Electrochemical Determination of Cyclopenthiazide using a Glassy Carbon Electrode by Cyclic Voltammetry

Saad Imran Al-Abadi*†, Muthana Saleh Mashkour‡

† College of Pharmacy, Ahl Al Bayt University, Karbala, Iraq; *email: Saadomranalbade@gmail.com
‡ Chemistry Department, Faculty of Science, University of Kufa, Iraq

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In this study, the electrochemical behavior of cyclopenthiazide was investigated at a glassy carbon electrode using cyclic voltammetry (CV). The oxidation of cyclopenthiazide was found to be completely irreversible over the scan rate range of 0.001–0.05 V s^{-1} and was controlled by diffusion. An irreversible oxidation peak was observed at approximately −0.889 V. Experimental parameters that affect the voltammetric response were optimized to achieve optimal analytical performance. Under the optimized conditions, the oxidation peak current showed a linear relationship with cyclopenthiazide concentration over the range of 20–200 μg mL^{-1}. The limits of detection (LOD) and quantification (LOQ) were calculated to be 7.276 and 22.05 μg mL^{-1}, respectively. The proposed method was successfully applied to the determination of cyclopenthiazide in pharmaceutical formulations. The developed electrochemical method is simple, rapid, cost-effective, and requires no complicated sample preparation, while providing satisfactory precision and accuracy.

Keywords: cyclopenthiazide, cyclic voltammetry, glassy carbon electrode, electrochemical analysis, pharmaceutical determination, voltammetric sensor

Introduction

Cyclopenthiazide is a thiazide diuretic widely used to treat hypertension and other cardiovascular disorders associated with fluid retention [1, 2]. Given its clinical importance and widespread pharmaceutical applications, the development of reliable analytical methods for its determination is essential for pharmaceutical quality control and therapeutic monitoring.

In recent years, electrochemical techniques have gained considerable attention in pharmaceutical analysis because of their high sensitivity, simplicity, rapid response, low operational cost, and minimal sample preparation requirements [3–6]. Electrochemical methods are particularly useful for studying the redox behavior of electroactive pharmaceutical compounds and provide valuable information regarding electron-transfer mechanisms and reaction kinetics [3, 4]. A typical electrochemical system consists of a working electrode, a counter electrode, and a reference electrode, which together provide stable and reproducible analytical measurements [5]. Among electrochemical techniques, cyclic voltammetry (CV) is one of the most widely used methods for investigating oxidation–reduction processes at electrode surfaces. Cyclic voltammetry has been successfully applied to the characterization and quantitative determination of various pharmaceutical compounds because of its simplicity, sensitivity, and rapid analysis time [6,7].

Cardiovascular diseases remain one of the leading causes of mortality worldwide, with hypertension considered a major risk factor contributing to serious complications such as myocardial infarction, stroke, and heart failure [8–10]. Therefore, the development of rapid and sensitive methods for the determination of antihypertensive drugs is of considerable pharmaceutical importance. Although several analytical methods have been reported for the determination of cyclopenthiazide [1], limited studies have focused on its electrochemical behavior and voltammetric determination using glassy carbon electrodes. Therefore, the present study aimed to investigate the electrochemical behavior of cyclopenthiazide at a glassy carbon electrode using cyclic voltammetry.

Experimental part

Reagents and solutions. Cyclopenthiazide standard (purity 99 %) was obtained from Nanjing Duly Biotechnology Co., Ltd. Phosphoric acid (H_3PO_4), acetic acid (CH_3COOH), and boric acid (H_3BO_3) were supplied by Dow Chemical Company, Eastman Chemical Company, and BASF, respectively. All reagents were of analytical grade.

Britton–Robinson (B–R) buffer solution (0.1 M) was prepared by mixing equal volumes of 0.1 M phosphoric acid, 0.1 M acetic acid, and 0.1 M boric acid solutions. The pH was adjusted within the range of 2.0–12.0 using 0.1 M sodium hydroxide solution.

All solutions were prepared using Milli-Q deionized

water. Unless otherwise stated, 0.1 M Britton–Robinson buffer was used as the supporting electrolyte. A fresh stock solution of cyclopenthiazide (100 μg mL^{-1}) was prepared daily in the supporting electrolyte solution.

Instrumentation. Electrochemical measurements were performed using a DY-2000 potentiostat/galvanostat (USA) coupled to a conventional three-electrode electrochemical cell. A glassy carbon electrode (GCE, 1 mm diameter, Detecto, Iran) served as the working electrode, while an Ag/AgCl electrode (3.0 M KCl, Detecto, Iran) and a platinum wire electrode were used as the reference and counter electrodes, respectively.

Before each measurement, the GCE surface was polished with diamond paste and alumina slurry, then subjected to electrochemical activation in 0.1 M Britton–Robinson buffer by cyclic voltammetry at 0.05 V s^{-1} for 20 cycles.

Cyclic voltammetric measurements were carried out in the potential range from 0.1 to −1.1 V at a scan rate of 0.05 V s^{-1} with a step potential of 0.001 V.

Pharmaceutical sample preparation. A commercial pharmaceutical formulation containing cyclopenthiazide (“Navidrex”, Arifrye, Sakarya, Turkey) was used for analytical application studies. Powdered tablets equivalent to the required amount of cyclopenthiazide were dissolved in 0.1 M Britton–Robinson buffer solution to prepare an approximately 200 μg mL^{-1} solution. The solution was sonicated for 10 min, filtered, and diluted with the supporting electrolyte to the desired concentration range.

Voltammetric measurements. The electrochemical behavior of cyclopenthiazide at the glassy carbon electrode was investigated using cyclic voltammetry. Cyclic voltammograms were recorded over the potential range from 0.1 to −1.1 V at scan rates ranging from 0.001 to 0.05 V s^{-1}. All measurements were performed in quintuplicate.

The effects of scan rate, pH, supporting electrolyte, and temperature on the voltammetric response of cyclopenthiazide were systematically investigated under optimized experimental conditions.

Results and discussion

Effect of Supporting Electrolyte. The effect of the supporting electrolyte on the voltammetric response of cyclopenthiazide was investigated by cyclic voltammetry using 0.1 M Britton–Robinson, acetate, and phosphate buffer solutions. As shown in Figure 1, the nature of the supporting electrolyte markedly influenced the oxidation peak current and peak shape. Among the tested media, Britton–Robinson buffer produced the highest anodic peak current and the best peak definition. Therefore, 0.1 M Britton–Robinson buffer was selected for subsequent experiments.

Effect of Scan Rate. The effect of scan rate was investigated over the range of 0.002–0.2 V s^{-1}. As shown in Fig. 2, the anodic peak current increased with the scan rate. A linear relationship between the anodic peak current (Ip) and the square root of the scan rate ($v^{1/2}$) was observed, indicating a diffusion-controlled electrode process. Furthermore, the linear dependence of log Ip on log v, with a slope of 0.4457, confirmed the diffusion-controlled nature of the oxidation process. The oxidation peak potential shifted toward more negative values as the scan rate increased, suggesting an irreversible electrochemical process. According to Laviron’s theory [13], the linear relationship between peak potential (Ep) and ln v indicated that two electrons participate in the electrooxidation mechanism of cyclopenthiazide at the glassy carbon electrode surface.

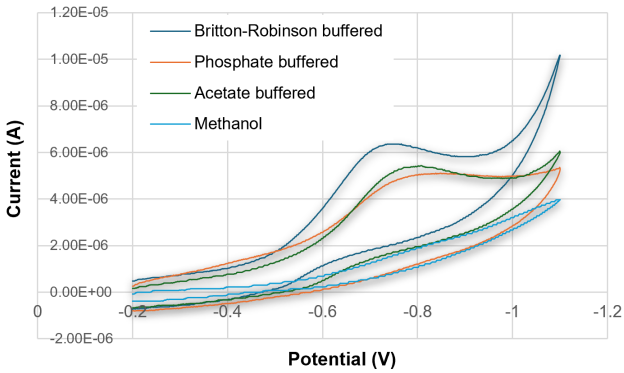

Fig. 1. Cyclic voltammograms of 100 μg mL^{-1} cyclopenthiazide recorded in different supporting electrolytes at the glassy carbon electrode (scan rate: 0.2 V s^{-1}).

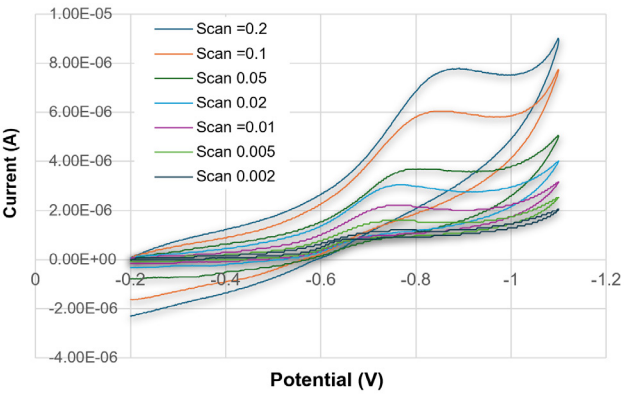

Fig. 2. Cyclic voltammograms of 100 μg mL^{-1} cyclopenthiazide in 0.1 M Britton–Robinson buffer at different scan rates.

Effect of pH. The effect of pH was investigated over the pH range of 2.0–12.0 using cyclic voltammetry. As shown in Fig. 3, the oxidation peak potential shifted toward lower values with increasing pH, indicating the participation of protons in the electrode reaction.

A linear relationship between Ep and pH was obtained according to the equation:

$$E_p\ (V) = -0.0598\,pH - 0.2528\ (R^2 = 0.9954).$$

The slope value (~59 mV pH^{-1}) indicates that equal numbers of electrons and protons participate in the electrooxidation process. Based on the obtained results, the oxidation mechanism of cyclopenthiazide at the glassy carbon electrode likely involves a two-electron/two-proton transfer process occurring at the sulfonamide moiety of the molecule. The electrochemical oxidation is accompanied by proton dissociation and formation of the corresponding oxidized sulfonamide derivative.

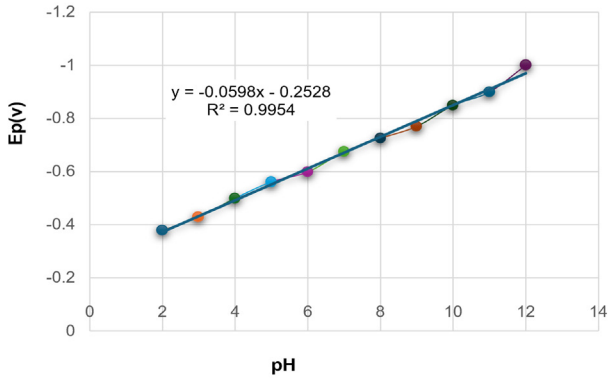

Fig. 3. Influence of pH on the oxidation peak potential (E_p) and peak current of cyclopenthiazide.

Effect of Temperature. The influence of temperature on the voltammetric response of cyclopenthiazide was investigated over the temperature range of 5–35 °C. The anodic peak current increased with temperature, indicating enhanced electron-transfer kinetics at higher temperatures (Fig. 4).

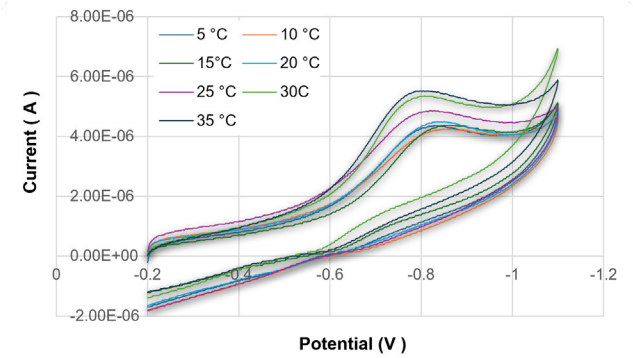

Fig. 4. Cyclic voltammograms of 100 μg mL^{-1} cyclopenthiazide recorded at different temperatures in 0.1 M Britton–Robinson buffer solution at a scan rate of 0.05 V s^{-1}.

Thermodynamic parameters, including activation energy (Ea), enthalpy change (ΔH), entropy change (ΔS), and Gibbs free energy change (ΔG), were calculated using the Arrhenius and Eyring equations. The positive value of ΔH indicates that the electrooxidation process is endothermic, whereas the negative value of ΔS suggests a decrease in disorder during the electrode reaction. In addition, the positive ΔG value indicates that the oxidation process is non-spontaneous under the experimental conditions. The calculated thermodynamic parameters are summarized in Table 1.

Table 1. Thermodynamic parameters for the electro-oxidation of cyclopenthiazide.

E_a (kJ mol^{-1})	ΔH (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})	ΔG (kJ mol^{-1})
2.44	0.114	−3.96	1.29

Interference Study. The selectivity of the proposed method was evaluated in the presence of common pharmaceutical excipients including starch, magnesium stearate, and lactose monohydrate. A 10-fold excess of these substances did not significantly affect the voltammetric response of cyclopenthiazide, indicating satisfactory selectivity of the proposed method (Fig. 5).

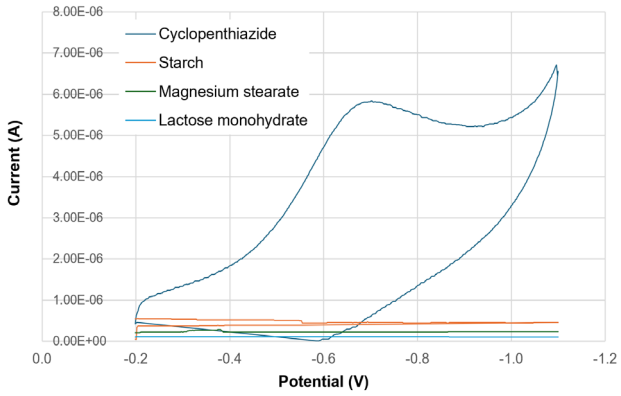

Fig. 5. Effect of common pharmaceutical excipients on the voltammetric response of cyclopenthiazide at the glassy carbon electrode**.**

Analytical parameters. Under the optimized experimental conditions, the anodic peak current increased linearly with cyclopenthiazide concentration over the range of 20–200 μg mL. The calibration equation is *Ipa* = 2 × 10^{-6} C + 2 × 10^{-5} (R^2 = 0.9972). The analytical performance parameters, including linear range, LOD, LOQ, and RSD, are summarized in Table 2

Table 2. Analytical parameters for the voltammetric determination of cyclopenthiazide at the glassy carbon electrode.

Parameter	GCE
Linearity range, μg mL^{-1}	20–200
Slope	2 × 10^{-6}
Intercept (A)	2 × 10^{-5}
Correlation coefficient (R^2)	0.9972
LOD (g mL^{-1})	7.28
LOQ (g mL^{-1})	22.1
SD (A)	4.41 × 10^{-6}
RSD %	7.74

Analytical Application. The applicability of the proposed voltammetric method was evaluated for the determination of cyclopenthiazide in commercial pharmaceutical formulations. Recovery studies were performed by the standard addition method using pre-analyzed samples containing known amounts of cyclopenthiazide. The obtained results demonstrated good agreement between the determined values and the labeled drug content, indicating satisfactory accuracy and reliability of the proposed method.

The anodic peak current increased linearly with increasing cyclopenthiazide concentration, confirming the suitability of the calibration graph for quantitative analysis. The analytical results for bulk samples and pharmaceutical formulations are summarized in Table 3.

Table 3. Determination of cyclopenthiazide in bulk samples and pharmaceutical formulations using cyclic voltammetry.

Sample	Taken, mg	Found, mg	Recovery,%	RSD, %
Bulk sample	13.00	12.95	100.38	3.50
Bulk sample	26.00	25.86	100.53	0.57
Bulk sample	32.00	32.08	99.75	0.19
Pharmaceutical formulation	25.00	25.06	99.76	0.52
Pharmaceutical formulation	50.00	49.88	100.24	0.19
Pharmaceutical formulation	75.00	74.95	100.06	0.07

Conclusions

The electrochemical behavior of cyclopenthiazide at a glassy carbon electrode was successfully investigated using cyclic voltammetry. The results demonstrated that cyclopenthiazide undergoes irreversible, diffusion-controlled electrooxidation. Among the investigated supporting electrolytes, 0.1 M Britton–Robinson buffer provided the highest anodic peak current and the best voltammetric response and was therefore selected for subsequent studies.

The proposed voltammetric method exhibited satisfactory selectivity, sensitivity, and reproducibility for the determination of cyclopenthiazide in pharmaceutical formulations. In addition, the method offers several advantages, including simplicity, low cost, rapid analysis, and minimal sample preparation.

The electrochemical oxidation mechanism of cyclopenthiazide was found to involve a two-electron/two-proton transfer process. The developed method was successfully applied to the quantitative determination of cyclopenthiazide in pharmaceutical samples, yielding satisfactory recovery. The proposed electrochemical method represents a promising alternative for the routine analysis of cyclopenthiazide in pharmaceutical preparations.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Authors' contribution

Saad Imran Al-Abadi wrote the manuscript. Muthana Saleh Mashkour checked and validated the results.

Declaration of AI-assisted technologies

During the preparation of this work, the authors used ChatGPT 5.0, a language model developed by OpenAI, to support text drafting and editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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