ ОБЛИЦИМА ПРИМЕНОМ БОРОМ ДОПИРАНЕ ДИЈАМАНТСКЕ ЕЛЕКТРОДЕ

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У овом раду је испитано електрохемијско понашање пропофола (PRO), једног од често коришћених интравенозних агенаса који делује седативно-хипнотички. У цикличној волтаметрији, агенс показује један иреверзибилан и дифузионо контролисан оксидациони пик у директном, као и један редукциони пик у повратном скену. Даљом циклизацијом, до мање позитивног потенцијала, јавља се нови пик као последица ре-оксидације редуковане форме лека. Испитиван је утицај процедуре припреме електроде на одговор PRO добијен применом волтаметрије правоугаоних таласа (SWV), са циљем постизања оптималне процедуре ради побољшања сигнала одговора у наредним испитивањима. Квантификација PRO је изведена на основу првог оксидационог пика применом SWV. После оптимизације одређених параметара, добијен је линеаран радни опсег за PRO Између 2,5 μg mL^{-1} ($1,4\times10^{-5}$ mol L^{-1}) и 160,0 μg mL^{-1} ($1,1\times10^{-3}$ mol L^{-1}, $n = 15$), са границом детекције од 0,71 μg mL^{-1} ($3,9\times10^{-6}$ mol L^{-1}). Нису детектоване значајније интерференције. Осим тога, развијена метода је примењена за квантификацију PRO у фармацеутским узорцима.

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