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Square-wave voltammetric determination of rosuvastatin calcium in pharmaceutical and biological fluid samples using a cathodically pretreated boron-doped diamond electrode

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ABSTRACT

The analytical potential of a boron-doped diamond electrode (BDD) and square-wave voltammetry (SWV) for the determination of rosuvastatin calcium (ROS) was investigated. The voltammetric response of the ROS molecule was evaluated with a BDD electrode that was subjected to anodic (positive polarization, +3.0 V for 5.0 s) or cathodic (negative polarization, −3.0 V for 15.0 s) pretreatments. The target analyte showed an irreversible anodic process at ≈1.4 V (vs. Ag/AgCl (3.0 mol L^{-1} KCl)) with an enhanced current response at a BDD electrode that was cathodically pretreated. Using the cathodically pretreated BDD electrode, other experimental conditions were optimized, including the supporting electrolyte and SWV parameters. Under optimized experimental conditions, the analytical curve was linear in the ROS concentration from 9.40 to 88.8 mg L^{-1} (9.40 to 88.8 μmol L^{-1}), with a correlation coefficient of 0.998 and limit of detection of 1.04 mg L^{-1} (1.04 μmol L^{-1}). The proposed method was successfully applied for ROS determination in pharmaceutical formulations and the electrochemically determined quantity of drug was in close agreement with the results obtained using a spectrophotometric method at the 95% confidence level. Additionally, biological fluid samples of urine and human serum were directly analyzed by the proposed voltammetric procedure, with excellent results of recovery.

1. Introduction

The pharmaceutical class of statins is the most known and widely consumed in the world for hypercholesterolemia treatment [1]. In this class, therefore, are included compounds of anti-lipid activity as its main pharmacological action, reducing the blood cholesterol levels and the risks of cardiovascular diseases [2,3]. Rosuvastatin calcium (ROS, Fig. 1) is the seventh statin approved by the US Food and Drug Administration Agency for commercialization [4]. Chemically, the ROS molecule has the same statin pharmacophore group common to the other statins, and the main structural difference is the presence of the pyrimidine ring (see Fig. 1), which provides the pharmacokinetic behavior changes [3]. In comparative assays, a higher efficiency for the reduction of low-density lipoprotein (LDL) cholesterol in blood was observed for the ROS statin than with another widely used statins, such as, atorvastatin, pravastatin and simvastatin [5]. Based in the pharmaceutical relevance of the ROS statin, analytical approaches of high efficiency for the rigid control of this important active principle in pharmaceutical formulations and different biological fluids are required.

Recent analytical methods dedicated to ROS quantification encompass high-performance liquid chromatography [6,7], electrophoresis [8], and spectrophotometry [9,10]. The application of these techniques is satisfactory with the generation of highly sensitive methods. However, most of these methods are relatively of high cost, generate a high amount of toxic organic solvent and are of low analytical frequency. These aspects can be covered using the electroanalytical methods, whose application fields have increased in the recent years [11,12]. Regarding to the electroanalytical determination of ROS, there are only two articles reported in the literature [13,14]. Altnoz and Uyar [13] used a hanging mercury drop electrode (HMDE) as working electrode for the square-wave voltammetric determination of ROS in pharmaceutical samples. Ramadan et al. [14] presented a differential pulse polarographic analysis (DPPA) method using a dropping mercury electrode (DME) for ROS determination. In these works, the authors explored the reduction reaction of the ROS molecule, and, in this paper, the electrochemical behavior of the ROS molecule was investigated on the boron-doped diamond (BDD) electrode involving the oxidation of this molecule. Despite the good results collected with the use of the mercury electrodes, mercury-based electrodic materials have been commonly replaced by alternative electrodes due to environmental issues [15].

Boron-doped diamond (BDD) electrodes gather a number of interesting electrochemistry properties which makes it ideal for electroanalysis

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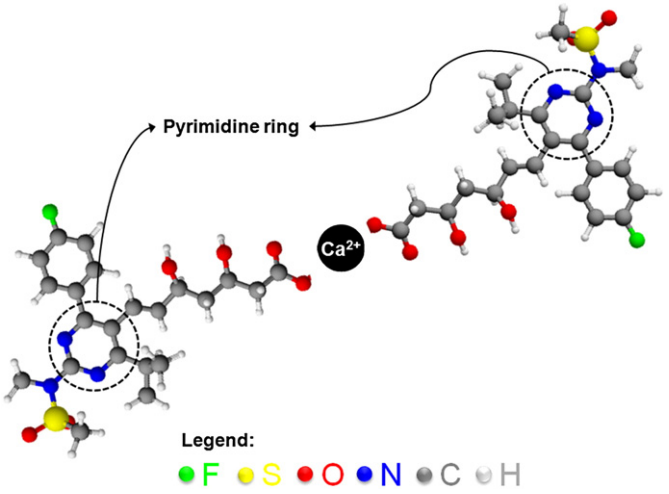

Fig. 1. Molecular structure of the rosuvastatin calcium. Two anionic rosuvastatin ions are contra-ions of a calcium cation.

applications, such as low and stable background current, wide working potential window, reduced adsorption effects, chemical and electrochemistry stability at aggressive media, and high precision of measurements [16–23]. From these properties, BDD electrodes have been used as working electrode to sensing of different target compounds of pharmaceutical [24–26], environmental [27–30], food [31–34] and biological [35–41] interest.

In this work, a BDD electrode was evaluated in the development of a square-wave voltammetric method for ROS determination in pharmaceutical formulation and different biological fluid samples. The proposed procedure is characterized by simplicity, with minimal sample treatment steps, fast analytical response, and high precision and accuracy.

2. Experimental

2.1. Reagents, solutions and samples

ROS standard was purchased from Calendula Pharmacy (molecular mass: 1001.14 g mol^{-1}; purity grade: 99%), and methanol and all the other chemical reagents used were purchased from the Sigma-Aldrich. Methanol was used as solvent for the diary preparation of 1.00×10^{-2} mol L^{-1} ROS stock solutions. The other solutions were prepared in ultra-pure water with resistivity greater than 18.0 MΩ cm supplied by a Millipore Milli-Q system (Billerica, USA). Pharmaceutical tablet samples were acquired in a local drugstore. The synthetic biological fluid samples of urine and human serum were prepared as previously reported by Laube [42] and Parham and Zargar [43].

2.2. Apparatus and BDD pretreatment procedures

The electrochemical assays were conducted in a potentiostat/galvanostat Autolab PGSTAT204 driven by the NOVA 1.10.4 software and using a 20 mL three-electrode electrochemical cell. The reference electrode was an Ag/AgCl (3.0 mol L^{-1} KCl), the counter electrode was a Pt spiral wire, and the working electrode was an anodically, or a cathodically, pretreated BDD electrode. The BDD film was synthesized on silicon wafers and with a boron content of 8000 ppm in the *Centre Suisse d'Electronique et de Microtechnique SA* (CSEM), Neuchâtel, Switzerland, using the hot filament chemical vapor deposition technique. For use as working electrode, the conducting silicon wafer substrate supporting the BDD film was fixed to a copper plate using tin solder and sealed with epoxy resin, leaving free only the BDD surface (exposed geometric area of 0.24 cm^2). Thus, the electrical contact was achieved in the backside of the conducting Si substrate. The BDD pretreatments were performed by positive or negative electrode polarization: anodic pretreatment, +3.0 V for 5.0 s and cathodic pretreatment, −3.0 V for 15.0 s [44]. The pretreatments were conducted in a 0.5 mol L^{-1} H_2SO_4 solution using a Pt plate as counter electrode and a DC Power Supply Minipa MPC-1303. For comparison and validation of the electrochemical assay, a spectrophotometric assay was also used for ROS quantification using a Shimadzu UV-2550 UV–vis spectrometer.

2.3. Analytical procedures

Initially, the voltammetric response of the ROS molecule was explored. After confirming the electroactivity of the ROS molecule, we performed optimization steps of the voltammetric response, as well as the investigation of the ROS electrochemistry features.

Regarding the optimization, we tested the effect of the BDD pretreatment, H_2SO_4 concentration as supporting electrolyte, and all parameters from the square-wave voltammetry (SWV). Under the optimized experimental conditions, the analytical curve for ROS was constructed. For this, appropriate aliquots of a standard ROS solution were added in the electrochemical cell containing 15.0 mL of supporting electrolyte followed by the registration of the correspondent SW voltammogram. The limit of detection (LOD) was calculated by the relation $(3 \times \sigma)/m$, being σ the standard deviation of ten blank measurements (only supporting electrolyte) and m is the analytical sensitivity.

Afterwards, commercial pharmaceutical samples of ROS were analyzed by the proposed voltammetric procedure. Two samples were employed and named as Sample *A* — 10 mg ROS/tablet and Sample *B* — 20 mg/tablet. For preparation of these samples, ten tablets of each sample were rigorously weighted and pulverized to a powder in a mortar and pestle. The correspondent mass of one tablet was weight and transferred to a 10.0 mL volumetric flask, and the flask volume completed with methanol for solubilization of the ROS compound. The additional excipient compounds non-solubilized were separated by vacuum filtration, obtaining, thus, the final ROS stock solution for each sample. Adequate volumes of each sample stock solution were added in the electrochemical cell, and the cell ROS concentration determined in triplicate using the standard addition method. Finally, the tablet ROS concentrations were calculated from the conversion of the cell ROS concentrations experimentally determined. The samples were also analyzed by a comparative spectrophotometric method at a wavelength of 244.0 nm [9]. The synthetic biological fluid samples of urine and human serum were spiked with a ROS concentration and directly analyzed in triplicate in terms of recovery percentage.

3. Results and discussions

3.1. Electrochemical response of the ROS molecule

Preliminary cyclic voltammetry assays were conducted for a ROS solution in order to determine the voltammetric response of this molecule on the BDD electrode. Cyclic voltammograms were recorded for a 0.1 mol L^{-1} H_2SO_4 solution containing 1.00×10^{-4} mol L^{-1} ROS, and using anodically (predominant oxygen–termination) or cathodically (predominant hydrogen–termination) pretreated BDD electrodes (Fig. 2). An oxidation process was verified during the anodic scanning when both electrodes were used: at +1.39 V on the anodically pretreated BDD and at +1.37 V on the cathodically pretreated BDD. No equivalent reduction voltammetric peak was noted after the potential scanning inversion, indicating that the ROS oxidation is an irreversible redox process. Moreover, the highest current peak was achieved using the cathodically pretreated BDD electrode (please see the Fig. 2 inset) and, therefore, the cathodic pretreatment was selected for the development of the procedure. Similar results have been reported for the voltammetric sensing of various organic compounds, including, e.g., pharmaceutical [24–26], environmental [27–29], food [31–33] and biological [36] substances employing cathodically pretreated BDD