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Short communication

Voltammetric behavior and assay of the antibiotic drug cefazolin sodium in bulk form and pharmaceutical formulation at a mercury electrode

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Abstract

The electrochemical behavior of the antibiotic drug cefazolin sodium (CFZ) in Britton–Robinson buffers (pH 2–11) at the mercury electrode was studied by means of dc-polarography, cyclic voltammetry, controlled-potential coulometry and square-wave adsorptive stripping voltammetry techniques. A validated square-wave adsorptive cathodic stripping voltammetric procedure was described for the trace determination of cefazolin in bulk form up to limits of detection and quantitation of 2.6×10^{-10} M and 8.6×10^{-10} M, respectively. The method was successfully applied for determination of cefazolin in pharmaceutical preparation without the necessity for samples pretreatment or any time-consuming extraction or evaporation steps prior to the analysis.

Keywords: Cefazolin; Dc-polarography; Cyclic voltammetry; Square-wave stripping voltammetry; Assay

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1. Introduction

Cefazolin sodium: 3-[(5-methyl-1,3,4-thiadiazol-2-yl) thiomethyl]-7-(tetrazol-1-ylacetamido)-3-cephem-4-carboxylic acid; is a semi synthetic cephalosporin antibiotic. Cefazolin (CFZ) is classified as a first generation cephalosporin having a broad spectrum of activity and exhibits somewhat greater activity against *klebsiella pneumoniae* [1]. It is active in vitro against many Gram-positive aerobic cocci but has a limited activity against Gram-negative bacteria [2].

Numerous analytical procedures were reported for the determination of CFZ including the use of fluorimetry [3], colourimetry and AAS [4], spectrophotometry [5–7], radiosensitivity [8], capillary zone electrophoresis [9], densitometry [10], liquid chromatography [11–13], high-performance liquid chromatography [14–18], and voltammetry [19–21]. Most of these methods required formation of CFZ-metal complexes [3–5] or samples pretreatment and time-consuming extraction steps prior to analysis of the drug [6–18]. The reported voltammetric methods achieved the detection limits of 1.5×10^{-5}–1×10^{-6} M CFZ [19–21], which are not sensitive enough for the trace assay of cefazolin.

The aim of this study was to investigate the electrochemical behavior of cefazolin at a mercury electrode and to describe a validated sensitive and precise square-wave adsorptive stripping voltammetric procedure for trace assay of cefazolin in bulk form and pharmaceutical formulation.

2. Experimental

2.1. Solutions

A standard solution (1×10^{-3} M) of cefazolin sodium was prepared daily in deionized water from the pure compound (Sigma, St. Louis, MO, USA). A series of Britton–Robinson (B-R) buffer of pH 2–11 was prepared [22] and used as a supporting electrolyte. Deionized water was obtained from a

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Purite Still Plus Deionizer attached to an Aquamatic bidistillation water system (Hamilton Laboratory Glass Ltd., Kent, UK). A Mettler balance (Toledo-AB 104, Switzerland) was used for weighing the solid materials. All the chemicals (Merck) were of analytical-reagent grade and were used without further purification.

2.2. Instrumentation

A polarograph Model 4001 (Sargent-Welch) was used for studying the polarographic behavior of CFZ. A polarographic cell with a dropping mercury electrode as a working electrode ($m = 1.03\ \mathrm{mg\,s^{-1}}$, $t = 3.3\ \mathrm{s}$ at mercury height = 60 cm) and a saturated calomel electrode (SCE) as a reference electrode was used. A computer-controlled Electrochemical Analyzer Model 394-PAR (Princeton Applied Research, Princeton, NJ, USA) with the software package 270/250 (PAR) was used for cyclic and square-wave measurements. The electrode assembly 303A (PAR) incorporated with a micro-electrolysis cell comprising of a hanging mercury drop electrode (HMDE) as a working electrode, an Ag/AgCl/KCl$_s$ as a reference electrode and a platinum wire as a counter electrode was used.

A potentiostat/galvanostat Model 173-PAR incorporated with a digital coulometer Model 179-PAR was used for the controlled-potential coulometric measurements at a mercury pool electrode. The number of electrons transferred per CFZ molecule in the B-R buffer of pH 2–11 was found to equal 2.

2.3. Procedures

2.3.1. Assay of bulk CFZ

A known volume of cefazolin sodium solution was pipetted into 10 ml calibrating flask and made up to the mark with a B-R buffer of pH 6. The solution was introduced into the electrolysis cell, and then deoxygenated with pure nitrogen for 10 min in the first cycle and 30 s for each successive cycle; the nitrogen was then kept over the solution. Preconcentration of CFZ onto the HMDE was performed at −0.6 V for 90 s while stirring the solution at 400 rpm with a magnetic stirrer. After an equilibrium time of 5 s was allowed for the solution to become quiescent, the stripping voltammogram was recorded by scanning the potential toward the negative direction using the square-wave waveform under the optimized conditions.

2.3.2. Assay of CFZ in formulation

Constitute sterile powder of the CFZ preparation (Cefazolin, 1 vial/1 g, produced by October Pharma S.A.E Egypt under license of Biochemie Austria) was dissolved in a volume of deionized water accurately measured corresponding to the volume specified in the labeling. An accurately measured volume of the prepared injection solution was diluted quantitatively with deionized water to obtain a 1×10^{-3} M. Cefazolin solution was then analyzed using the optimized voltammetric procedure.

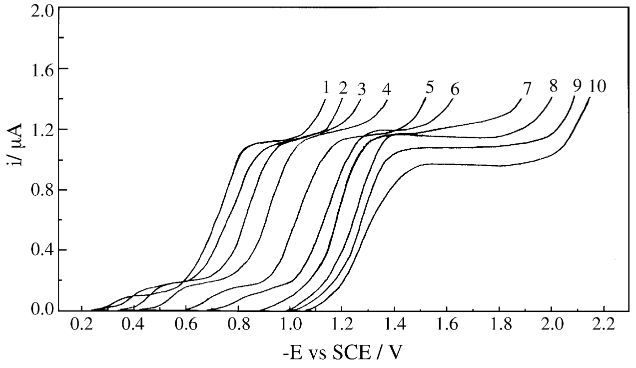

Fig. 1. Dc-polarograms of 2.5×10^{-4} M cefazolin in (1) 0.1 M HCl solution (pH 1) and in B-R buffers of various pH values: (2) 1.8; (3) 3.0; (4) 4.0; (5) 5.0; (6) 6.0; (7) 7; (8) 8.0; (9) 10.0; and (10) 11.0.

3. Results and discussion

3.1. Dc-polarography

Polarograms of CFZ in B-R buffers of pH 2–11 exhibited a single 2-electron irreversible cathodic wave with almost pH-independent limiting current which could be due to the reduction of the –CH$_2$–S– moiety of CFZ molecule [21,23–26]. In addition a pre-wave was appeared at less negative potential in solutions of pH <7 (Fig. 1). A similar behavior was obtained in 0.1 M HCl solution (pH 1), Fig. 1, curve 1. The pre-wave may be an adsorption one due to the reduction of the adsorbed CFZ species. Gibbs energy of adsorptive CFZ species makes the reduction of the adsorbed species easier than that of CFZ species in bulk solution [27]. Sulfur atoms of CFZ molecule play a crucial role in the adsorption phenomena of the analyte onto the mercury electrode surface [28]. Plots of $E_{\mathrm{d.e.}}$ against $\log(i/i_{\mathrm{d}} - i)$ [29] at the various pH values were straight lines with the slope values reported in Table 1 (slope, mV = $S_1 = 59/\alpha n_{\mathrm{a}}$, where α is the transfer coefficient and n_{a} is the number of electrons involved in the rate—determining step). The estimated values of αn_{a} and α indicated the irreversible nature of the reduction process of CFZ at the mercury electrode and the number of electrons (n_{a}) involved in the rate-determining step equals 2. The half-wave potential ($E_{1/2}$) of the polarographic wave of CFZ shifted to more negative values with the increase of pH up to 8, which indicated the involvement of protons in the rate-determining step of the reduction process [30] within this pH range.

The $E_{1/2}$–pH plot (Fig. 2, curve *a*) composed of two segments; the linear segment (pH $\leq$8) follows the equation: $E_{1/2} = -0.50 - 0.086$ pH while at higher pH values the effect of pH is almost negligible. From slope values (S_2) of the linear segment of the $E_{1/2}$–pH plot $\{\delta E_{1/2}/\delta\,\mathrm{pH} = S_2, \mathrm{mV} = (59/\alpha n_{\mathrm{a}})\, Z_{\mathrm{H}}{}^{+}\}$, where $Z_{\mathrm{H}}{}^{+}$ is the number of protons participated in rate-determining step of the reduction process$\}$, and those (S_1) of the $E_{\mathrm{d.e.}}$ versus $\log(i/i_{\mathrm{d}} - i)$ plots at various pH values, the number of protons ($Z_{\mathrm{H}}{}^{+}$) participated in the rate-determining