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Simultaneous determination of hydrochlorothiazide and valsartan in combined dosage forms: Electroanalytical performance of cathodically pretreated boron-doped diamond electrode

Ana Paula Pires Eisele, Guilherme Roberto Mansano, Fernanda Midori de Oliveira, Juliana Casarin, César Ricardo Teixeira Tarley, Elen Romão Sartori *

Universidade Estadual de Londrina (UEL), Centro de Ciências Exatas, Departamento de Química, Rodovia Celso Garcia Cid, PR 445 Km 380, Londrina – PR, C.P. 10.011, 86057-970, Brazil

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ABSTRACT

This work deals with simultaneous determination of hydrochlorothiazide (HCTZ) and valsartan (VAL) by square-wave voltammetry using a cathodically pretreated boron-doped diamond electrode. The method exhibits linear responses to HCTZ and VAL in the concentration range 1.97–88.1 μmol L^{-1} and 9.88–220 μmol L^{-1}, respectively, in a Britton–Robinson buffer solution (pH 5.0), with detection limits of 0.639 μmol L^{-1} and 0.935 μmol L^{-1}, respectively. The proposed method was successfully applied in the simultaneous determination of both antihypertensives in combined dosage forms and the results are in close agreement with those obtained using high performance liquid chromatography method.

1. Introduction

Hydrochlorothiazide (HCTZ) is a diuretic, often prescribed in combination with valsartan (VAL), an angiotensin II receptor antagonist [1]. The use of the mixture of HCTZ and VAL in combined dosage forms is well established in commercial pharmaceutical formulations. This combination is more effective than either drug alone to achieve better blood pressure control, especially for patients not responding to monotherapy. Thus, the development of an analytical method for simultaneous determination of both analytes is of great interest and significance for quality control.

The combination of HCTZ and VAL is available in several different strength combinations. The official method recommended by United State Pharmacopoeia [2] for HCTZ–VAL mixture determination involves the high performance liquid chromatography (HPLC) with UV detection, using glacial acetic acid, water and acetonitrile as mobile phase.

Some of the analytical procedures for determining HCTZ and VAL simultaneously in pharmaceutical formulations and biological samples have been recently reported, based on thin layer chromatography and high performance liquid chromatography with different modes of detection [3–7], capillary electrophoresis [8], and spectrophotometry [9–12]. In general, these procedures are unsuitable for field use, because they have extensive preliminary sample treatment, time-consuming derivatization steps and high implementation costs, thus justifying the need for reliable, low cost and simpler methods.

No voltammetric studies on HCTZ and VAL simultaneously in pharmaceutical formulations or biological samples have been found in the literature. These methods have many inherent advantages such as low-cost instrumentation, high sensitivity, good stability, and simplicity in preparation of sample. Boron-doped diamond electrode (BDDE) has many possibilities for application in electroanalysis because of their stability, fouling resistance, weak molecular adsorption, and wide working potential window, due to the high overpotentials for oxygen and hydrogen evolution, which can be larger than 3.5 V [13–19]. Moreover, BDDE exhibit less tendency to become fouled by adsorbed reaction products than do other common electrodes, which reduced adsorption might contribute for the signal stability during the measurements [16,18]. This electrode has been useful for compounds that are not easily oxidized in conventional electrode materials, such as acetylsalicylic acid [20] and orphenadrine [21], as well as for those compounds, such as propylthiouracil, that suffer from strong adsorption effects, thus making it possible the direct determination of analyte for a long time with the same response [22].

* Corresponding author. Tel.: +55 43 3371 4811; fax: +55 43 3371 4286.
E-mail address: elensartori@uel.br (E.R. Sartori).

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Several voltammetric methods with different electrodes have been reported in the literature for the individual determination of HCTZ in pharmaceutical formulations and biological samples, such as glassy carbon electrode (GCE) [23], GCE modified with multi-walled carbon nanotubes [24], ferrocenedicarboxylic acid modified carbon paste electrode (CPE/FDC) [25], multiwall carbon nanotubes/silicone rubber composite electrode (SRE/MWCNTs) [26], benzoylferrocene modified multi-walled carbon nanotube paste electrode (BF/CNPE) [27]. More recently, HCTZ was determined simultaneously with other antihypertensives by voltammetric methods using graphene/ferrocene composite carbon paste (GR/Fc/CP) [28], BDDE [29], carbon paste electrode modified with 5-amino-20-ethyl-biphenyl-2-ol and carbon nanotubes (5AEB/CNPE) [30], and GCE [31]. Few voltammetric methods employing mercury film electrode (MFE) [32], hanging mercury drop electrode (HMDE) [33], and GCE [34] have been developed for individual determination of VAL in pharmaceutical formulations. However, despite their advantages, mercury electrodes and conventional sp^2 carbon electrodes still suffer drawbacks. The use of mercury electrode has been avoided for analytical applications due to its toxicity. Furthermore, in high oxidation potentials, sp^2 carbon can corrode and at the very least undergo microstructural and surface chemical changes that adversely affect the oxidation response for analytes and leads to the need for frequent time-consuming pretreatment or activation [35]. Compared with other electrodes, BDDE does not suffer from these complications/problems and, therefore, this electrode material should be quite useful for analytes that require positive potentials for detection, such as HCTZ and VAL.

In this sense, we reported the use of a cathodically BDDE to development of simple, reproducible, and sensitive procedure for the simultaneous determination of HCTZ and VAL by square-wave voltammetry (SWV). This electrode, among other advantages, has a wide potential window in aqueous solutions, which allows for the detection of both antihypertensives without the interference of water decomposition and its resistance to molecular adsorption and electrode fouling. The proposed method was applied in simultaneous determination of HCTZ and VAL in real samples (combined dosage forms). The obtained results have been statistically compared with those obtained using high performance liquid chromatography (HPLC) as comparative method [11].

2. Experimental

2.1. Reagents and solutions

All chemicals were of analytical grade (HCTZ and VAL from Sigma–Aldrich; methanol from Synth; boric acid, acetic acid, orthophosphoric acid, and sodium hydroxide from Merck) and all solutions were prepared with ultra-purified water supplied by a Milli-Q system (Millipore®) with resistivity greater than 18 MΩ cm. Two different concentration combinations of commercial tablets were purchased from a local drugstore, in city of Londrina, state of Paraná, in Brazil, labeled to contain HCTZ and VAL in concentrations of 12.5:160 mg and 25:160 mg.

Britton–Robinson (BR) buffer solution was chosen as supporting electrolyte. This solution was prepared by mixing 0.04 mol L^{-1} in acetic, orthophosphoric, and boric acids, with pH adjusted to 5.0 with a 0.2 mol L^{-1} NaOH solution.

A 10.0 mmol L^{-1} stock solution of HCTZ and VAL were prepared in a BR buffer solution (pH 5.0) containing 30% methanol (v/v). Both HCTZ and VAL working solutions were prepared by appropriated dilution of these stock solutions with the BR buffer solution (pH 5.0).

2.2. Apparatus

The voltammetric measurements were carried out using a PalmSens potentiostat/galvanostat controlled with the PalmSens PC software. The pretreatment of the BDDE was carried out in a MQPG-01 potentiostat (Microquímica). The electrochemical experiments were conducted in a three-electrode single-compartment glass cell (with degassing facilities for bubbling N_2), including a BDDE (8000 ppm doping level; 0.30 cm^2 exposed geometrical area; Adamant Technologies SA, Switzerland) as working electrode, a Pt wire as auxiliary electrode, and an Ag/AgCl (3.0 mol L^{-1} KCl) as reference electrode, to which hereinafter all working electrode potentials are referred. Detailed information on the preparation of the diamond films was reported elsewhere [36]. Prior to the experiments, the BDDE 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). With the cathodic pretreatment, the BDDE surface is made predominantly hydrogen terminated [37–39].

A Shimadzu liquid chromatograph equipped with a LC-20AT gradient pump, a UV–VIS diode array detector, a manual injector fitted with a 20 μL loop and a CLC-ODS (M) column (column size: 250 mm × 4.6 mm i.d., particle size: 5 μm) was used in the accuracy study.

2.3. Analytical procedures

Cyclic voltammetry (CV) and square-wave voltammetry (SWV) were employed for investigation and determination of HCTZ and VAL.

After optimizing the experimental parameters for the proposed method, the analytical curve was obtained by addition of aliquots of the previously prepared HCTZ and VAL standard solutions into the measurement cell containing 10.0 mL of the BR buffer solution (pH 5.0). Square-wave voltammograms were obtained after each aliquot addition. All measurements were carried out in triplicate for each concentration. Detection limit (LOD) and quantification limit (LOQ) was calculated as three and ten times the standard deviation for the blank solution, respectively, divided by the slope of the analytical curve [40].

To prepare the solutions of the commercial pharmaceutical samples of HCTZ and VAL, 10 tablets of each pharmaceutical formulation were reduced to a homogeneous fine powder in a mortar with a pestle. These powders were weighed and transferred to 10 mL calibrated volumetric flasks containing methanol; after sonication for 20 min, the volumes of the flasks were completed with methanol; when needed, non-dissolved solids were filtered using a filter paper. Then, 200 μL of these solutions were diluted to 2 mL using the BR buffer solution (pH 5.0). For each sample, an aliquot of this solution was directly transferred to the electrochemical cell containing 10 mL of the BR buffer solution (pH 5.0), after which the voltammogram was obtained. Finally, the HCTZ and VAL concentrations in each sample solution were determined directly by interpolation in the previously obtained analytical curves.

The accuracy of proposed method was checked by means of addition and recovery studies (done in triplicate) as well as by using HPLC as a comparative technique. For assessing the addition and recovery studies (done in triplicate), aliquots of the standard solution of HCTZ and VAL were added to the solutions of the commercial pharmaceutical samples of both antihypertensives and the recovery values were calculated.

For the analysis of pharmaceutical formulations by HPLC, the tablets of each pharmaceutical formulation were firstly prepared in similar way to proposed voltammetric method. After sonication and filtration procedure, an aliquot of the solution was diluted in the mobile phase 0.02 mol L^{-1} phosphate buffer (pH 3.2) – acetonitrile