Diamond & Related Materials 39 (2013) 41–46

Contents lists available at ScienceDirect

Diamond & Related Materials

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

Fast and simultaneous determination of nimesulide and paracetamol by batch injection analysis with amperometric detection on bare boron-doped diamond electrode

Polyana Fernandes Pereira [a], Mariana Cardoso Marra [a], Amanda Barbosa Lima [b], Wallans Torres Pio dos Santos [c], Rodrigo Alejandro Abarza Munoz [a], Eduardo Mathias Richter [a,*]

[a] Instituto de Química, Universidade Federal de Uberlândia, Av. João Naves de Ávila, 2121, Uberlândia, MG, Brazil
[b] Departamento de Química, Universidade Federal dos Vales do Jequitinhonha e Mucuri, 39100-000 Diamantina, MG, Brazil
[c] Departamento de Farmácia, Universidade Federal dos Vales do Jequitinhonha e Mucuri, 39100-000 Diamantina, MG, Brazil

ARTICLE INFO

Article history:
Received 16 May 2013
Received in revised form 15 July 2013
Accepted 30 July 2013
Available online 7 August 2013

Keywords:
Batch injection analysis (BIA)
Flow injection analysis (FIA)
Unmodified boron-doped diamond
Multiple pulse amperometry

ABSTRACT

A fast and simple procedure for simultaneous determination of nimesulide and paracetamol (acetaminophen) was carried out by batch injection analysis with multiple pulse amperometric detection (BIA-MPA). The purpose is achieved with a unique and simple injection of a sample aliquot (150 μL) onto the unmodified boron-doped diamond (BDD) electrode immersed in a BIA system. The analytical characteristics of our proposed method include elevated analytical frequency (up to 46 injections per hour), high stability (RSD < 1.3%; $n = 12$), low detection limits (0.293 and 0.297 mg L^{-1} for paracetamol and nimesulide, respectively) and minimal waste generation. The proposed method presented similar results to those obtained by liquid chromatography at a 95% confidence level.

Published by Elsevier B.V.

1. Introduction

Nimesulide (NIM) or [N-(4-nitro-2-phenoxyphenyl)] methanesulfonamide is a widely used drug due to its good analgesic, anti-inflammatory and antipyretic properties [1]. However, the use of excess of NIM can cause severe side effects including hepatic, renal and gastrointestinal problems [2]. According to some studies, if NIM is combined with paracetamol (PAR) in pharmaceutical formulations, less dosage of NIM is required (synergic effect) and side effects can be prevented [3]. Therefore, some companies have introduced NIM and PAR combined in tablets at a ratio of 1:3 or 1:5, and claim that this combination has faster onset and longer duration of analgesic and antipyretic effects than either drug individually [4].

Some analytical methods have been reported for simultaneous determination of NIM and PAR, including liquid chromatography [5–9], thin layer chromatography [10], and UV spectrophotometry [1,11]. Although NIM [2,12–14] and PAR [15–18] are electrochemically active, to our knowledge there is no reported study about the use of electrochemical methods for simultaneous determination of NIM and PAR. In addition, as informed in the literature [19], if NIM is electrochemically reduced, a progressive blockage of the electrode surface can occur, yielding irreproducible results or even the complete inhibition of the electronic transfer processes. This problem usually impedes the use of unmodified solid electrodes in electrochemical determination of this type of molecules.

As well described in the literature, boron doped diamond (BDD) electrodes present advantages over conventional solid electrodes in terms of high stability (low adsorption of organic molecules), chemical inertness, wide potential window and low background current [20–23]. However, despite these desirable characteristics (high stability mainly), if certain organic molecules are oxidized or reduced using BDD as working electrode, a gradual blockage (adsorption of oxidation or reduction products) of the electrode surface tends to occur [24–26]. To circumvent or minimize such a limitation, pulsed-amperometric detection under hydrodynamic conditions can be used. This technique allows the application of an additional potential pulse for constant cleaning (protection) of the electrode surface from adsorption of oxidation or reduction products and reproducible results can be obtained [24–28].

Recently, our group demonstrated the use of batch injection analysis with multiple-pulse amperometric (BIA-MPA) detection for simultaneous determination of two analytes using a single working electrode [29,30]. A sequence of potential pulses was selected in such a way that one analyte is selectively detected at the first potential pulse and both analytes at a second potential pulse. A simple correction factor [24,25,30] is used to have access of the current coming from the second analyte (not detected at the first potential pulse). The possibility of

Abbreviations: BIA-MPA, batch injection analysis with multiple pulse amperometric detection; BDD, boron-doped diamond; NIM, nimesulide; PAR, paracetamol; FIA, flow injection analysis.

* Corresponding author at: Av. João Naves de Ávila, 2121, Campus Santa Mônica — Bloco 1D, CEP: 38.400-902 — Caixa Postal 593, Uberlândia, MG, Brazil. Tel.: +55 34 3239 4143x206; fax: +55 34 3239 4208.
E-mail address: emrichter@iqufu.ufu.br (E.M. Richter).

0925-9635/$ – see front matter. Published by Elsevier B.V.
http://dx.doi.org/10.1016/j.diamond.2013.07.010

simultaneous determinations using a single working electrode also made possible the implementation of the internal standard method in FIA [31] and BIA [32] systems with multiple-pulse amperometric detection.

In this work, we propose the simultaneous determination of PAR and NIM using batch injection analysis with multiple pulse amperometric (BIA-MPA) detection. The application of four potential pulses provided PAR detection by its electrochemical oxidation (at +0.9 V for 100 ms) and NIM detection by its electrochemical reduction (at −0.7 V for 100 ms) without electrode contamination (applying of two potential pulses for electrode cleaning). Results were validated in relation to linearity, repeatability, recovery, detection and quantification limits, and by comparison with the results from HPLC analysis.

2. Experimental

2.1. Reagents and samples

Paracetamol (PAR) and nimesulide (NIM) were obtained from Synth (Diadema — Brazil) and All Chemistry (São Paulo/SP — Brazil), respectively. All solutions were prepared with deionized water (Millipore Direct-Q3) with a resistivity not less than 18 MΩ cm. Reagents were of analytical grade and were used without further purification. Sulfuric acid (0.1 mol L^{-1}) in water/ethanol (70:30) medium was used as the supporting electrolyte. Pharmaceutical formulations (tablets) containing PAR and NIM were obtained from local drugstore. For the analyses, ten tablets were weighed, grounded to a fine powder and homogenized. Some portions were taken and weighed, dissolved in ethanol and diluted to an adequate concentration in supporting electrolyte solution.

2.2. Instruments and apparatus

Electrochemical measurements were performed with a three electrode BIA cell system employing a μAutolab Type III potentiostat (Metrohm Autolab B.V.) controlled by GPES 4.9.007 software. For multiple-pulse amperometry (MPA) measurements, a mini Ag/AgCl sat. with KCl [33] and platinum wire were employed as the reference and auxiliary electrodes, respectively. A thin film (around 1.2 μm) of boron-doped diamond (BDD) with a doping level of around 8000 ppm deposited on a polycrystalline silicon wafer (0.7 × 0.7 cm) with 1.0 mm of thickness (Adamant Technologies SA, La Chauxde-Fonds, Switzerland) was used as the working electrode. Prior the first use (new material), the BDD electrode was anodically pretreated by applying 0.01 A for 1000 s in 0.04 mol L^{-1} Britton–Robinson buffer solution 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 [34,35]. After the first pretreatment, the BDD electrode was pretreated only cathodically once at the beginning of the workday. If the electrode is not used for a few days, both pretreatments (anodic and cathodic) are again required. Glassy carbon and gold (∅ = 0.3 cm; Metrohm) were also employed as working electrodes. The cleaning of these electrodes was mechanically performed on a felt-polishing pad using an alumina powder suspension (0.3 μm) and subsequent rinsing with deionized water.

BIA measurements were carried out using a homemade cell as previously described [36]. In this cell, one piece of BDD material (0.7 × 0.7 cm) is used and the electrode area is delimited by using a rubber O-ring of diameter 0.4 cm (electrode area = 0.13 cm^2). The electrochemical pretreatment was performed with the BDD electrode positioned in the BIA cell. All experiments were carried out with the solution under stirring. A micro DC-motor was adapted to the BIA cell and used in the solution stirring [37]. The stirring rate could be easily changed by varying the voltage from a universal AC/DC voltage regulator (3 to 12 V). All studies were performed at a constant stirring rate of 2700 ± 10 rpm (with the application of 9 V). Injection solutions were performed with a motorized electronic micropipette (Eppendorf Multipette® stream) with a constant distance from the working electrode to Multipette® Combitip® (≈2 mm), as recommended in a previous work [38].

Results for the simultaneous determination of PAR and NIM were compared to those obtained by using high performance liquid chromatography (HPLC). A Hitachi pump L-2130, Hitachi LC-4250 UV–VIS detector and, a Shim-pack CLC-ODS column (25 mm × 4.6 mm; Shimadzu) was used. The mobile phase was composed of acetonitrile/methanol/water (35:40:25, v/v; pH adjusted to 4.20 with phosphoric acid), and the flow rate was 1.0 ml min^{-1}. The detector was fixed at 276 nm [6]. The retention times were 2.75 and 3.90 min for PAR and NIM, respectively.

3. Results and discussion

The electrochemical behavior of PAR and NIM are well known. PAR can be oxidized to N-acetyl-p-benzoquinoneimine, which can subsequently be reduced at more negative potentials (reversible or quasi-reversible behavior) [16,18,39,40]. Other information available in the literature is that the oxidation product of PAR (N-acetyl-p-benzoquinoneimine) can catalytically react with other sample components, and therefore, errors can occur when performing simultaneous determinations. However, if PAR is oxidized in acid medium, this catalytic reaction is inhibited (slow kinetics) [39], and therefore, more appropriate for simultaneous determinations. On the other hand, NIM can be reduced and oxidized [2,41]. The nitro group can be reduced to a hydroxylamine derivative, which can be oxidized (quasi-reversible behavior) to a nitroso derivative in the forward sweep at more positive potentials. Posteriorly, a reduction of the electrogenerated nitroso compound can be observed on the second sweep from positive to negative potentials (reversible behavior of the nitroso group). The anodic signal of NIM (detected without previous reduction) could be attributed to oxidation of the methylsulfonamide group. Electrochemical studies involving NIM were usually performed in hydro alcoholic solutions due to its low solubility in water [2]. For this reason, a hydroethanolic solution containing 30/70% (v/v) hydroethanolic solution with 0.1 mol L^{-1} H_2SO_4 was used as a supporting electrolyte for simultaneous determination of NIM and PAR.

Fig. 1 shows cyclic voltammograms obtained at a BDD electrode before (—) and after addition of PAR (····) or NIM (----).

Under this condition, PAR is oxidized to N-acetyl-p-benzoquinoneimine at about 0.92 V and no cathodic current peak was observed in the reverse scan, which differs from other data available in the literature on PAR [39,40]. Probably, this occurred due to the use of hydroethanolic solution as electrolyte. NIM is reduced to the corresponding hydroxylamine derivative at about −0.59 V and an anodic current peak was observed in the reverse scan at about +0.50 V (hydroxylamine oxidation to nitroso derivative). The reduction of the nitroso group was also observed in a following sweep (−0.1 V),

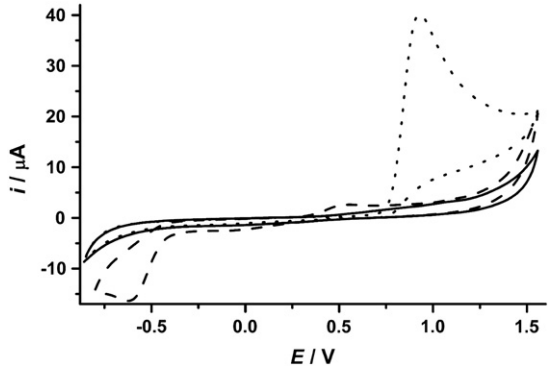

Fig. 1. Cyclic voltammograms of BDD working electrode in 30/70% (v/v) hydroethanolic solution with 0.1 mol L^{-1} H_2SO_4 before (—) and after addition of 370 mg L^{-1} NIM (----) or 263 mg L^{-1} PAR (····). Scan rate: 50 mV s^{-1}; step potential: 5 mV.