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REVIEW ARTICLE

Anodic behaviour of fulvestrant and its voltammetric determination in pharmaceuticals and human serum on highly boron-doped diamond electrode using differential pulse adsorptive stripping voltammetry

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Abstract The electrochemical oxidation of fulvestrant was made on highly boron-doped diamond electrode using differential pulse adsorptive stripping voltammetry. The highest current intensities were obtained by applying +1.10 V during 150 s for boron-doped diamond electrode. For boron-doped diamond electrode, linear responses were obtained for the concentrations between 1×10^{-6} and 8×10^{-5} M in standard samples and between 1×10^{-6} and 4×10^{-5} M in serum samples. The repeatability of the method was 0.55 RSD% for differential pulse adsorptive stripping voltammetry. The analytical values of the method are demonstrated by quantitative determination of fulvestrant in pharmaceutical formulations and human serum, without the need for separation or complex sample preparation, since there was no interference from the excipients and endogenous substances. Selectivity, reproducibility, and accuracy of the developed methods were demonstrated by recovery studies.

Keywords Fulvestrant · Drug analysis · Human serum · Boron-doped diamond electrode · Adsorptive stripping voltammetry

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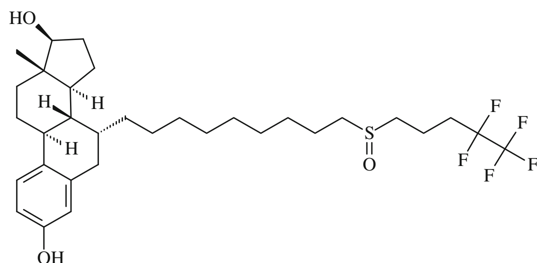
1 Introduction

Endocrine therapy is the treatment of choice for postmenopausal women with hormone receptor-positive advanced breast cancer owing to its favorable tolerability profile versus cytotoxic chemotherapy. However, tolerability concern associated with some endocrine treatments and the potential for cross-resistance has helped to drive the need for new, effective, and better-tolerated agents. Fulvestrant, a new type of oestrogen receptor antagonist with no agonist effects, in phase-II trials, has been shown to be at least as effective as the third-generation aromatase inhibitor anastrozole in the treatment of postmenopausal women with advanced breast cancer progressing on tamoxifen therapy. Fulvestrant has low bioavailability and presystemic metabolism after oral administration. A long-acting intramuscular administration of fulvestrant gives adequate bioavailability and allows controlled release of the drug.

Fulvestrant has a steroidal structure 7-alpha-(9-((4,4,5,5,5-pentafluoropentyl) sulfinyl) nonyl) estra-1,3,5(10)-triene, 3,7 beta-diol) (Scheme 1), which when complexed with oestrogen receptors, prevents its dimerisation and renders the receptor transcriptionally inactive [1–4].

No report has been published on quantitative determination of fulvestrant in pharmaceutical formulations. Moreover, no monograph of fulvestrant has been reported in the official pharmacopoeias as of today.

The widespread use of this compound and the need for clinical and pharmacological studies require fast and sensitive analytical techniques to assay the drug in pharmaceutical dosage forms and biological samples. These may also be used for monitoring patient compliance and establishing relationship between blood concentration and the therapeutic effects, which are not always fully understood.



Scheme 1 Structure of fulvestrant

Electroanalytical methods have long been used for the determination of a wide range of drug compounds due to their simplicity, low cost, and relatively short analysis time when compared to other techniques. Furthermore, the knowledge of the electrochemical properties of a drug is an important pharmaceutical tool mostly because it can be vital to understand its metabolic fate or in vivo redox processes and pharmacological activity.

Pure diamond is a very good electrical insulator and the material may be doped with boron to produce electrodes with semiconducting or semimetallic properties. Each carbon atom in the bulk of diamond is tetrahedrally bonded to four others using sp3-hybrid orbital. In the electrically conducting doped form, diamond adds a very useful new electrode material to the range of electrode types available in electroanalysis. Compared to classical carbon electrodes and other metallic electrodes, diamond electrodes open up new opportunities for working under extreme conditions, such as extremely high anodic potentials, or extremely aggressive media (e.g., strongly acidic) [5, 6].

The use of diamond electrodes, especially boron-doped diamond electrode, has been proposed for many electrochemical applications such as pharmacological applications and determination of hostile environments and pharmaceutical dosage forms. Diamond electrodes also possess attractive features such as stability, low voltammetric background currents, a wide potential window in aqueous and non-aqueous electrolytes, high thermal conductivity, high hardness and chemical inertness, very low capacitance, and high electrochemical stability [6–8].

Among the electroanalytical techniques currently available for boron-doped diamond electrodes and various electrodic surfaces, differential pulse voltammetry is an extremely sensitive method for the detection of pharmaceutical compounds [9]. The analytical sensitivity of differential pulse voltammetry can be improved by using adsorptive steps, involving an initial accumulation step to preconcentrate the analyte into, or onto, and the working electrode, which is then electrochemically oxidized or reduced in the current measurement step [10–12].

The use of adsorptive steps allied to the differential pulse voltammetry technique is well established. These steps provide high sensitivity and prove an advantage for the determination of both organic and inorganic compounds, since they are relatively simple and fast. Moreover, they cause insignificant effects on the components of the samples [10]. In addition,up to now there is only one published literature on quantitative determination of drug molecules at boron-doped diamond electrode using stripping voltammetry [11].

This study therefore investigated the electrochemical behavior of fulvestrant and developed an analytical procedure to quantify this compound in commercial formulations employing differential pulse adsorptive stripping voltammetry (DPAdSV) using boron-doped diamond (BDD) electrode.

2 Experimental

2.1 Apparatus

Voltammetric experiments were performed using a BAS 100 W (Bioanalytical System, USA) electrochemical analyzer associated to one-compartment glass electrochemical cell equipped with a three-electrode system consisting of a BDD (Windsor Scientific Ltd; ϕ: 3 mm, diameter) working electrode, a platinum wire counter electrode and an Ag/AgCl saturated KCl reference electrode. Before each experiment, BDD electrode was polished manually with aqueous slurry of alumina powder (0.01 µm, diameter) on a damp smooth polishing cloth (BAS velvet polishing pad). All measurements were performed at room temperature.

The pH measurements were made using a model 538, WTW pH-meter (Austria) with a combined electrode (Glass-reference electrodes) with an accuracy of pH $\pm$ 0.05.

The experimental conditions for differential pulse adsorptive stripping voltammetry (DPAdV) were as follows: scan rate of 20 mV/s, pulse amplitude of 50 mV, pulse width of 50 ms, and pulse period of 200 ms.

2.2 Chemicals and standards

Fulvestrant and its pharmaceutical dosage form were kindly supplied by Astra Zeneca (Istanbul, Turkey). Model compounds, levodopa, carbidopa, benserazide, epirubicine, and doxorubicine were kindly supplied from different pharmaceutical companies in Turkey. Other chemicals were reagent grade (Merck or Sigma).

Stock solutions of fulvestrant (1×10^{-3} M) were prepared in acetonitrile and kept in the dark at 4 °C. Fulvestrant working solutions for voltammetric investigations were prepared by dilution of the stock and contained 30%

acetonitrile. Four different supporting electrolytes, sulfuric acid solution (0.1 and 0.5 M), phosphate buffer (0.2 M H_3PO_4; 0.2 M $NaH_2PO_4 \cdot 2\ H_2O$; 0.2 M Na_2HPO_4; pH 2.0–8.0), Britton-Robinson buffer (0.04 M H_3BO_3; 0.04 M H_3PO_4, and 0.04 M CH_3COOH; pH 2.0–10.0), and acetate buffer (0.2 M CH_3COOH; pH 3.5–5.5), were used for electrochemical measurements. All solutions were protected from light and were used within 24 h to avoid decomposition. All measurements were carried out at the ambient temperature of the laboratory (23–27 °C). The calibration curve for DPAdSV analysis was constructed by plotting the peak current versus the fulvestrant concentration.

The ruggedness and precision were checked at different days. The results were given as repeatability (within day) and reproducibility (between days). Relative standard deviations (RSD) were calculated to check the ruggedness and precision of the method [13–20].

The accuracy and precision of the developed methods are described in a quantitative fashion by the use of relative errors (Bias %). An example of the Bias% is the accuracy which describes the deviation from the expected results.

2.3 Pharmaceutical dosage form assay procedure

1.21 mL of Faslodex® injectable solution, claim to contain 250 mg fulvestrant per 5 mL of the solution, was dissolved in 100 mL of acetonitrile. An aliquot of this solution was transferred to a 10.0 mL volumetric flask and diluted to the mark with supporting electrolyte and the voltammogram was recorded.

The nominal content of the injectable solution is determined from corresponding regression equations using BDD electrodes.

2.4 Analysis of serum

Drug-free human blood, obtained from healthy volunteers (after obtaining their signed consent), was centrifuged (5,000 rpm) for 30 min at room temperature. The separated serum samples were stored frozen until assay. An aliquot volume of the serum sample was fortified with fulvestrant dissolved in acetonitrile to achieve final concentration of 1×10^{-3} M. This solution contained acetonitrile as serum precipitating agent. Acetonitrile removed serum proteins effectively, by the addition of 1 to 1.5 volumes of the serum. The mixture was vortexed for 30 s, centrifuged for 10 min at 5,000 rpm to remove serum protein residues and the supernatant was taken carefully. Appropriate volumes of the supernatant were transferred to the volumetric flask and diluted to the chosen volumes with 0.1 M sulfuric acid solution. The concentration of fulvestrant in the prepared solutions was varied in the range of 1×10^{-6}–4×10^{-5} M using DPAdSV technique with BDD electrode in human serum samples.

Quantifications were performed by means of the calibration curve method from the related calibration equation.

3 Results and discussion

Boron-doped diamond electrodes for application in electroanalytical determination have been receiving increasing attention, mainly due to the number of their advantages over traditionally employed electrodes (e.g., glassy carbon or metal electrodes), such as high corrosion resistances, extreme hardness, chemical inertness, high thermal conductivity, low sensitivity of dissolved oxygen, very low and stable background currents, and a wide working potential window in aqueous solutions.

Fulvestrant appears to be an electroactive drug, but there are no reports about the electrooxidation. In order to understand the electrochemical behavior occured on BDD electrode, cyclic (CV) and linear sweep voltammetry were carried out. Differential pulse adsorptive stripping (DPAdSV) voltammetric technique was developed for the quantitative determination of fulvestrant using BDD electrode.

Fulvestrant is manifested on current–potential curves recorded by CV by one anodic wave. Cyclic voltammogram of 2×10^{-5} M fulvestrant using BDD electrode (sweep rate 100 mV/s) exhibited a single irreversible oxidation wave at +1.00 V. This wave was obtained more clearly from further successive segments (Fig. 1).

It is well known that pH of the supporting electrolyte has a major impact on the response in most analytical

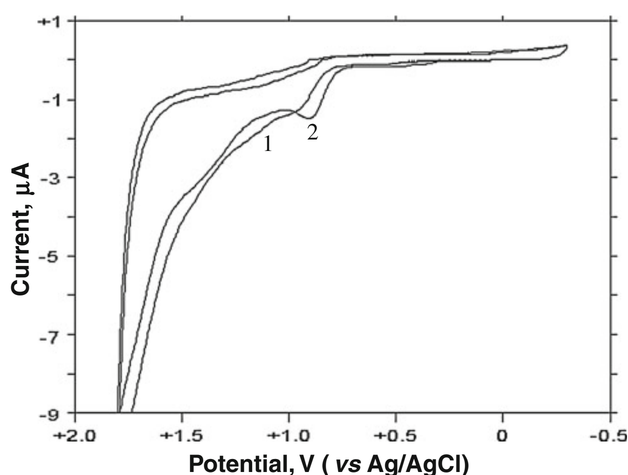


Fig. 1 (*1*) First cycle and (*2*) second cycle of the repetitive voltammograms for 8×10^{-5} M fulvestrant solution in 0.1 M sulfuric acid with BDD electrode. Curve is from 0 to +1.8 V. Scan rate is 100 mV/s

determinations of organic and inorganic compounds. We examined the involvement of this parameter in the oxidation process on BDD electrode. The pH-dependent oxidation of fulvestrant was studied systematically in a pH range between 1.80 and 12.00. The voltammetric response was markedly dependent on pH.

Before starting the pH studies on BDD electrode, the circumstances of the stripping parameters were optimized. Next, these parameters are used for the following experiments. Accumulation time and accumulation potential were individually optimized and chosen as +1.05 V and 90 s, respectively, for pH investigations. Besides, the DPAdSV behavior of 2×10^{-5} M fulvestrant using BDD electrode yielded one well-defined peak in strongly acidic solutions such as 0.1 M sulfuric acid, pH 3.0 Britton-Robinson, or pH 2.0 phosphate buffer (Fig. 2).

As pH increased, the wave gave a small shoulder. When exceeded 9.0, fulvestrant did not give any measurable or detectable electrochemical response. Therefore, only anodic process will be discussed hereafter.

The peak potential (E_p) versus pH plot created a straight line (Fig. 3a) between pH 1.0 and 9.0. The slope of the below equation is found 29.45 mV/pH for the main oxidation process. This slope is found close to the expected theoretical value of 30 mV/pH. According to the obtained slope value of this equation, same amount of electron and proton is involved in the rate-determining steps [21].

$$E_p = 954.83 - 29.45\,\text{pH}; \quad r = 0.991$$

(SE of intercept: 7.08, SE of slope: 1.32)

(Acetate, phosphate, and BR buffer between pH 1.0 and 9.0)

The intersection of the E_p–pH curves is located around pKa value of drugs. pH 10.03 which may correspond to the pKa value of fulvestrant according to the literature [22]. Unfortunately, this value could not be set with BDD electrode due to the lack of any peaks or waves beyond pH 9.0.

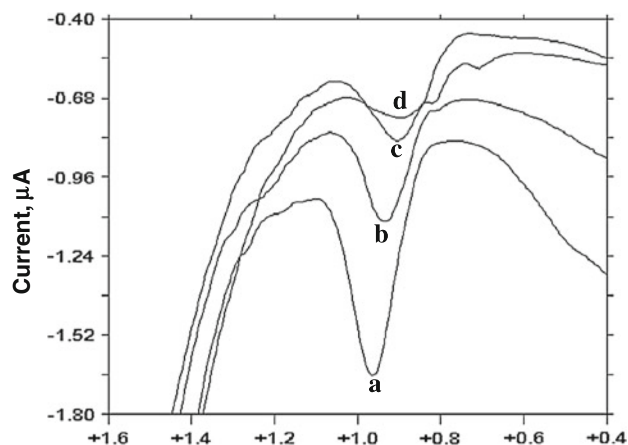


Fig. 2 DPAdS voltammograms of 2×10^{-5} M fulvestrant on BDD electrode. (*a*) 0.1 M sulfuric acid; (*b*) pH 2 phosphate buffer; (*c*) pH 3 BR buffer; (*d*) pH 5 BR buffer solutions. Accumulation time: 90 s; accumulation potential: +1.05 V

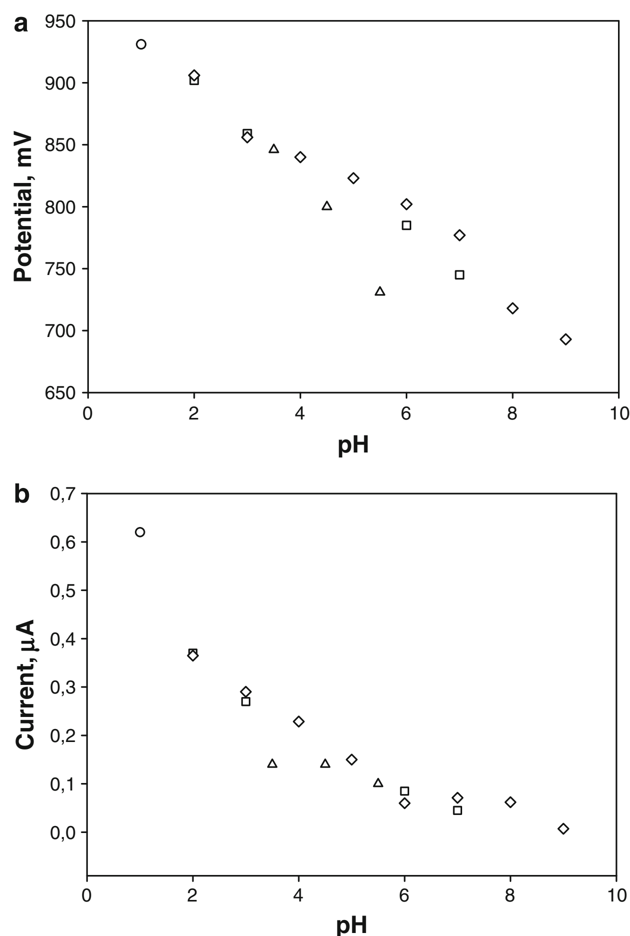


Fig. 3 Effect of pH on fulvestrant anodic peak potential (**a**) and peak current (**b**); fulvestrant concentration: 2×10^{-5} M. 0.1 M sulfuric acid (*open circle*); 0.2 M phosphate (*open square*); 0.2 M acetate (*open triangle*); 0.04 M BR buffers (*open diamond*)

The effect of pH (within the range of 1.8–12.0) on the peak current of fulvestrant was investigated also Fig. 3b. The plot of I_p vs. pH indicated that the peak current reached a maximum for 0.1 M H_2SO_4. Therefore, 0.1 M H_2SO_4 was chosen as the supporting electrolyte for the quantitative determination part of the study. This supporting electrolyte was chosen with respect to sharp response and better peak shape for the calibration equation of pharmaceutical dosage forms and biological samples.

For BDD electrode, however, the peak potential shifted to more positive potentials (about 230 mV) to the anodic direction when the scan rate increased. This can be expressed by the following equation:

$$E_p\,(\text{mV}) = 0.42\ v\,(\text{mV/s}) + 1189.30;\quad r = 0.971,\quad n = 6\,(\text{for } 5\text{–}250\ \text{mV/s})$$

$$(\text{SE of intercept: } 6.04,\quad \text{SE of slope: } 5.18 \times 10^{-2})$$

The rate increased to the observed potential until 250 mV/s and levelled off thereafter.

When the scan rate was varied from 5 to 1,000 mV/s in 4×10^{-5} M fulvestrant, a linear dependence of the peak intensity I_p (μA) upon the square root of the scan rate ($v^{1/2}$) (mV/s) was found, demonstrating an adsorptive behaviour.

The equation is for BDD electrode in 0.1 M H_2SO_4 solution:

$$I_p\,(\mu\text{A}) = 0.14\,v^{1/2}\,(\text{mV/s}) - 0.39;\quad r = 0.987,\ n = 10$$

$$(\text{SE of intercept: } 1.35 \times 10^{-1},\ \text{SE of slope: } 8.11 \times 10^{-3})$$

It followed from the variation of the logarithm of the peak current as a function of the logarithm of the sweep rate in the range of 5–1,000 mV/s that the process was adsorptive controlled, since the value of the straight line $\log I_p = f(\log v)$ was equal to 0.69. This showed that the process had an adsorptive component.

Tafel plot was obtained with a scan rate of 5 mV/s beginning from a steady-state potential in 0.1 M sulfuric acid for BDD electrode and from the slope of the linear part and αn was 0.33. The exchange current density (I_o) was 1.35×10^{-11} A cm^{-2} for this system. These values and the absence of cathodic waves in cyclic voltammetry indicated electrochemical irreversibility of the oxidation reaction.

The anodic oxidation of oxygen-containing compounds appears to be a complex process and different reaction pathways might be possible and still continues to be an active area of research. The mechanism of oxidation of fulvestrant may be postulated by oxidation of the hydroxyl group on the aromatic ring. Comparative studies on levodopa, carbidopa, benserazide, epirubicine, and doxorubicine related for the hydroxyl group of fulvestrant were carried out by cyclic voltammetry on BDD electrodes—as a function of pH—in order to identify the other oxidation step of fulvestrant. The cyclic voltammograms of these selected compounds closely matched the more positive part of the voltammograms of fulvestrant. In general, the oxidation of phenol in a solution at high pH will generate the phenoxy radical giving additional oxidation and reduction process. We assumed that the oxidation process, via an initial oxidation of equal amount electrons and protons, via conversion of hydroxyl group to quinone, might be occurring together on the selected compounds and the hydroxy group of the molecule, which was electroactive in both acidic and basic media.

3.1 Analytical applications and validation of the analytical procedure

Pulse voltammetric techniques such as DPV, square wave voltammetry, and adsorptive stripping pulse techniques are effective and rapid electroanalytical techniques with well-established advantages including good discrimination against background currents and low detection limits [23, 24]. Short adsorption times (1–5 min) result in a very effective interfacial accumulation. This technique has been shown to be highly suitable for measuring organic drug compounds.

Adsorption of the analyte was confirmed by the results obtained with cyclic voltammetry. The plot of logarithm of the peak current versus logarithm of the scan rate has a slope of 0.69, close to the theoretical value of 1.0 which is expressed for an ideal reaction of the adsorption controlled electrode process for BDD electrode. Also, adsorptive stripping parameters such as accumulation time, potential, etc. were investigated in 0.1 M H_2SO_4. The spontaneous accumulation of fulvestrant can be exploited for effective preconcentration prior to the voltammetric scan. Figure 4a displays the resulting peak current versus accumulation potential for 2×10^{-5} M fulvestrant in 0.1 M sulfuric acid solution. An adsorption potential of +1.1 V was adopted for analytical determination of fulvestrant in 0.1 M sulfuric acid solution. Figure 4b shows the resulting peak current versus. preconcentration time profile for 2×10^{-5} M of fulvestrant.

The rate increased to the current observed at a short preconcentration time and was followed by a leveling-off. The plots did not pass through the origin possibility because of the strong adsorption of the analyte on the electrode surface at the equilibrium time, which was fixed to 10 s. Hence for the maximum sensitivity, a 150-s accumulation time was used for the subsequent quantitative determinations with DPAdSV method. However, the ultimate decision on accumulation time must depend on the concentration range studies.

DPAdSV for BDD electrode was developed for the quantitative determination of fulvestrant. 0.1 M sulfuric acid solution proved the best medium for the analytical applications.The plot of the calibration curve was linear between 1×10^{-6} and 8×10^{-5} M for DPAdSV method. Characteristics of these graphs are reported in Table 1.

The precision of the method was investigated by repeatedly ($n = 5$) measuring peak potential and peak current of fulvestrant within a day and over three consecutive days. LOD and LOQ were calculated as (3 σ/m) and (10 σ/m), respectively, where σ is the standard deviation of response (three runs) and m the slope of the calibration

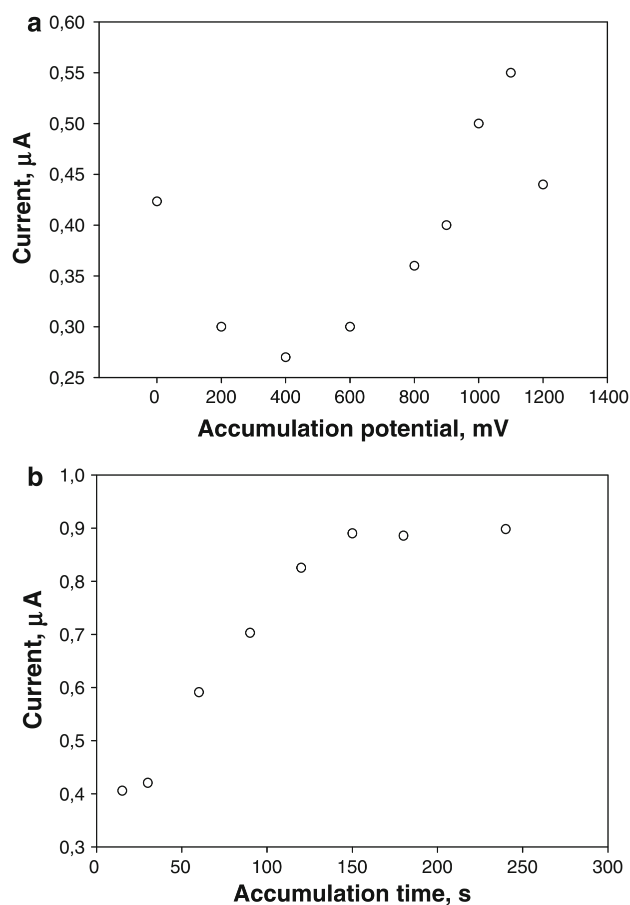


Fig. 4 **a** Effect of accumulation potential on the peak current with 150 s of accumulation time. **b** Effect of accumulation time on the peak current, with an accumulation potential at +1.10 V for 2×10^{-5} M fulvestrant in the presence of 0.1 M sulfuric acid using DPAdSV method for BDD electrode

curve. LOD and LOQ values confirmed the sensitivity of the proposed methods were shown in Table 1.

The low values of SE of slope, the intercept, and a correlation coefficient greater than 0.99 in the supporting electrolyte and human serum samples confirmed the precision of the proposed method.

The stability of the reference substance and sample solutions was checked by analyzing prepared standard solution of fulvestrant in the supporting electrolyte aged at +4 °C in the dark against freshly prepared sample. The results demonstrated that the working reference solutions were stable at least for 3 days. The fulvestrant response for the assay reference solutions over 3 days did not change considerably.

The developed techniques were validated according to the ICH guidelines [25]. The results are summarized in Table 1. Accuracy, precision, specificity, selectivity, reproducibility, LOD, and LOQ of the proposed technique

Table 1 Regression data of the calibration curve and quantitative determination of fulvestrant by DPAdSV in standard solution and human serum for BDD electrode

	BDD electrode	
	Standard solution	Serum
Measured potential (V)	1.00	0.98
Linearity range (M)	1×10^{-6}–8×10^{-5}	1×10^{-6}–4×10^{-5}
Slope (µA M^{-1})	3.52×10^{4}	5.77×10^{4}
Intercept (µA)	-9.02×10^{-2}	-1.12×10^{-1}
Correlation coefficient	0.999	0.998
SE of slope	4.17×10^{2}	1.40×10^{3}
SE of intercept	1.46×10^{-2}	2.33×10^{-7}
LOD (M)	2.36×10^{-7}	2.33×10^{-7}
LOQ (M)	7.88×10^{-7}	7.76×10^{-7}
Repeatability of peak current (RSD%)	0.55	0.95
Repeatability of peak potential (RSD%)	0.66	0.67
Reproducibility of peak current (RSD%)	1.50	1.28
Reproducibility of peak potential (RSD%)	0.71	0.71

were assessed by performing replicate analysis of the standard solutions in the supporting electrolyte and human serum samples within calibration curves. The selected concentrations were prepared in both media, assayed with the related calibration equations to determine repeatability and reproducibility, and were shown as RSD% values in Table 1. The validation results shown in Table 1 demonstrate good precision, accuracy, and reproducibility.

3.2 Determination of fulvestrant in pharmaceutical formulations

When working on standard solutions and occurring to the obtained validation parameters, the results encouraged the use of the proposed methods described for the assay of fulvestrant in injectable dosage form. Pretreatment was not required for the samples prior to the analysis. The developed voltammetric technique was applied to the direct determination of fulvestrant in pharmaceutical dosage forms, using the related calibration straight line. The results showed that the proposed method was successfully applied for the assay of fulvestrant in its dosage forms (Table 2). The accuracy of the proposed method was determined by its recovery during spiked experiments. Recovery studies were carried out after the addition of known amounts of pure drug to various preanalyzed formulations of fulvestrant.

Table 2 Results obtained from the determination and recovery experiments in injectable dosage form for DPAdSV with BDD electrode

	BDD electrode
Labeled claim (mg 5 mL^{-1})	250.00
Amount found[a]	250.33
RSD%	0.66
Bias%	−0.13
Added fulvestrant (mg)	20.00
Found fulvestrant (mg)[a]	20.18
Average recovery%	100.88
RSD% of recovery	1.63
Bias%	−0.88

[a] Each value means five experiments

In order to detect interactions of excipients, the standard addition technique was applied to the same pharmaceutical preparations, which were analyzed by the calibration curve. Recovery experiments using the developed assay procedures further indicated the absence of interference from commonly encountered pharmaceutical excipients used in the selected formulations (Table 2). The results indicated the validity of the proposed techniques for the determination of fulvestrant in injectable dosage form (Table 2).

3.3 Determination of fulvestrant in spiked human serum

The optimized procedure was successfully applied to the determination of fulvestrant in protein-free spiked human samples. Acetonitrile was used as a serum precipitating agent. The best results were obtained with 5.4 mL of acetonitrile. No extraction or evaporation other than the centrifugal protein separation was required prior to assay for the drug. The measurements of fulvestrant in serum samples were performed as described in Sect. 2.

The applicability of the proposed method to the human serum samples and the calibration equation were obtained

Table 3 Results obtained from fulvestrant determination from spiked serum

	BDD electrode
Added fulvestrant concentration (M)	4×10^{-5}
Obtained fulvestrant concentration (M)	4.01×10^{-5}
Number of experiments	5
Average recovery%	100.25
RSD% of recovery	0.85
Bias%	−0.25

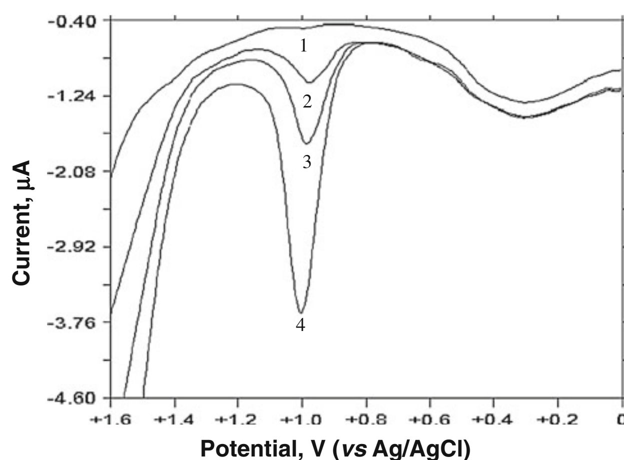


Fig. 5 DPAdS voltammograms on BDD electrode in 0.1 M sulfuric acid for the determination of fulvestrant in spiked human serum samples; (*1*) blank serum extract, (*2*) extract containing 1×10^{-5} M, (*3*) extract containing 2×10^{-5} M, (*4*) extract containing 4×10^{-5} M

in spiked human serum samples. Calibration equation parameters and necessary validation data were shown in Table 1. The recovery results of fulvestrant in serum samples were calculated from the related linear regression equation, which were given in Table 1. Obtained recovery results of spiked human serum samples were given in Table 3.

Analysis of drugs from serum samples usually requires extensive time-consuming sample preparation, use of expensive organic solvents and other chemicals. In this study, the serum proteins and endogenous substances in serum samples were precipitated by the addition of acetonitrile and centrifugation at 5,000 rpm. The supernatant was taken and diluted with the supporting electrolyte and directly analyzed. Typical DPAdSV curves of fulvestrant for BDD electrode examined in serum samples were shown in Fig. 5. As shown in Fig. 5, no oxidation compounds and no extra noise peaks presented in biological material peak occured in the potential range where the analytical peak appeared.

Stability of serum samples kept in cold (+4 °C) was tested with five consecutive analysis of the sample over a period of approximately 5 h. There were no significant changes in the peak currents and potentials between the first and last measurements.

4 Conclusions

BBD electrode showed perfect accomplishment for analysis of fulvestrant using DPAdSV.

The electrochemical process proved an irreversible oxidation at all of pH values and buffers that were

investigated. The analyses were performed without any interference by the additives in injection solution and human serum samples. The analytical results obtained from pharmaceutical dosage forms or human serum samples for DPAdSV with BDD electrode.

The use of electrochemical techniques to study mechanism directly with the electrodes and the determination of compounds of pharmaceutical interest has been become more popular [26].

In this study, possible oxidation pathways were tried to identify the functional groups responsible from the oxidation. For this reason, the oxidation process of fulvestrant was compared with those of some model compounds. Comparative studies on levodopa, carbidopa, benserazide, epirubicine, and doxorubicine related for the hydroxyl group of fulvestrant were performed by cyclic voltammetry on BDD electrode, as a function of pH, in order to identify the oxidation step of fulvestrant. The oxidation mechanism of fulvestrant seems to be the oxidation of the hydroxyl group on the aromatic ring.

Validated DPAdS voltammetric procedures were developed. Proposed method was fully validated. Once the instrument was set, just by changing the analyte within about 2 min, the amount of fulvestrant could be determined, indicating its potential in high throughput analysis of a large number of samples. We believe that the above-presented technique is appropriate for determining fulvestrant in pharmaceutical formulations and spiked serum samples. The proposed methods might be an alternative to the HPLC techniques in therapeutic drug monitoring or the experimental data might be used for the development of HPLC-EC method.

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