Sensors and Actuators B 212 (2015) 411–418

Contents lists available at ScienceDirect

Sensors and Actuators B: Chemical

journal homepage: www.elsevier.com/locate/snb

Simultaneous determination of captopril and hydrochlorothiazide on boron-doped diamond electrode by batch injection analysis with multiple pulse amperometric detection

Denise Tofanello Gimenes*, Mariana Cardoso Marra, Jhonys Machado de Freitas, Rodrigo Alejandro Abarza Muñoz, Eduardo Mathias Richter*

Instituto de Química – Universidade Federal de Uberlândia, Av. João Naves de Ávila, 2121, Uberlândia, MG, Brazil

ARTICLE INFO

Article history:
Received 31 October 2014
Received in revised form 7 January 2015
Accepted 28 January 2015
Available online 13 February 2015

Keywords:
Captopril
Hydrochlorothiazide
Boron-doped diamond
Multiple pulse amperometry
Batch injection analysis
Screening test

ABSTRACT

This work describes a new, simple, and fast electrochemical method for simultaneous determination of captopril (CAP) and hydrochlorothiazide (HCT) using a boron-doped diamond (BDD) electrode associated with batch-injection analysis with multiple-pulse amperometric (BIA–MPA) detection. A sequence of potential pulses was selected in such a way that HCT was selectively detected at +1.4 V/50 ms and both (HCT + CAP), were detected at +1.8 V/50 ms. CAP was quantified without interference of HCT by subtracting the currents detected at +1.8 V and +1.4 V (using a correction factor). The proposed BIA method requires minimal sample manipulation (dissolution and dilution in electrolyte) and the simultaneous determination is achieved with a single injection step of 150 μL of a sample solution (100 injections h^{-1}). The results obtained with the BIA method were compared to those obtained by capillary electrophoresis and similar results were obtained (at 95% of confidence level). A simple and rapid test for detecting the presence or absence of electroactive interferents was also proposed (fast screening test).

1. Introduction

Hypertension is a major risk factor associated with cardiovascular morbidity and with end-stage renal failure [1]. Only half of hypertensive patients respond to monotherapy treatment. Evidence suggests that the use of combination drugs from different classes is approximately 5 times more effective in lowering blood pressure than increasing the dose of one drug. Therefore, the combination therapy is the preferred initial strategy in the treatment of high blood pressure [2].

Thiazide diuretics, such as hydrochlorothiazide (HCT), have been used in antihypertensive therapy since the advent of chlorothiazide in 1957, because they reduce the active sodium reabsorption and peripheral vascular resistance [1]. HCT is often indicated in combination with other antihypertensive drugs such as β-blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (AEBs), or potassium sparing diuretics [3]. The combination of these drugs with HCT is highly efficient especially in patients not responding to monotherapy.

Captopril (CAP) is an ACE inhibitor widely used in the treatment of hypertension and some types of congestive heart failure [4]. In vitro studies indicate that CAP functions as an antioxidant either by scavenging reactive oxygen species or by increasing the activities of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase [5]. Unfortunately, administering CAP for therapeutic purpose leads to undesirable side effects. Preliminary research indicated significant loss of zinc in urine due to the intake of CAP [6]. In order to prevent or reduce possible secondary effects, CAP is often commercialized combined with HCT in order to improve its action without increasing the dose [4].

There are some analytical methods in the literature focusing on the simultaneous quantification of CAP and HCT. Techniques such as HPLC [7,8] and spectrophotometry [9,10] were used in these works. One of the important limitation of the majority of these methods is the fact that CAP presents relatively low UV absorption, and thus derivatization procedures were required (increasing cost and time of analysis) [4,8,11,12]. Electrochemical techniques provide alternative methods widely used in pharmaceutical applications. They are usually easy and rapid to perform and less expensive than chromatographic methods. In addition, the sensitivity of electrochemical methods is often greater than spectrophotometric procedures [12].

* Corresponding authors. Tel.: +55 34 3239 4143x206; fax: +55 34 3239 4208.
E-mail addresses: denisetoff@yahoo.com.br (D.T. Gimenes), emrichter@iqufu.ufu.br (E.M. Richter).

http://dx.doi.org/10.1016/j.snb.2015.01.132
0925-4005/

To the best of our knowledge, only one report on the simultaneous electrochemical determination of CAP and HCT was previously shown [4]. In this work, differential pulse voltammetry (DPV) on a modified electrode (graphene/ferrocene carbon paste composite) was used to achieve this goal. Linear responses over the concentration ranges of 1.0–430 μmol L^{-1} for CAP and 0.5–390 μmol L^{-1} for HCT ($r^2 > 0.99$) and LOD values of 0.87 and 0.38 μmol L^{-1}, respectively, were obtained. However, no information was given regarding electrode surface contamination or intra-day and inter-day precision of this analytical method. In the literature, there are no previous reports on the simultaneous electrochemical determination of CAP and HCT using an unmodified electrode.

Flow-injection analysis (FIA) or batch-injection analysis (BIA) systems with amperometric detection can be used for fast and simultaneous determinations without a previous separation step (e.g. HPLC or CE). The objective can be achieved by injecting a single sample aliquot in a FIA [13–19] or BIA [20–27] system coupled to single, dual or array working electrodes. If dual [18] or array [16] electrodes were used, a bi [18] or multi-potentiostat [16] is required in order to current acquisition at each electrode. If a single working electrode was used, a technique known as multiple-pulse amperometry (MPA) has been employed [14,15,17,20,27]. MPA technique allows the application of up to ten potential pulses and simultaneous acquisition of ten independent amperograms (current versus time) [17,20].

Boron-doped diamond (BDD) thin-film electrode is one of the new promising materials for electrochemical applications due to its unique and extremely useful properties [28], such as high stability and hardness, very low and stable background current, wide potential window in aqueous electrolyte solutions, slight adsorption of polar organic molecules, high resistance to deactivation via fouling, and good activity toward some redox analytes without any conventional pretreatment. The principal reasons for these properties are that the diamond surface is relatively nonpolar when hydrogen terminated and contains no extended π-electron system [29].

Batch-injection analysis (BIA) is a newly developed analytical technique, which involves the injection of a small analyte plug (from a micropipette tip) directly onto an electrode surface that is immersed in a relatively large volume of electrolyte [30]. The response to the injection is similar to FIA, except that in the BIA technique there is no continuous flowing carrier solution [31]. Disadvantages associated with pump, valves, and excessive disposal of carrier solutions of the FIA system, are eliminated [32–34]. BIA in combination with electrochemical detectors provides additional advantages of electrochemical sensors such as high sensitivity, fast response (high throughput), and easy implementation of strategies to prevent or minimize the gradual fouling of the electrode surface (common limitation of solid electrodes) [32,35].

In this work, we report a fast electrochemical method for the simultaneous determination of CAP and HCT. The proposed method is based on batch-injection analysis with multiple-pulse amperometric (BIA–MPA) detection using BDD as working electrode. The amperometric method involved the continuous application of three sequential potential pulses to the BDD electrode. HCT was monitored at the first potential pulse and CAP at the second potential pulse. The third potential pulse was applied in order to avoid electrode fouling.

2. Experimental

2.1. Reagents and samples

Highly pure deionized water (resistivity not less than 18 MΩ cm) obtained from a Millipore Direct-Q3 water purification system (Bedford, MA, USA) was used to prepare all aqueous solutions. All reagents were of analytical grade and were used without further purification. Captopril (CAP), scopolamine (internal standard) and hydrochlorothiazide (HCT) were purchased from Attivos Magistrais (São Paulo, SP, Brazil), triethanolamine (TEA) from Sigma–Aldrich (Milwaukee, WI, USA) and sodium hydroxide and oxalic acid (OXA) from Synth (Diadema, SP, Brazil). Acetic, sulfuric, and phosphoric acids were purchased from Synth (Diadema – Brazil). Acetic acid/acetate buffer (0.1 mol L^{-1}) was used as the supporting electrolyte in the BIA–MPA experiments. CAP and HCT samples and standard stock solutions were prepared daily in NaOH.

Pharmaceutical formulations containing CAP (50 mg) and HCT (25 mg) were obtained from local drugstore. Ten tablets from each sample were accurately weighed and powdered in a mortar. An adequate amount of the powder was dissolved in NaOH and sonicated for 5 min in an ultrasonic bath. The sample and standard stock solutions were further diluted in a suitable electrolyte for subsequent injection in the BIA–MPA system.

2.2. Instrumentation and apparatus

Electrochemical measurements were performed using μ-Autolab Type III potentiostat/galvanostat (Metrohm Autolab, Utrecht, The Netherlands) connected to a microcomputer and controlled by Autolab Software GPES version 4.9.007. The reference and counter electrodes were a miniaturized Ag/AgCl (saturated KCl) [36] and a platinum wire, respectively. A thin-film (around 1.2 μm) of boron-doped diamond (BDD) with a doping level of 8000 ppm on a polycrystalline silicon wafer (Adamant Technologies SA, La Chauxde-Fonds, Switzerland) was used as the working electrode. Before the use for the first time, the BDD electrode was anodically pretreated by applying +0.01 A for 1000 s in a 0.04 mol L^{-1} Britton-Robinson buffer solution (pH = 2.0) and then cathodically pretreated by applying −0.01 A for 1000 s in a 0.1 mol L^{-1} H_2SO_4 solution. This pretreatment is similar to that used in previously published works [37,38]. After the first pretreatment, the BBD electrode was pretreated only cathodically once at the beginning of the workday. If the electrode is not used for a few days, both electrochemical pretreatments (anodic and cathodic) are again required.

The homemade BIA cell developed by our research group is similar to that previously described [39]. All experiments were carried out with the solution under stirring. A micro DC-motor was adapted to the BIA cell and used for solution stirring when necessary [40]. Injections of solutions (standards and samples) were carried out using an Eppendorf® electronic micropipette (Multipette® stream), which permits injections from 10 to 1000 μL (using a 1 mL Combitip®) at a programmable dispensing rate (from 28 to 250 μL s^{-1}). A constant distance was maintained between the working electrode and the multipette® combitip® (≈2 mm), as recommended in a previous work [33].

Electrophoresis experiments were performed using an in-house made CE equipment with two compact and high-resolution capacitively coupled contactless conductivity detectors (CE-C^4D) [41]. The detectors were positioned along the capillary at 10 cm from each end. The fused-silica capillary used in all experiments was 40 cm long (effective length of 10 and 30 cm) and 50 μm inner diameter, 375 μm outer diameter (Agilent, Folsom, CA, USA). The capillaries were preconditioned by flushing with 0.1 mol L^{-1} NaOH for 15 min, with deionized water for 10 min, and finally with background electrolyte for 10 min. The samples were injected hydrodynamically for 0.5 s at 25 kPa. The separation potential adopted was +25 kV (injection side). A buffer solution containing 11.3 mmol L^{-1} TEA, 1.8 mmol L^{-1} OXA (pH 8.7) was used as a background electrolyte (BGE). The migration time of HCT and CAP was approximately 43 and 64 s, respectively.