

Original Research

**ELECTROCHEMICAL DETERMINATION OF CEFTRIAXONE USING
A GRAPHITE ROD ELECTRODE**

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Abstract

Ceftriaxone (CEF) is a widely used third-generation cephalosporin antibiotic frequently detected in environmental samples. In this study, the electrochemical behavior of ceftriaxone was investigated using cyclic voltammetry (CV) and differential pulse voltammetry (DPV) on a graphite rod electrode in Britton–Robinson (BR) buffer at pH 2. CV measurements showed a well-defined irreversible oxidation peak at approximately 1.0 V vs. SCE. Increasing the scan rate resulted in higher peak current and a movement of the oxidation peak toward higher potentials. DPV measurements revealed that the peak current increased with increasing ceftriaxone concentration from 2×10^{-5} to 5×10^{-4} mol/L. The graphite rod electrode exhibited good electrochemical response, low cost, and simple preparation.

Keywords: ceftriaxone, electrochemistry, cyclic voltammetry, differential pulse voltammetry, graphite rod electrode.

INTRODUCTION

Antibiotics are an important group of drugs that have been used widely to treat various bacterial infections. They are classified according to different criteria, such as mechanism of action, spectrum of activity, and method of administration. The most common classification is based on their molecular structure. In addition to medical use, antibiotics are also used for food preservation and transport. They can be used to treat sick animals, promote animal growth, improve animal feed quality, and in aquaculture [1].

Cephalosporins

Cephalosporins (Figure 1) are a class of β -lactam antibiotics used to treat various bacterial infections. The β -lactam antibiotic group also includes penicillins, carbapenems, and monobactams. Their β -lactam ring enables binding to bacterial penicillin-binding proteins (PBPs) and inhibits peptidoglycan formation during bacterial cell wall synthesis. The

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differences among these antibiotic groups are related to the structure of the β -lactam ring. Penicillins have a five-membered thiazolidine ring, cephalosporins contain a six-membered dihydrothiazine ring, carbapenems have a modified five-membered ring without a sulfur atom, while monobactams contain only a single β -lactam ring. β -Lactam antibiotics are among the most commonly prescribed antibiotics and have been in clinical use for the longest period, beginning with the production of penicillin in 1945 and continuing to the most recent cephalosporin, cefiderocol, approved in the United States in 2019 and in Europe in 2020. The first cephalosporin, cefazolin, became clinically available in 1974, and since then, six generations of cephalosporins have been developed. Within each generation, differences in chemical structure, particularly in the acyl side chain, result in significant variations in antibacterial spectrum and stability against β -lactamase enzymes [1,2].

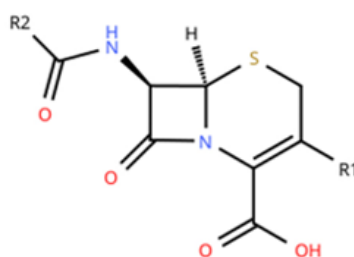


Figure 1 General chemical structure of cephalosporins [1]

Ceftriaxone

Ceftriaxone (CEF) (Figure 2) is a well-known antibiotic used to treat infections. It is one of the most widely used antibiotic drugs. Ceftriaxone belongs to the third generation of cephalosporins and acts by inhibiting the formation of mucopeptides in the bacterial cell wall. It is widely used in clinical practice due to its strong antibacterial activity, high resistance to β -lactamase enzymes, proven clinical effectiveness, low toxicity and low risk of allergic reactions. This drug is used to treat of diseases such as urinary tract infections, respiratory tract infections, and sinusitis [3,4]. The strong antibacterial activity of ceftriaxone and other antibiotics in disease treatment has led to their widespread use. Antibiotics are also widely used in veterinary medicine where they are added to animal feed. The uncontrolled use of antibiotics results in the presence of antibiotic residues and their degradation products in the environment. The main sources of antibiotic contamination are the pharmaceutical industry, livestock farming, hospitals, and household wastewater. Some antibiotics exit the body unchanged, while others used in livestock farming and aquaculture can accumulate in food products such as meat, eggs, and milk, which are then eaten by humans. Conventional water treatment methods are often not effective in removing antibiotic residues from water. As a result, these compounds are often found in surface water, groundwater, and drinking water at very low concentrations (ng/L). It is believed that the high use of antibiotics contributes to the development and spread of bacterial resistance. Infections caused by resistant bacteria are more difficult to treat and may cause serious health problems and higher death rates. Therefore, it is important to develop fast, reliable, and low-cost methods for antibiotic detection.

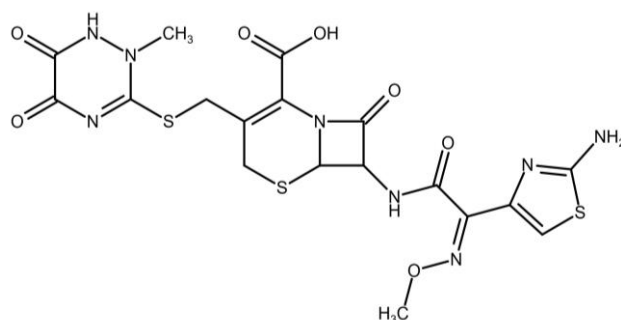


Figure 2 Molecular structure of ceftriaxone [3]

For the determination of ceftriaxone (CEF), conventional analytical methods such as high-performance liquid chromatography (HPLC), ultra-performance liquid chromatography (UPLC), UV spectroscopy, IR spectroscopy, and spectrofluorimetry are commonly used. Other methods reported in the literature include spectrophotometric methods, chromatographic methods, and capillary electrophoresis. However, these methods often require expensive instruments, complex procedures, complicated sample preparation, and long analysis times [4–6]. Due to these limitations, there is a need for fast, simple, and low-cost analytical methods [7]. Electrochemical methods are widely used for determining electroactive compounds because they are sensitive, simple, rapid, and inexpensive. Electrochemical methods for ceftriaxone determination also allow *in situ* analysis and usually do not require complicated sample preparation [4,6]. These methods are based on oxidation or reduction processes that occur on the electrode surface. Additionally, electrochemical systems can be miniaturized and used in portable devices [7]. Modern electrochemical techniques include voltammetric, amperometric, and potentiometric methods. Among these, cyclic voltammetry and pulse voltammetry are widely used for studying redox reactions. In cyclic voltammetry, the potential is swept forward and backward over a selected range, while the current is measured simultaneously. This method provides information on redox behavior and reaction kinetics, but it is mainly used for qualitative analysis [8]. Pulse voltammetry techniques, such as differential pulse voltammetry (DPV) and square-wave voltammetry (SWV), use potential pulses instead of continuous scanning. These techniques are highly sensitive and reduce background current effects. They also offer rapid analysis and low detection limits [7,8]. Electrodes are essential components of electrochemical systems and can be made from materials such as glassy carbon, platinum, gold, and modified electrode materials. Carbon-based electrodes are widely used because they are inexpensive, stable, and exhibit good electrochemical performance. Graphite rod electrodes and carbon paste electrodes can also be prepared from waste batteries, making them low-cost and environmentally friendly materials for electrochemical analysis [8].

MATERIALS AND METHODS

Electrochemical measurements were performed using a potentiostat (IVIUM XRE, IVIUM Technologies, Eindhoven, the Netherlands) in a three-electrode system. A graphite rod electrode from waste zinc-carbon batteries was used as the working electrode, a saturated

calomel electrode (SCE) as the reference electrode, and a platinum electrode as the counter electrode. Before each measurement, the graphite rod electrode was mechanically polished with aluminum oxide paste ($0.3\ \mu\text{m Al}_2\text{O}_3$), rinsed with distilled water, and dried at room temperature. Britton Robinson (BR) buffer at pH 2 was used as the supporting electrolyte. Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were used to study the electrochemical behavior of ceftriaxone (CEF) on the graphite rod electrode surface. Solutions with different concentrations of ceftriaxone were prepared in BR buffer for DPV measurements. For CV measurements, a ceftriaxone solution with a concentration of 5×10^{-5} mol/L was used. CV measurements were performed in the potential range from 0.5 V vs. SCE to 1.6 V vs. SCE at different scan rates (10, 25, and 50 mV/s) in BR buffer at pH 2 (Figure 3). The effect of scan rate on ceftriaxone oxidation was studied by observing changes in peak current and peak potential. Differential pulse voltammetry measurements were performed in the potential range from 0.5 V vs. SCE to 1.3 V vs. SCE using a pulse amplitude of 50 mV, pulse time of 20 ms, potential step of 5 mV, and scan rate of 50 mV/s. Measurements were carried out for different CEF concentrations (5×10^{-4} , 8×10^{-5} , 5×10^{-5} , and 2×10^{-5} mol/L) in BR buffer at pH 2 (Figure 4). For comparison, the blank BR buffer solution was measured under the same conditions.

RESULTS AND DISCUSSION

The cyclic voltammetry results showed a pronounced and sharp oxidation peak of ceftriaxone in BR buffer at pH 2 at approximately $E \approx 1.0$ V (Figure 3). As the scan rate increased from 10 to 50 mV/s, the peak current also increased, while the peak potential moved toward more positive values. The oxidation peak current increased linearly with scan rate. The corresponding equation could be expressed as follows:

$$I_p(\mu\text{A}) = 1.2245 + 0.098v; R^2 = 0.959 \quad (1)$$

This behavior indicates an irreversible electrochemical oxidation process of ceftriaxone on the graphite rod electrode surface [3,4]. The blank BR buffer solution showed no electrochemical response in the investigated potential range, confirming that the observed signal originated from ceftriaxone oxidation. Additionally, the absence of a cathodic peak during the reverse scan further confirmed the irreversible nature of the electrochemical process.

The DPV measurements showed that the oxidation peak current of ceftriaxone increased as the concentration increased. As the concentration rose from 2×10^{-5} to 5×10^{-4} mol L⁻¹, the peak current gradually increased, while the peak potential remained nearly constant (Figure 4). All voltammograms displayed a well-defined peak at approximately $E \approx 1.0$ – 1.1 V vs. SCE for all concentrations, indicating a stable oxidation process. The highest peak current was observed at 5×10^{-4} mol L⁻¹. When the concentration decreased (8×10^{-5} , 5×10^{-5} and 2×10^{-5} mol L⁻¹), the peak current also decreased. The linear increase in peak current with concentration confirmed the good sensitivity and analytical performance of the DPV method for quantitative electrochemical determination of ceftriaxone [10,11]. The

corresponding equation, in the examined concentration range of ceftriaxone, can be expressed as follows:

$$I_p(\mu A) = 0.3416 + 0.0074x; R^2 = 0.9676 \quad (2)$$

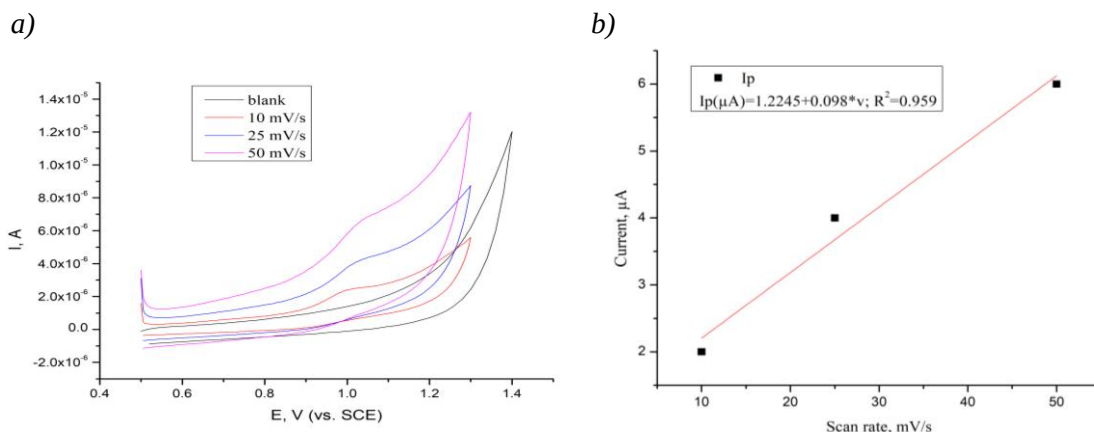


Figure 3 a) The effect of scan rate on the peak intensity of ceftriaxone; b) Dependence of peak current of 50.0 μM ceftriaxone on the scan rate

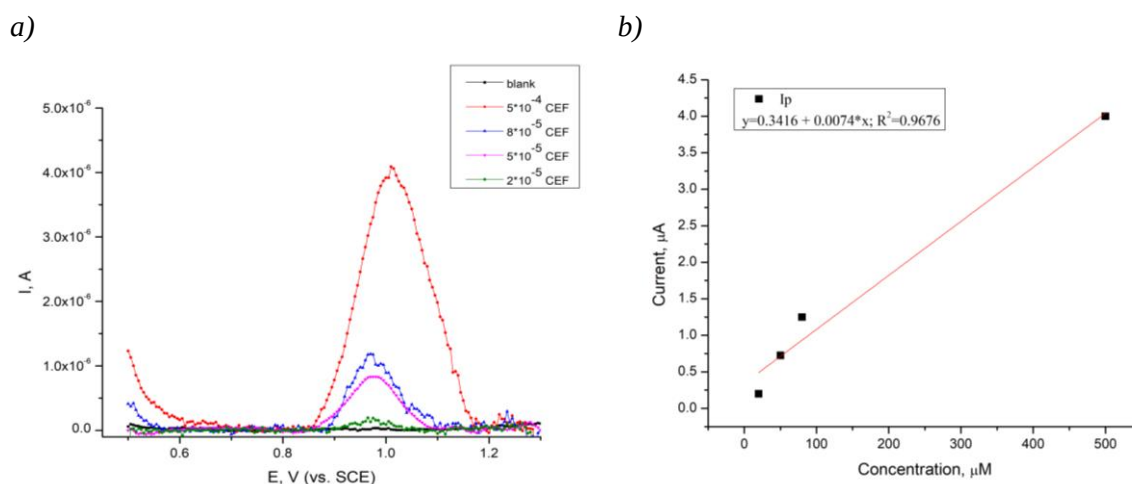


Figure 4 a) The effect of concentration on the peak intensity of ceftriaxone; b) The dependence of peak current on ceftriaxone concentration (investigated concentration range 20 μM – 500 μM)

CONCLUSION

The electrochemical behavior of ceftriaxone was studied using cyclic voltammetry and differential pulse voltammetry on a graphite rod electrode in Britton–Robinson buffer solution at pH 2. Cyclic voltammetry measurements showed a distinct irreversible oxidation peak of ceftriaxone at approximately 1.0 V vs. SCE. Increasing the scan rate resulted in higher peak currents and a shift of the peak potential toward more positive values, indicating irreversible oxidation. Differential pulse voltammetry measurements showed that the oxidation peak current increased with higher ceftriaxone concentrations, while the peak potential remained nearly constant. These results confirmed that DPV is suitable for quantitative determination of ceftriaxone. The graphite rod electrode provided good

electrochemical response and advantages such as low cost, simple preparation, and easy handling. Therefore, this electrochemical method can serve as a simple and reliable alternative for ceftriaxone determination in pharmaceutical and environmental samples.

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