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Stripping voltammetric detection of nephrotoxic drug cefitizoxime in wastewater

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ABSTRACT

The objective of the present work is to develop the stripping voltammetric method for determination of nephrotoxic drug cefitizoxime in pharmaceutical formulation and its application to wastewater analysis. Solubilized system of different surfactants viz. cationic, anionic and non-ionic influences the electrochemical response of cefitizoxime. Solubilized system of CTAB containing cefitizoxime enhanced the peak current while anionic and non-ionic showed an opposite effect. The current signal due to the reduction process is a function of concentration of the cefitizoxime, pH of medium, type of surfactant and accumulation time at electrode surface. The proposed SWCAdSV (Squarewave Cathodic Adsorptive Voltammtery) and DPCAdSV (Differential Pulse Cathodic Adsorptive Voltammetry) are linear over concentration range 1.732–6.901 μg/mL and 4.792–30.672 μg/mL with detection limit of 0.76 ng/mL and 2.63 ng/mL, respectively. The method is successfully applied for determination of cefitizoxime in pharmaceutical formulation and wastewater with mean percentage recovery of 99.73% and 98.51%, respectively.

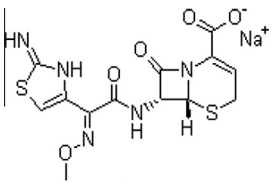
1. Introduction

Pharmaceuticals are an important group of emerging contaminants in the environment [1]. Many drug residues have been found in water and analysis of drug residues is increasing in importance day by day [2]. Pharmaceuticals are manufactured each year and by consumption or improper disposal, they end up in wastewater. Often wastewater treatment plants cannot degrade these substances and so loads of pharmaceuticals end up in the environment. Only recently, the attention has been drawing towards this pollution in the environment. In recent years, many reports have been made on the occurrence of the large, differentiated group of pharmaceuticals in wastewater, surface water, ground water and in soil [3–5]. Acute toxicity is the biggest concern we are facing and these biologically active chemicals can have acute effects on aquatic plants and organisms [6].

The political world has also noticed the problem of pharmaceutical pollution in the environment. Two directives have been written (2001/83/EC for human pharmaceuticals, 2001/82/EC for animal pharmaceuticals) to demand an environmental assessment for the approval of new drugs coming on the market [7,8]. In this regard, there has to be made a lot of effort concerning research toward environmental assessment of pharmaceuticals.

Recent advances in technology have allowed the development of beta-lactams that were too reactive to be isolated in the early decades of the antibiotic era, but unfortunately also increase their toxic side effects. Although the penicillins are almost completely free of renal toxicity, several cephalosporins and most of the broadly effective beta-lactam antibiotics developed so far are nephrotoxic [9–13]. This toxicity has been severe enough with certain cephalosporins to preclude their clinical use. Administration of nephrotoxic beta-lactam antibiotics cause acute proximal tubular necrosis.

Cefitizoxime sodium is a sterile, semisynthetic, beta-lactamase resistant antibiotic, having high bactericidal activity against streptococci, staphylococci, proteus and shigella [14]. This broad-spectrum compound has a synmethoxyimino chain at the 7-position that confers, 3-lactamase stability [15]. The bactericidal action of cefitizoxime results from inhibition of cell-wall synthesis [16].



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To date only few analytical methods have been reported for the estimation of cefitizoxime, these include liquid chromatography [17], high performance liquid chromatography [18] and high performance liquid chromatography with anion-exchange extraction technique [19].

The interest in developing electrochemical sensing devices for use in environment monitoring, clinical assays or process control is growing rapidly. Electroanalytical techniques have long been used for the determination of a wide range of drug compounds with the advantages that there is no need for derivatizations and these techniques are less sensitive to matrix effects compared to other analytical techniques [20,21].

Solubilized system of surfactants heavily influences the electrochemical processes of electroactive species [22] and is widely used in electroanalytical chemistry to improve the sensitivity and selectivity [23,24]. The aggregates of surfactants, such as micelles, liquid crystalline, vesicles, etc. could enhance the stabilized content and the control of release behavior of drugs are widely studied as drug delivery systems. The uses of surfactants as drug carriers make necessary to the study the interaction of drugs with micellar systems, implying the elucidation of the nature of these interactions. In addition, micellar systems are considered primitive model systems for biological membranes [25]. The current electroanalytical research is based on voltammetric determination of nephrotoxic drug cefitizoxime in pharmaceutical formulation and waste water in presence of less hazardous surfactant media comparison to toxic organic solvents.

2. Experimental

2.1. Materials and methods

Cefitizoxime (99% purity) is obtained from Glaxo SmithKline Pharmaceuticals and is used as received. Injection containing cefitizoxime (*cefizox*) labeled 1.0 g is obtained from commercial sources. KCl (1.0 mol/L) solution was prepared in double distilled water and used as supporting electrolyte. All chemicals used are of analytical reagent grade quality and were employed without further purification.

2.2. Procedure

2.2.1. Cefitizoxime measurement in pharmaceutical formulation

A stock solution of cefitizoxime (1.0 mg/mL) was prepared in DMF, cetyltrimethyl ammonium bromide (CTAB), sodium dodecyl sulfate (SDS) and in Tween 20. Solution is introduced into a 10 mL volumetric flask and then completed to a volume with a B–R buffer of selected pH value and 1.0 mol/L KCl. The solution was transferred into the voltammetric cell, and a pure nitrogen stream was passed for 5 min before analysis. The analyte was preconcentrated by accumulation parameters; t_{acc} = 140 s and E_{acc} = −0.5 V while stirring the solution. At the end of the preconcentration time the stirring was stopped and 5 s were allowed for the solution to become quiescent. Then the voltammograms are recorded by scanning the potential towards the negative direction under the optimized instrumental and operational parameters (frequency = 100 Hz, scan increment = 10 mV and pulse height = 50 mV).

2.2.2. Cefitizoxime analysis in wastewater

Wastewater samples were collected from municipal discharge station in Gwalior city Madhya Pradesh, India and filtered through Whatman filter paper. A stock solution of cefitizoxime 1.0 mg/mL was prepared in industrial wastewater samples to give a final concentration over the range 2.13–28.48 μg/mL. Other optimization parameters are same as above for analysis of cefitizoxime in wastewater.

$$\text{Cefitizoxime concentration} = C_{std} \times I_{samp}/A_{istd}$$

where C_{std} is the concentration of the standard and I_{samp} and A_{std} are the currents for sample and standard, respectively.

2.3. Instrumentation

Electrochemical measurements were performed using a μ-Autolab type III (Eco-Chemie B.V., Utrecht, The Netherlands) potentiostat–galvanostat with 757VA computrace software. The utilized electrodes are hanging mercury drop electrode (HMDE) as working electrode, graphite rod as counter electrode and Ag/AgCl (3.0 mol/L KCl) as reference electrode. The electrochemical cell is a Metrohm 663 VA stand. All pH-metric measurements were made on a Decible DB-1011 digital pH meter fitted with a glass electrode and a saturated calomel electrode as reference, which was previously standardized with buffers of known pH.

Chromatographic experiments are performed on the HPLC apparatus comprised of UV variable wavelength Model SPD-20AU Prominence (Shimadazu Corporation Japan), Isocratic Pump LC-20AD Prominence, a Model 7125 injection valve with a 20 μL sample loop (Rheodyne, Cotati, CA, USA). Data acquisition and processing are performed by Spinchrom CFR. Injection is accomplished with a 20 μL loop injector (Model 701 syringe 50 μL; Hamilton, Bonaduz, Switzerland). ODS column (250 mm × 4.6 mm i.d., 5 μm) YMC is used for separation. Elution was isocritical at a flow-rate of 1.5 mL/min and the eluent is monitored at 310 nm.

3. Results and discussion

3.1. Cefitizoxime measurement in solubilized system

On comparing the voltammetric behavior (CV (Cyclic Voltammetry), DPV (Differential Pulse Voltammetry), SWV (Square Wave Voltammetry)) of cefitizoxime in DMF and in solubilized system of CTAB (Table 1), it is observed that cefitizoxime shows substantial increase in peak current and the limit of detection is found to be lower in CTAB (Fig. 1) while neutral and anionic surfactants showed an opposite effect. The reason for

Table 1
Comparison between electrochemical parameters of ceftizoxime in 4.0×10^{-3} mol/L CTAB and in DMF using different voltammetric methods.

Operational method	4.1 μg/mL cefitizoxime + 4.0×10^{-3} mol/L CTAB		4.1 μg/mL cefitizoxime + DMF	
	[a] I_{pc}/μA	[b] E_{pc}/V vs. Ag/AgCl	[a] I_{pc}/μA	[b] E_{pc}/V vs. Ag/AgCl
CV	0.92	−1.28	0.62	−1.23
SWV	1.20	−1.29	0.89	−1.22
DPV	0.28	−1.26	0.23	−1.22

[a] Cathodic peak current.
[b] Cathodic peak potential.