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Article

Determination of Propylthiouracil in Pharmaceuticals by Differential Pulse Voltammetry Using a Cathodically Pretreated Boron-Doped Diamond Electrode

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Um procedimento simples é descrito para a determinação de propiltiouracil (PTU) por voltametria de pulso diferencial (DPV) usando um eletrodo de diamante dopado com boro (BDD) pré-tratado catodicamente. Estudos por voltametria cíclica indicam que a oxidação do PTU é irreversível a um potencial de pico de 1,42 V (*vs.* Ag/AgCl (KCl 3,0 mol L^{-1})) em uma solução tampão de Britton-Robinson (BR) (pH 2,0). Sob condições otimizadas, a curva analítica obtida foi linear (r = 0,9985) na faixa de concentração de PTU de 1,0 a 29,1 µmol L^{-1} em solução tampão BR (pH 2,0), com um limite de detecção de 0,90 µmol L^{-1}. O método proposto foi aplicado com sucesso na determinação de PTU em amostras farmacêuticas, com resultados concordantes (a um nível de 95% de confiança) com aqueles obtidos empregando um método titulométrico oficial.

A simple procedure is described for the determination of propylthiouracil (PTU) by differential pulse voltammetry (DPV) using a cathodically pretreated boron-doped diamond (BDD) electrode. Cyclic voltammetry studies indicate that the oxidation of PTU is irreversible at a peak potential of 1.42 V (*vs.* Ag/AgCl (3.0 mol L^{-1} KCl)) in a Britton-Robinson (BR) buffer solution (pH 2.0). Under optimized conditions, the obtained analytical curve was linear (r = 0.9985) for the PTU concentration range of 1.0 to 29.1 µmol L^{-1} in a BR buffer solution (pH 2.0), with a detection limit of 0.90 µmol L^{-1}. The proposed method was successfully applied in the determination of PTU in pharmaceutical samples, with results in agreement at a 95% confidence level with those obtained using an official titration method.

Keywords: propylthiouracil determination, 6-propyl-2-thiouracil, BDD electrode, cathodic pretreatment, differential pulse voltammetry

Introduction

Propylthiouracil (PTU; 6-propyl-2-thiouracil, Figure 1) is widely used in the treatment of hyperthyroidism, a disease caused by overactivity of the thyroid gland. This drug inhibits the activity of the thyroid gland peroxidase and blocks the conversion of tetraiodothyronine (T4) to triiodothyronine (T3).[1] Therefore, the development of a sensitive and selective method for the determination of PTU in pharmaceuticals is highly desirable, especially for quality control purposes.

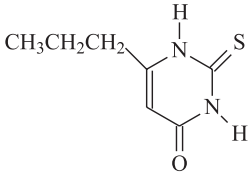

Figure 1. Chemical structure of propylthiouracil.

Several methods for the determination of PTU have been reported in the literature for pharmaceutical formulations and biological samples, such as high-performance liquid chromatography (HPLC) with post column iodine-azide reaction monitored at UV[2] or HPLC with chemiluminescence detection,[3] spectrophotometric kinetic method based on the PTU inhibitory effect of the Pd(II)-catalyzed reaction between pyronine G and

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the hypophosphite anion,[4] titration,[5] and electrochemical techniques, such as potentiometric and coulometric titration[6] and voltammetry.[7-11]

Sarna and Fijalek[7] determined PTU in 0.1 mol L^{-1} NaOH by cyclic voltammetry (CV) using a gold electrode; the obtained analytical curve was linear for the concentration range of 0.10 to 0.50 mmol L^{-1}. Kasprzak *et al.*[8] used a hanging mercury drop electrode for the determination of PTU in pharmaceutical formulations by cathodic stripping voltammetry (CSV). The obtained analytical curve was linear for the concentration range of 0.020 to 0.24 μmol L^{-1} in an acetate buffer solution (pH 3.9), with detection limit of 0.0010 μmol L^{-1}. Shahrokhian and Jannat-Rezyani[9] developed a differential pulse voltammetric method for PTU determination in pharmaceutical preparations using a carbon-paste electrode modified with a Schiff-base complex of cobalt (Co(II)-4-chlorosalophen). A linear response was attained for the concentration range of 5.0 to 750 μmol L^{-1}, with a detection limit of 2.0 μmol L^{-1}. Shahrokhian and Saberi[10] developed an indirect method (using catechol as redox mediator) for the determination of PTU in pharmaceutical and biological fluids by differential pulse voltammetry (DPV) using a glassy-carbon (GC) electrode. A linear analytical curve was obtained for the concentration range of 0.1-10 μmol L^{-1}, with a detection limit of 0.05 μmol L^{-1}. More recently, Oliveira *et al.*[11] used a GC electrode modified with multiwalled carbon nanotubes within a poly(allylamine hydrochloride) film for the determination of PTU in pharmaceuticals by CSV. The obtained analytical curve was linear for concentrations in the range of 5.0 to 58.0 μmol L^{-1} in a Britton-Robinson (BR) buffer solution (pH 2.0), with a detection limit of 1.0 μmol L^{-1}, applying an accumulation potential of 1.0 V for 60 s.

Boron-doped diamond (BDD) has been widely used in electroanalytical determinations of organic compounds in pharmaceutical formulations.[12-23] BDD electrodes present several advantages compared to other conventional electrodes (e.g., GC or Pt electrodes), such as stability against corrosion in very aggressive media, very low and stable background current, extreme electrochemical stability in both alkaline and acidic media, high response sensitivity, and a very wide working potential window.[24-26] Previously, these unique properties of BDD allowed the direct determination of acetylsalicylic acid in pharmaceutical formulations,[12] without the previous alkaline hydrolysis step that is necessary when other types of electrodes are used.

In this article, we report on the development of a novel method for the determination of PTU in pharmaceutical formulations by DPV using a cathodically pretreated BDD electrode. We show that the voltammetric responses are much better than those obtained using a GC electrode. The proposed method is simple, rapid, precise, and accurate for quantitative determinations of PTU. Moreover, the obtained results are statistically equal to those from the official British Pharmacopoeia method.[5]

Experimental

Reagents and solutions

All chemicals were of analytical grade: PTU (Sigma-Aldrich) and boric acid, acetic acid, orthophosforic acid, and methanol (Merck). The PTU pharmaceutical samples were purchased from a local drugstore.

A 0.1 mol L^{-1} PTU methanolic stock solution was prepared before use. All PTU working solutions were prepared by dilution of this stock solution with a Britton-Robinson (BR) buffer solution (pH 2.0). This BR buffer was prepared by mixing 0.04 mol L^{-1} acetic, orthophosphoric, and boric acid solutions; the final pH was adjusted by adding suitable amounts of a 2.0 mol L^{-1} sodium hydroxide solution.

Equipments and electrodes

Voltammetric measurements and electrochemical pretreatments of the BDD electrode were carried out using an Autolab PGSTAT-30 (Ecochemie) potentiostat/galvanostat controlled with the GPES 4.0 software. The voltammetric experiments were conducted in a three-electrode single-compartment glass cell at room temperature (25.0 ± 0.5 °C), including a Pt wire as the auxiliary electrode, an Ag/AgCl (3.0 mol L^{-1} KCl) as the reference electrode (to which all potentials hereinafter will be referred to), and BDD (8000 ppm; 0.36 cm^2 exposed area; Adamant, Switzerland) or GC (Tokay Carbon Co., Japan) as working electrode. Detailed information on the preparation of the BDD films is reported elsewhere.[27] Prior to the experiments, the BDD electrode was electrochemically pretreated in a 0.5 mol L^{-1} H_2SO_4 solution: first an anodic pretreatment (0.5 A cm^{-2}, 30 s), which was followed by a cathodic one (−0.5 A cm^{-2}, 150 s); thus, the BDD surface was first rid of any impurities and then made predominantly hydrogen terminated.[28] The selection of this pretreatment procedure is discussed in detail in section 3.1.

The GC electrode (5 mm diameter) was carefully polished to a mirror finish, starting with metallographic abrasive paper (No. 6) and finishing with slurries of 0.3 and 0.05 μm alumina. After being rinsed with doubly distilled water, sonicated for 5 min in absolute ethanol and then in ultrapure water, the polished GC electrode was left to dry at room temperature.

The pH was measured at 25.0 ± 0.5 °C using an Orion pH-meter, Expandable Ion Analyser, model EA-940, employing a combined glass electrode with an Ag/AgCl (3.0 mol L^{-1} KCl) external reference electrode.

Analytical procedures

CV, DPV, and square-wave voltammetry (SWV) were employed to investigate the electrochemical behavior or the quantification of PTU. Analytical curves were obtained by adding small volumes of the PTU methanolic stock solution to the BR buffer solution (pH 2.0). DP and SW voltammograms were obtained after each aliquot addition. Thus, the analytical parameters were compared and the best results were used to quantify PTU in the commercial samples.

To prepare solutions of the PTU commercial samples, ten tablets (100 mg of PTU per tablet) were accurately weighed and then reduced to a homogeneous fine powder in a mortar with a pistil. A suitable amount of this powder, corresponding to a methanolic 0.1 mol L^{-1} PTU stock solution, was weighed, transferred to a 5 mL calibrated flask and dissolved to volume. After, suitable aliquots of the supernatant were transferred to 10 mL calibrated flasks and completed to volume with the BR buffer solution (pH 2.0). An aliquot of each sample solution was directly transferred to the electrochemical cell containing the supporting electrolyte, after which the DP voltammograms were obtained. The PTU concentration in each sample solution was determined using the regression equation of the previously plotted analytical curve obtained with standard solutions.

For the recovery studies, aliquots of the PTU standard solution were added to real samples prepared from pharmaceutical tablets. Sets of triplicate enrichments were carried out with increasing PTU concentration. The recovery of PTU was calculated using the corresponding regression equation of the previously plotted analytical curve.

The results obtained with the proposed DPV method were compared with those obtained with the titration method of the British Pharmacopoeia.[5] Thus, an accurate representative amount of powder of each PTU sample was dissolved in a sodium hydroxide solution with the aid of gentle heating. This solution was acidified with acetic acid and titrated with mercury nitrate until a pinkish violet color was obtained using 1,5-diphenylcarbazone as indicator.

Results and Discussion

PTU electrochemical behavior

Initially, the cyclic voltammogram for 1.0 mmol L^{-1} PTU in the BR buffer (pH 2.0) was obtained using the BDD electrode. As can be seen in Figure 2, an anodic current peak is present at a potential of 1.42 V due to the oxidation of PTU. No reduction peaks were observed on the reverse scan, indicating that on BDD this is an irreversible charge-transfer process.

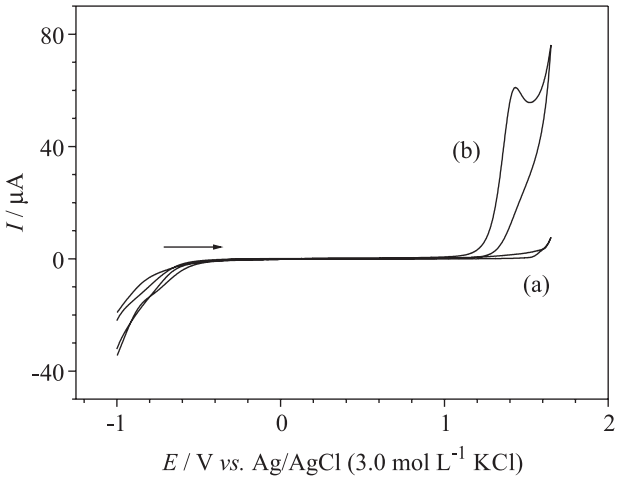

Figure 2. Cyclic voltammograms (50 mV s^{-1}) obtained using a cathodically pretreated BDD electrode for a: (a) BR buffer solution (pH 2.0); (b) 1.0 mmol L^{-1} PTU solution in the BR buffer (pH 2.0).

Taking into account that the analytical performance of BDD electrodes depends on their surface termination (e.g., hydrogen or oxygen terminated),[28-29] the effect of different electrochemical pretreatments of the BDD electrode on its analytical response for a 1.0 mmol L^{-1} PTU solution in the BR buffer (pH 2.0) was investigated. Thus, the BDD electrode was anodically (+0.5 A cm^2, 20 s) or cathodically (–0.5 A cm^2, 80 s) pretreated in a 0.5 mol L^{-1} H_2SO_4 solution, and then its analytical response was assessed (see Figure 3). As can be seen in this figure, the cathodic pretreatment led to a less positive PTU oxidation potential and a better current peak definition (a better repeatability was also found), indicating that this pretreatment of the electrode led to a higher electrochemical activity for PTU oxidation, as previously observed for several other analytes.[12-17,30-35] Next, the influence of the duration (120 to 180 s) of the cathodic pretreatment of the BDD electrode on its analytical signal was investigated; a less positive PTU oxidation potential along with a higher current peak magnitude was attained with the 150 s pretreatment. Thus, all subsequent PTU analytical determinations were carried out with the BDD electrode cathodically pretreated (–0.5 A cm^{-2}, 150 s), which ensured a predominantly hydrogen-terminated electrode surface. This pretreatment, which was carried out daily before starting the voltammetric measurements, was always preceded by an anodic pretreatment (0.5 A cm^{-2}, 30 s) that cleaned the electrode surface by oxidizing any contaminant present on it. This coupled pretreatment

procedure led to an excellent repeatability in the PTU determinations.

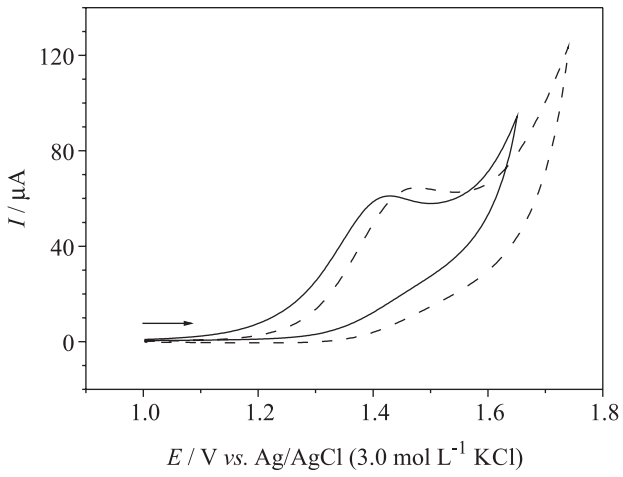

Figure 3. Cyclic voltammograms (50 mV s^{-1}) obtained for a 1.0 mmol L^{-1} PTU solution in the BR buffer (pH 2.0) using a BDD electrode after it underwent an anodic (dashed line) or cathodic (solid line) pretreatment (see text).

The number of electrons (n) transferred in the electrooxidation of PTU on the BDD electrode can be estimated by $E_p - E_{p/2} = 47.7\ mV/\alpha n$.[36] In the voltammogram for PTU oxidation obtained using a cathodically pretreated BDD electrode (Figure 3), the E_p and $E_{p/2}$ values are 1.42 V and 1.32 V, respectively. If the value of the transfer coefficient (α) is assumed as equal to 0.5, n can be estimated as 0.95, i.e., approximately 1. Consequently, assuming $n = 1$, we propose that the oxidation of PTU is represented by the reaction shown in Figure 4. This result indicates that PTU is oxidized to its corresponding free-radical product via a one-electron transfer process (Figure 4, step (I)), followed by its dimerization to a disulfide compound (–S–S–) (Figure 4, step (II)), as reported or discussed in previous studies with same and similar molecules.[11,37,38] It should be noted that no adsorption of the disulfide formed in the PTU oxidation was observed on the surface of the BDD electrode, as it occurs on a GC electrode,[11] which led to an improvement of the repeatability between measurements.

Effects of pH, supporting electrolyte composition, and scan rate

The effect of the BR buffer pH on the voltammetric response of a 1.0 mmol L^{-1} PTU solution was investigated in the pH range of 2.0 to 6.0, at the scan rate of 50 mV s^{-1} (Figure 5). We found that the current magnitude decreased and the peak potential shifted to less positive values as the pH was increased. Hence, the best voltammetric response using the BR buffer occurred when its pH was 2.0.

Next, the effect of the composition of the supporting electrolyte was comparatively investigated for sulfuric acid and phosphate or BR buffer solutions at pH 2.0. The BR buffer yielded the best response: less positive oxidation peak potential and higher peak current magnitude; hence, this buffer solution was used as the supporting electrolyte for all the additional studies.

Once again using a 1.0 mmol L^{-1} PTU solution in the BR buffer (pH 2.0), CV scan rate (0.005-0.500 V s^{-1}) studies were carried out to assess whether the electrodic processes at the BDD electrode were under diffusion or adsorption control. We found that the PTU oxidation peak potential shifted toward more positive values as the scan rate increased, a characteristic of irreversible electrochemical reactions.[39] At the same time, a linear

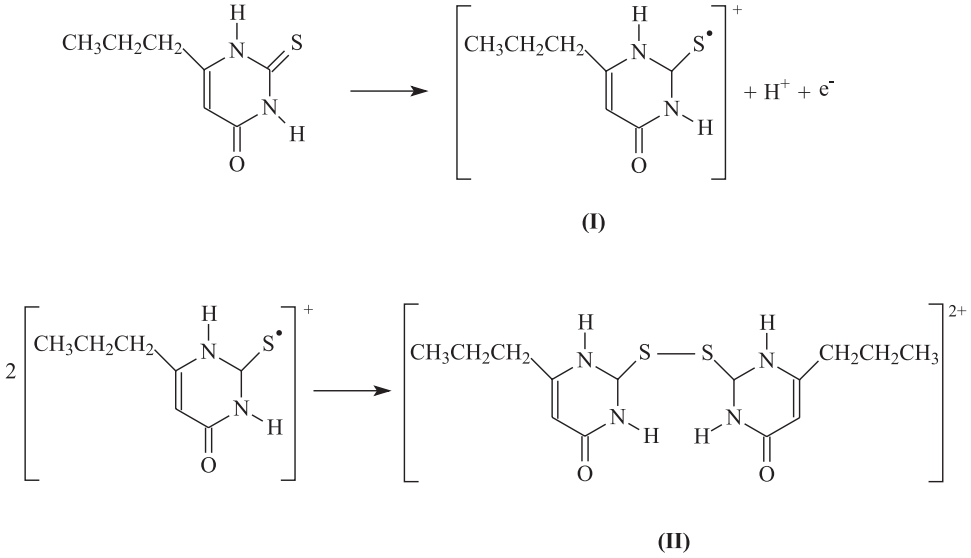

Figure 4. Proposed oxidation mechanism for propylthiouracil and its dimerization to a disulfide compound.

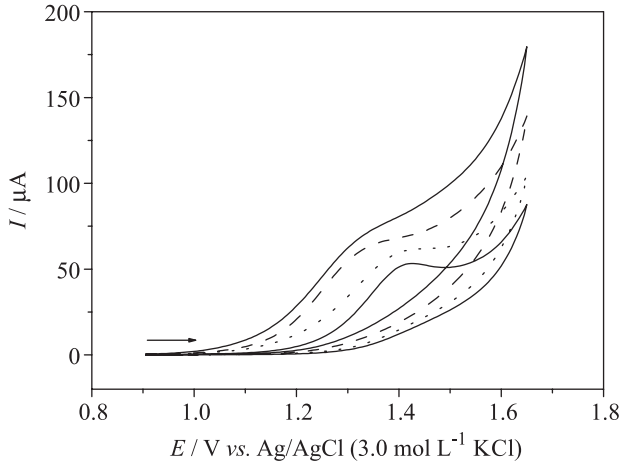

Figure 5. Cyclic voltammograms (50 mV s^{-1}) of 1.0 mmol L^{-1} PTU solutions in BR buffers of different pH values: 2.0 (solid thick line), 3.0 (dotted line), 4.0 (dashed line), and 5.0 (solid line) using a cathodically pretreated BDD electrode.

dependence of the peak current with the square root of the scan rate was found (Figure 6). On the other hand, a plot of the logarithm of the oxidation peak current *vs.* the logarithm of the scan rate yielded a straight line with a slope of 0.47, close to the theoretically expected value (0.5) for a diffusion-controlled behavior.[39] The number of electrons (n) transferred in the electrooxidation of PTU on the BDD electrode may also be estimated by applying Laviron's equation for an irreversible electrode process.[40] The obtained αn value was 0.673; hence, assuming that α is equal to 0.5, n can be estimated as 1.3, i.e., approximately 1, in reasonable agreement with the value obtained above from the $E_p - E_{p/2} = 47.7\ mV/\alpha n$ equation and confirming the involvement of one electron per molecule in the oxidation of PTU, as shown in Figure 4.

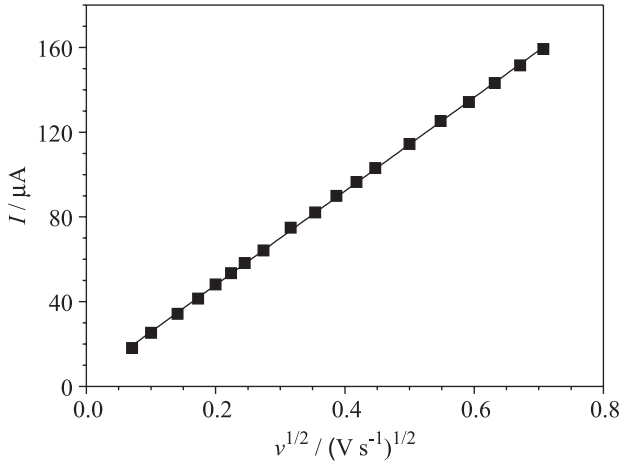

Figure 6. Linear dependence of the peak current (I_{ap}) with the square root of the scan rate ($v^{1/2}$) for cyclic voltammograms of a 1.0 mmol L^{-1} PTU solution in the BR buffer (pH 2.0) using a cathodically BDD electrode at different scan rates (0.005-0.500 V s^{-1}).

Analytical curves

First, the influence of the values of the operational parameters associated to each voltammetric technique (SWV and DPV) was investigated using the cathodically pretreated BDD electrode and a 100 μmol L^{-1} PTU solution in the BR buffer (pH 2.0).

For SWV, the investigated value ranges were: 10-150 Hz, for the square-wave frequency (f); 10-60 mV, for the pulse amplitude (a); 1-8 mV, for the scan increment (ΔE_S). The obtained optimized values were f = 50 Hz, a = 40 mV, and ΔE_S = 3 mV.

For DPV, the investigated value ranges were: 10-250 mV, for the pulse amplitude (a); 2.5-50 mV s^{-1}, for the scan rate (ν); 2-10 ms, for the modulation time (t). The obtained optimized values were a = 150 mV, ν = 40 mV s^{-1}, and t = 3 ms.

After optimization of these operational parameters, the analytical curves for PTU in the BR buffer solution (pH 2.0) were obtained for both voltammetric techniques. The analytical parameters associated to these curves are summarized in Table 1. As can be inferred from the values of these parameters, especially from those of the peak potential and sensitivity (slope), DPV yielded the best results and, hence, was selected for the determination of PTU. Despite the higher slope value, the DPV calculated detection limit (LOD) value (0.90 μmol L^{-1}) was similar to the SWV one (0.92 μmol L^{-1}); this occurred because the standard deviation of the blank solution was higher for DPV.

Table 1. Analytical parameters for the voltammetric determination of PTU in the BR buffer solution (pH 2.0) by square-wave voltammetry (SWV) and differential pulse voltammetry (DPV), using a cathodically pretreated BDD electrode.

	SWV	DPV
Peak potential / V	1.37	1.30
Linear range / (μmol^{-1} L)	1.0-29.1	1.0-29.1
Correlation coefficient, r	0.9989	0.9985
Slope / (μA μmol^{-1} L)	0.13	0.49
Intercept / μA	0.079	–0.62
Detection limit[a] / (μmol^{-1} L)	0.92	0.90

[a]Calculated as equal to three times the standard deviation of the blank solution divided by the slope of the analytical curve.

The DP voltammograms obtained for PTU reference solutions at different concentrations (1.0 to 29.1 μmol L^{-1}) in the BR buffer solution (pH 2.0) are presented in Figure 7. The insert in this figure depicts the respective analytical curve obtained for PTU (r = 0.9985), whose corresponding regression equation is

$$I_{ap} / \mu A = -0.62 + 0.49 \{[PTU] / (\mu mol\ L^{-1})\} \quad (1)$$

where I_{ap} is the anodic peak current.

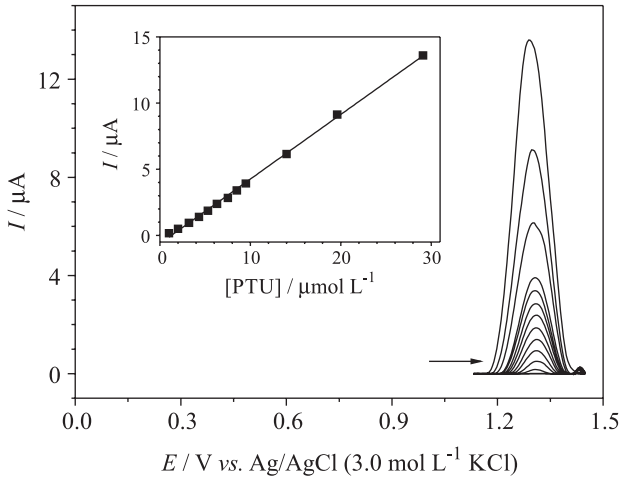

Figure 7. Differential pulse voltammograms obtained using the cathodically pretreated BDD electrode for (1) 1.0, (2) 2.0, (3) 3.2, (4) 4.3, (5) 5.3, (6) 6.3, (7) 7.5, (8) 8.5, (9) 9.5, (10) 14.0, (11) 20.0, and (12) 29.1 μmol L^{-1} PTU solutions in the BR buffer (pH 2.0). Insert: corresponding analytical curve.

The intra-day repeatability of the magnitude of I_{ap} was determined by successive measurements (n = 10) of a 7.0 μmol L^{-1} PTU solution in the BR buffer (pH 2.0), where a relative standard deviation (*RSD*) of 0.84% was obtained. The inter-day repeatability of the magnitude of I_{ap} was evaluated by measuring its value for similar fresh solutions over a period of 5 days, resulting in an *RSD* of 3.6%.

Table 2 presents a comparison between the analytical performances of the here-reported method and other voltammetric methods for the determination of PTU previously reported in the literature. These results reveal that the LOD value for PTU obtained in this work is lower than that obtained with a modified carbon paste electrode,[9] but higher than those obtained by CSV using a mercury electrode[7] and by DPV with a GC electrode using catechol as redox mediator.[10] However, the use of the cathodically pretreated BDD electrode for the determination of PTU is direct, with no need for renewal of the electrode surface; moreover, adsorption on the BDD surface of PTU oxidation products was not observed. On the other hand, the other procedures reported in the literature using solid electrodes require either mechanical polishing or surface renewal prior to the experiments to assure a reproducible electrode surface.

Next, the voltammetric response of the cathodically pretreated BDD electrode was compared to that of a GC electrode. Figure 8A shows the DP voltammograms obtained on these electrodes for a 500 μmol L^{-1} PTU solution in the BR buffer solution (pH 2.0). As can be seen, a higher magnitude of the PTU oxidation peak current was obtained on the BDD electrode, with an excellent repeatability (*RSD* < 1.0%, for n = 6; data not shown). Furthermore, the magnitude of the PTU oxidation peak current obtained on the GC electrode decreases with successive measurements (see Figure 8B), clearly indicating that the disulfide adsorbs on the surface of the GC electrode.

Determination of PTU in pharmaceutical formulations

The effect of some possible interferent compounds (starch, magnesium stearate, povidone, and calcium carbonate) was investigated for a 7.0 μmol L^{-1} PTU solution in the BR buffer (pH 2.0) at the concentration ratios (standard solution:interferent compound) 1:1, 1:10, and 10:1 (*m*/*m*). The corresponding current signals were compared with that obtained in the absence of any interferent compound. The obtained responses (data not shown) allowed to conclude that these compounds do not interfere with the determination of PTU at the used working conditions.

Next, PTU was determined in three different commercial pharmaceutical samples (tablets) by their dissolution in the BR buffer solution (pH 2.0) and using the cathodically pretreated BDD electrode. The results obtained employing the here-proposed method and the official titration method of the British Pharmacopoeia[5] for the determination of PTU in several commercial tablets are presented in Table 3. As can be inferred from the data in this table, no significant

Table 2. Comparison of the analytical parameters obtained using different electrodes and/or techniques for the determination of PTU

Electrode	Technique	Concentration range / (mol L^{-1})	LOD / (μmol L^{-1})	Reference
Au disc	CV	$1.0 \times 10^{-4} - 5.0 \times 10^{-4}$	-	7
Dropping mercury	CSV	$2.0 \times 10^{-8} - 2.4 \times 10^{-7}$	0.0010	8
CoClSal-carbon paste	DPV	$5.0 \times 10^{-6} - 7.5 \times 10^{-4}$	2.0	9
GC/indirect using catechol	DPV	$1.0 \times 10^{-7} - 1.0 \times 10^{-5}$	0.05	10
GC/PAH-MWCNTs	CSV	$5.0 \times 10^{-6} - 5.8 \times 10^{-5}$	1.0	11
BDD	DPV	$1.0 \times 10^{-6} - 2.9 \times 10^{-5}$	0.90	This work

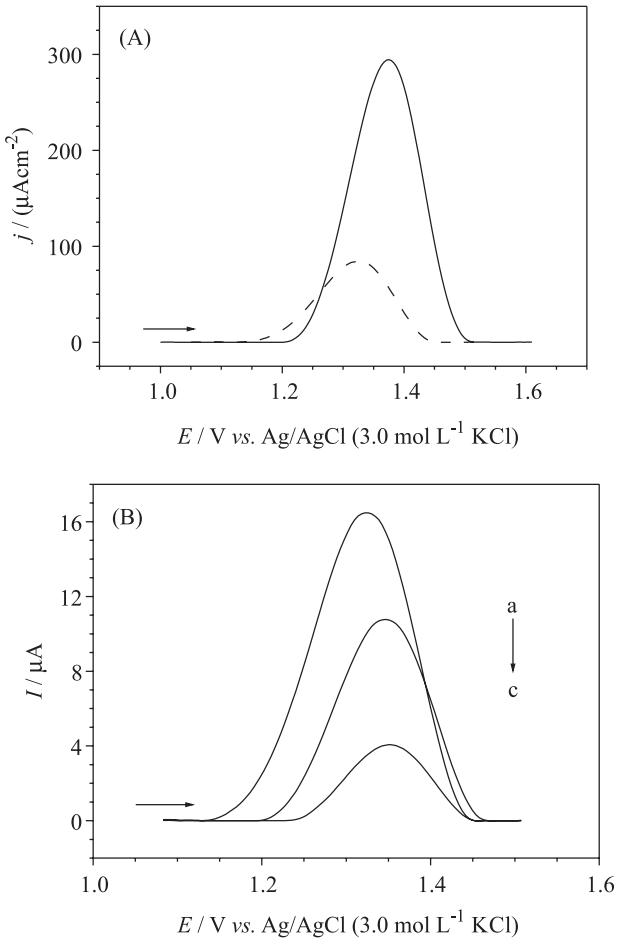

Figure 8. Differential pulse voltammograms for a 500 μmol L^{-1} PTU solution in the BR buffer (pH 2.0) obtained on: (A) GC (dashed line) and BDD (solid line) electrodes; (B) a GC electrode for the (a) first, (b) second, and (c) third scans.

differences were observed between the values found for the amounts of PTU in the tablets using the proposed DPV method and the standard titration method. Besides, considering that the paired *t*-test[41] was applied to these results and the calculated *t* value (0.242) is smaller than the critical value (4.303, $\alpha = 0.05$), the results obtained with either method are not statistically different, at a 95% confidence level.

Table 3. Results ($n = 3$) obtained for the determination of PTU in pharmaceutical formulations (tablets) using the here-proposed DPV method with a cathodically pretreated BDD electrode and a reference titration method[5]

Samples	PTU / mg			RE[a] / %
	Label value	Reference method	DPV method	
A	100	98.7 ± 0.9	99.8 ± 0.3	1.1
B	100	102.8 ± 0.8	104.6 ± 0.4	1.8
C	100	101.4 ± 0.9	97.1 ± 0.2	–4.2

[a]Relative error = [100 × (DPV method – reference method)] / reference method.

Finally, an addition and recovery study was carried out. Known amounts of standard solutions were added to a given sample and the resulting solution was analyzed by the here-proposed method. The obtained results yielded adequate average recoveries, ranging from 93.3% to 108% for the commercial tablets, indicating that there were no matrix interferences for these samples when analyzed by the proposed DPV method.

Conclusions

The results here reported demonstrate that a cathodically pretreated BDD electrode along with the DPV technique can be used to determine PTU in pharmaceutical formulations. After optimization of all the experimental parameters using a BR buffer solution (pH 2.0), a PTU detection limit of 0.90 μmol L^{-1} was attained. Furthermore, adequate relative standard deviations for 7.0 μmol L^{-1} PTU solutions of 0.84% and 3.6% were attained for intra-day ($n = 10$) and inter-day ($n = 10$) repeatability, respectively. On the other hand, an addition-recovery study yielded results statistically equal to those of a reference titration method. Moreover, the use of the cathodically pretreated BDD electrode did not lead to any adsorption effect, which allowed the use of the electrode for a long time with the same response. Clearly, the here-proposed method is simple, rapid, precise, and accurate for analytical determinations of PTU. Furthermore, the proposed voltammetric method does not involve the inconvenient use of mercury nitrate, as is the case with the official method of the British Pharmacopoeia.

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