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Differential pulse voltammetric determination of acyclovir in pharmaceutical preparations using a pencil graphite electrode

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ABSTRACT

In this study, a new selective and sensitive voltammetric procedure for determination of acyclovir (ACV) was proposed using a disposable electrode, pencil graphite electrode (PGE). Cyclic and differential pulse voltammograms of ACV were recorded in Britton–Robinson buffer solution containing 0.10 M KCl with pH of 4.0 at PGE. The PGE displayed a very good electrochemical behavior with significant enhancement of the peak current compared to a glassy carbon electrode (GCE). Under experimental conditions, the PGE had a linear response range from 1.0 μM to 100.0 μM ACV with a detection limit of 0.3 μM (based on 3 S_b). Relative standard deviations of 4.8 and 3.6% were obtained for five successive determinations of 10.0 and 50.0 μM ACV, respectively, which indicate acceptable repeatability. This voltammetric method was successfully applied to the direct determination of ACV in real pharmaceutical samples. The effect of various interfering compounds on the ACV peak current was studied.

1. Introduction

Acyclovir (9-carboxymethoxymethyl guanine; Scheme 1) (ACV) is an antiviral drug that acts as a specific inhibitor of herpes virus family such as herpes simplex, varicella-zoster, (chickenpox) and herpes zoster (shingles). It has also been investigated for the treatment of herpes labialis applied using an iontophoretic device [1,2]. ACV made from guanosine is a nucleic acid analogue. It causes a reduction in the production of DNA viruses. ACV may lead to nephrotoxicity (crystallization of ACV within renal tubule enhancement of serum creatinine, transient) and neurotoxicity (coma, hallucinations, lethargy, seizures, tremors) [1,2]. Therefore, the amount of ACV in medicine or biological fluids must be strictly controlled. Thus, achieving sensitive and selective determination of ACV has attracted a lot of attention and a number of qualitative and quantitative methods have already been developed for ACV determination [3–23]. For this aim, chromatographic methods such as HPLC [3–6] and LC/MS [6,7], electrophoretic [8], spectrophotometric [9–11], spectrofluorimetric [11,12] and chemiluminescence [13] methods have been mainly used for the determination of ACV. However, these methods are generally time consuming and need expensive equipment and tedious operations, such as optimization of chromatographic conditions, pretreatment of samples for HPLC analysis, and low detection limit for spectroscopic methods. Therefore, development of an alternative analytical methodology for determination of ACV has become necessary, in particular, a method that is sensitive, inexpensive and less complex.

One of the most efficient approaches in pharmaceutical analysis is the use of modern electroanalytical methods, which have the advantage of easy application, high sensitivity, accuracy and selectivity, simplicity and fast (less time-consuming) detection and low cost [24–34]. In the construction of electrochemical sensors and biosensor, carbon nanomaterials are good candidate for constructing electrodes because of high surface area and conductivity [35–37] ACV is an electrochemically active molecule due to oxidation of guanine group to 8-oxoguanine, which can be oxidized on the electrode surface. However, the use of unmodified bare electrodes suffers from sluggish electron transfer and fouling of surface which result in poor sensitivity and selectivity. In order to improve sensitivity and avoid fouling, modified electrode such as a multi-wall carbon nanotubes (MWNTs)-dihexadecyl hydrogen phosphate (DHP) film coated glassy carbon electrode (GCE) [23], copper nanoparticles (CuNP) modified carbon paste electrode (CPE) [21], 2-mercaptobenzothiazole-[5,10,15,20-tetrakis-(3-methoxy-4-hydroxyphenyl) porphyrinato]copper(II) modified Au electrode [20], fullerene-C_{60}-modified GCE [19], polyvinylpyrrolidone (PVP) modified CPE [18], a modified electrode obtained from polymerization of β-cyclodextrin (β-CD) on electrochemically pretreated pencil graphite electrode (PGE) [17], ruthenium hexachloroplatinate or hexacyanocobaltate film coated GCE [16], MWCNT/tiron-doped polypyrrole modified GCE [15], and poly(*p*-amminobenzen sulfonic acid) modified GCE [14] have been proposed for sensitive and selective determination of ACV.

In this study, PGE was used for sensitive and selective voltammetric determination of ACV without using any modification procedure. When compared with other carbon-based electrodes, PGEs have the same advantages, such as high electrochemical reactivity, commercial availability, good mechanical rigidity, disposability, low cost, low technology

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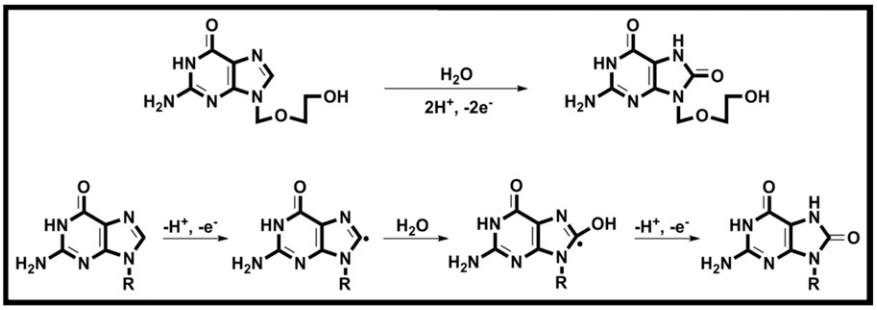

Scheme 1. Proposed mechanism for electrochemical behavior of ACV at PGE.

and ease of modification [17,31–42]. In addition, it was reported that pencil lead electrodes offer a renewal surface which is simpler and faster than polishing procedures, common with solid electrodes, and result in good reproducibility for individual surface [31]. Thus, many scientists have recently focused on the use of these electrodes in various electroanalytical applications due to the useful properties of PGEs [17,31–42]. Although the above-mentioned modified electrodes for determination of ACV demonstrated very good sensitivity and a low detection limit, these methods are time-consuming due to preparation of modified electrodes and the electrode materials are more expensive than PGEs. Taking into account the good properties of PGEs in electroanalysis, in this work we used PGE for ACV determination using the differential pulse voltammetric technique with improved qualities such as easy availability, simplicity, disposability and low cost of electrode, wider linear range, low detection limit, and high selectivity.

2. Materials and methods

2.1. Apparatus and chemicals

H_3PO_4 (85%, d: 1.71 g mL^{-1}), CH_3COOH (96%, d: 1.05 g mL^{-1}), H_3BO_3, NaOH and KCl were purchased from Merck (Darmstadt, Germany) and Acyclovir (ACV) was purchased from Sigma (USA). A stock standard solution of acyclovir (10^{-2} M) was prepared in methanol and water (1:1) and kept in the dark. The required concentration of ACV in aqueous buffer solutions was then prepared from the stock standard solution. Britton–Robinson buffer solutions (BRRS) in the pH range 2.0–10.0 were prepared from 0.04 M H_3PO_4, 0.04 M H_3BO_3 and 0.04 M CH_3COOH containing 0.1 M KCl in ultrapure water. The pH of the solution was adjusted by adding 0.2 M NaOH containing 0.1 M KCl.

Cyclic and differential pulse voltammetric experiments were performed in a traditional three-electrode system using a platinum wire as the counter electrode, an $Ag/AgCl/KCl_{sat}$ as the reference electrode and a PGE as the working electrode. A pencil lead with a diameter of 0.5 mm (Ultra-Polymer, 2B), a total length of 60 mm (Tombow, Japan) and a mechanical pencil Model T 0.5 (Rotring, Germany), which was used as the holder for the pencil lead, were purchased from a local bookstore. Electrical contact to the lead was obtained by wrapping a metallic wire to the metallic part of the holder. For each measurement, a total of 10 mm of lead (active electrode area was calculated as 15.9 mm^2) was immersed into the solution.

All electrochemical experiments were carried out using a Compactstat Electrochemical Interface (Ivium Technologies, Eindhoven, The Netherlands). Scanning electron microscopy (SEM) images of electrodes were recorded using a JEOL SEM-7100-EDX. Raman scattering measurements were performed at room temperature using a RENISHAW inVia Raman Microscope in the Bulent Ecevit University (Zonguldak, Turkey). The spectrometer is controlled by using Renishaw WiRE version 3.3 software. A HI 221 Hanna pH-meter with a combined glass electrode (Hanna HI 1332) was used to follow the pH values of the solutions. All the solutions were prepared with ultrapure water from Elga Option Q7B water purification system (18.2 MΩ cm).

2.2. Procedure

In the electrochemical measurements, PGE was directly used, while GCE (3 mm diameter, geometric surface area = 7.1 mm^2) was used after it was polished with alumina slurry on the polishing cloth, washed with deionized water and sonicated with ethanol and water in an ultrasonic bath, respectively. Firstly, the electrochemical behavior of ACV at PGE and also GCE was investigated by recording cyclic voltammograms in the BRBS in the pH range of 2.0–10.0. For this, 5.0 mL of supporting electrolyte was placed in the electrochemical cell and after a total of 10.0 mm of pencil graphite was immersed into the supporting electrolyte, the cyclic voltammograms were recorded at a scan rate of 50 mV s^{-1} using a potential range from 0.5 to 1.3 V. Then, the cyclic voltammograms of 0.14 mM ACV were recorded under the same conditions after the required volume of ACV solution had been added to the cell. Similar experiments were repeated for the GCE. Pure argon was purged from the supporting electrolyte for 5 min before all electrochemical experiments.

Then, the differential pulse voltammetric technique was used for the determination of ACV. Firstly, the effect of the pH in the BRBS on differential pulse voltammograms of 0.14 mM ACV was investigated. Differential pulse voltammograms were recorded in a potential range 0.5–1.3 V at a scan rate of 50 mV s^{-1} and using optimized pulse amplitude (10 mV) and pulse time (25 ms). The parameters for analytical performance, such as dynamic calibration range, limit of detection, limit of quantification, reproducibility, selectivity, *etc.*, were investigated by recording differential pulse voltammograms. After each successive differential pulse voltammetric measurement, argon gas was purged into the supporting electrolyte for 20 s prior to the next measurement.

2.3. Analysis of pharmaceutical sample

Applicability of the PGE was also investigated for the determination of ACV in an antiviral drug tablet which includes 200 mg ACV per one tablet (it is about 701.8 mg ACV/g tablet). This pharmaceutical tablet was purchased from a local pharmacy in Turkey.

Four tablets of pharmaceutical formulation (AKLOVIR, each tablet (about 285 mg), containing 200 mg of ACV) were accurately weighed and finely powdered in a porcelain mortar. An adequate amount of this powder was weighed and transferred into a 50.0 mL flask, then dissolved with methanol:water (1:1) and sonicated for 10 min. An aliquot of this solution (about 20 μL) was added into the electrochemical cell that contained 5.0 mL of BRBS (pH 4.0) containing 0.1 M KCl and then the differential pulse voltammograms were recorded following the already outlined voltammetric procedure. The standard addition method was applied by adding successive aliquots of 20 μL of 2.5×10^{-3} M ACV standard solution to the electrochemical cell. After each addition, differential pulse voltammograms were also recorded. The recovery of the tablet solutions was calculated by evaluating the peak current obtained from standard addition method.