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# Differential pulse voltammetric determination of albendazole in pharmaceutical tablets using a cathodically pretreated boron-doped diamond electrode

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ABSTRACT

A sensitive, simple, and rapid electrochemical method was developed for the determination of albendazole (ABZ) in anthelminthic pharmaceutical formulations using differential pulse voltammetry (DPV) with a cathodically pretreated boron-doped diamond (BDD) electrode and 0.05 mol $L^{-1}$ $H_2SO_4$ as supporting electrolyte. The electrochemical behavior of ABZ obtained with cyclic voltammetry (CV) showed two oxidation peaks at 0.95 and 1.30 V *vs.* Ag/AgCl (3.0 mol $L^{-1}$ KCl). The total number of electrons (four) transferred during the oxidation process was estimated from the scan rate dependence of this CV response. The proposed method resulted in an analytical curve ranging from 0.0797 to 8.36 μmol $L^{-1}$, with a detection limit (based on 3-sigma) of 0.0625 μmol $L^{-1}$. This novel DPV method was successfully applied to determine ABZ in three pharmaceutical formulations (tablets), with results similar to those obtained using a reference HPLC method.



## 1. Introduction

Anthelmintic drugs are widely used in both veterinary and human medicine with the purpose of protecting or treating against different types of parasitic worms. Albendazole (ABZ), methyl [5-propylthio-1*H*-benzimidazol-2-yl]carbamate, is an anthelmintic compound that belongs to the class of the benzimidazole methylcarbamates. As concluded by van den Enden [1] in a review on the pharmacotherapy of helminth infection, ABZ is one of the most important anthelmintic drugs available (along with praziquantel and ivermectin), being easy to use and presenting activity against most helminths. From animal studies, it is known that the major active ABZ metabolite is ABZ sulfoxide, which is further metabolized to an apparently inactive form, ABZ sulfone [2].

Anthelmintic drugs generally present very low toxicity to mammalian hosts, but congenital malformation resulting from administration of ABZ during gestation in ewes has been observed; nevertheless, ABZ use during pregnancy is not contra-indicated to cattle [3,4]. On the other hand, the safety of exposing children under one year old, during pregnancy and lactation, has been questioned [4,5]. To avoid problems, an acceptable daily intake that can be ingested on a daily basis over a lifetime without an appreciable health risk has been established, for example, in the legislation of Mercosul for ABZ residues (albendazole 2-aminosulphone) in food of animal origin, per unit of bodyweight: 0–50 μg $kg^{-1}$ [6].

Several methods have been proposed for the determination of ABZ or its main metabolites, solely or simultaneously; for instance, spectrophotometric [7] and chromatographic [2,8–11] methods. However, there are few studies reported in the literature about the electrochemical behavior and the quantification of ABZ using electrochemical techniques [12–15]. Msagati and Ngila [12] developed a voltammetric method to determine benzimidazole anthelminthics using a glassy-carbon rotating-disk electrode modified with poly(3-methylthiophene). For ABZ, the obtained detection limit using square-wave voltammetry (SWV) was 0.33 μmol $L^{-1}$, for a linear concentration range of 3.90–29.3 μmol $L^{-1}$. De Oliveira and Stradiotto [14] developed voltammetric methods for the determination of ABZ in pharmaceutical formulations by dissolving commercial tablets in aqueous HCl solutions and using linear sweep voltammetry, SWV, and differential-pulse voltammetry (DPV) with a glassy-carbon electrode. The obtained detection limits using these voltammetric techniques were 0.30, 0.62, and 0.40 μmol $L^{-1}$, respectively. Abu Zuhri et al. [15] determined ABZ by differential pulse adsorptive cathodic stripping voltammetry at a hanging drop Hg electrode using the reduction peak of its copper (II) complex after its accumulation at a less negative electrode potential. The obtained calibration

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curve was linear in the range from 0.030 to 0.90 μmol $L^{-1}$ and the detection limit was 0.010 μmol $L^{-1}$, after accumulation for 180 s.

The use of boron-doped diamond (BDD) films as electrodes is very attractive for electrochemical studies mainly due to properties such as low background current, stability against corrosion in very aggressive media, extreme electrochemical stability in both alkaline and acidic media, high response sensitivity, good resistance to fouling, and a wide working potential window in aqueous solutions (up to ~3.5 V) [16], which are significantly different when compared with the properties of conventional electrodes (e.g. glassy-carbon and metal electrodes). The quantity and kind of the doping agent, morphologic factors and presence of impurities ($sp^2$ carbon), and type of surface termination (hydrogen or oxygen) commonly affect the properties of BDD electrodes [17–20]. Recently, in our research group, it has been observed that the analytical performance of BDD electrodes greatly depends on their surface termination, i.e. whether they are predominantly hydrogen or oxygen terminated [21]; the predominance of a termination type can be attained by proper electrochemical pretreatments. This effect of surface termination was observed, for instance, in the determination of additives in food products [22–24] and of drugs in pharmaceutical formulations [25–28], when cathodically pretreated (predominantly hydrogen-terminated) BDD electrodes presented better performances.

In this study, we report on the use of a cathodically pretreated BDD electrode for the development and optimization of a sensitive method for the determination of ABZ in pharmaceutical formulations by DPV. The proposed method is very attractive compared to the other few electroanalytical methods reported in the literature for the determination of ABZ, which show disadvantages (despite lower detection limit) such as indirect determination with long time for analyses and use of Hg [15], use of a modified electrode (with higher detection limit) [12], or simply higher detection limit [14].

## 2. Experimental

### 2.1. Apparatus

All voltammetric experiments (cyclic voltammetry – CV, DPV, and SWV) were carried out using an Autolab PGSTAT-30 (Ecochemie) potentiostat/galvanostat controlled with the GPES 4.9 software. A three-electrode cell system (volume of 10 mL) was used, with a BDD electrode (0.56 $cm^2$ exposed area) as working electrode, a platinum wire as auxiliary electrode, and an Ag/AgCl (3.0 mol $L^{-1}$ KCl) electrode as reference, to which all electrode potentials hereinafter are referred. The voltammograms using DPV and SWV were base-line-corrected by the moving average method (peak width: 0.003) and smoothed with a Savicky and Golay algorithm using the GPES 4.9 software.

The BDD film (8000 ppm) on a p-silicon wafer, obtained from Adamant Technologies (lot # 1374), Switzerland, was prepared as described elsewhere [29]. Prior to use, the BDD electrode was anodically or cathodically pretreated (daily) in a 0.50 mol $L^{-1}$ $H_2SO_4$ solution by applying 0.5 A $cm^{-2}$ during 30 s or −0.5 A $cm^{-2}$ during 180 s, respectively. Once the cathodic pretreatment was chosen for the final development of this work, the galvanostatic pretreatment procedure carried out on the BDD electrode once at the beginning of every work day was: use of the anodic pretreatment to clean the electrode surface, followed by the cathodic pretreatment to attain predominance of hydrogen terminations on the electrode surface.

The ABZ determination by high-performance liquid chromatography (HPLC), for comparative purposes, was carried out using a LC-10 AT Shimadzu system, with an UV–Vis detector (SPD-M10-AVP) set at 315 nm. A Shim-Pack CLC-ODS (4.6 × 150 mm, 5 μm) chromatographic column was used. The mobile phase was an acetonitrile/methanol/water mixture (45:35:75, *V*/*V*) at a flow rate of 1.0 mL $min^{-1}$, while the injection volume was 50 μL.

### 2.2. Reagents and standards

All reagents were of analytical grade. Stock solutions (1.0 mmol $L^{-1}$) of ABZ (Sigma–Aldrich) were freshly prepared in 1.0 mol $L^{-1}$ HCl (Synth) and stored protected from light. For dilutions, a supporting electrolyte was used. The following solutions were tested as supporting electrolyte: $H_2SO_4$ (0.1 and 0.5 mol $L^{-1}$), HCl (0.1 and 0.5 mol $L^{-1}$), and a Britton–Robinson (BR) buffer (0.04 mol $L^{-1}$ in acetic, orthophosphoric, and boric acids, with pH adjusted to 2.1 with a NaOH solution). 0.5 mol $L^{-1}$ $H_2SO_4$ (Synth) solutions were prepared and appropriate dilutions were made. All solutions were prepared with ultra-pure water of resistivity not less than 18 MΩ cm obtained with a Millipore Milli−Q system.

### 2.3. Measurement procedures

The electrochemical behavior of ABZ was investigated using three different voltammetric techniques. CV was used for preliminary studies, followed by a systematic study of SWV and DPV parameters to find the best conditions for ABZ determination. After optimizing the experimental parameters for the investigated methods, analytical curves were obtained by successive addition of aliquots of the ABZ stock solution into the electrochemical cell already containing 10 mL of a 0.05 mol $L^{-1}$ $H_2SO_4$ solution; each concentration was measured in triplicate. The detection limit was calculated as equal to three times the standard deviation of the current response for the blank solution ($n = 10$) divided by the slope of the analytical curve.

### 2.4. Pharmaceutical samples

Commercial samples of pharmaceutical formulations of ABZ (400 mg tablets) from different manufacturers were purchased in a local market. Ten tablets of each analyzed pharmaceutical formulation were accurately weighed and finely powdered in a mortar, transferred into a calibrated flask, which was completed to volume with a 1.0 mol $L^{-1}$ HCl solution to prepare a solution equivalent to an ABZ stock solution. After that, appropriate aliquots were diluted with the supporting electrolyte. The standard addition method was used to analyze the pharmaceutical samples. The excipients present in the samples were magnesium stearate, povidone, saccharin, sodium carbonate, citric acid, lactose, starch, and sodium bicarbonate.

## 3. Results and discussion

### 3.1. Effect of supporting electrolyte and investigation of the electrochemical behavior

Firstly, the electrochemical behavior of ABZ on a BDD electrode was investigated by CV for a 99 μmol $L^{-1}$ ABZ (in 0.05 mol $L^{-1}$ $H_2SO_4$) solution. As can be seen in Fig. 1, two oxidation peaks were observed, at the electrode potentials of 0.95 and 1.3 V. The former oxidation peak potential was chosen to develop the proposed electroanalytical method because it occurs at a less positive value, thereby reducing the possibility of any interference.

Next, CV was also used to investigate the effect of supporting electrolytes on the redox activity of ABZ. For such, $H_2SO_4$ (0.1 and 0.5 mol $L^{-1}$), HCl (0.1 and 0.5 mol $L^{-1}$), and BR buffer (pH = 2.1) solutions were used in this study; here, it should be