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Voltammetric analysis of Cu (II), Cd (II) and Zn (II) complexes and their cyclic voltammetry with several cephalosporin antibiotics

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Abstract

Both osteryoung square wave voltammetry and cyclic voltammetry have been utilized to elucidate and confirm the possible complexation reaction that occur between the various cephalosporin antibiotics and either the toxic, non-essential metal ion, viz. Cd (II), or the essential but toxic (when their concentration exceeds certain level in serum) metal ions, viz. Cu (II) and Zn (II).

Voltammetric measurements indicated the existence of 1:1 metal-to-ligand ratio (as in cephalexin and cephapirin complexes), 1:2 ratio (such as in cefamandole, cefuroxime and cefotaxime complexes) and 2:1 ratio in case of ceftazidime complexes. Adsorption behavior was evidenced for Cu (II)–cefuroxime or ceftazidime complexes as well as for those for Zn (II)–cephalexin or cephapirin. This phenomenon could be used for the determination of either the antibiotic or the metal ion using adsorptive stripping voltammetry. Detection limits down to 7×10^{-10} M have been easily achieved.

Keywords: Cephalosporin antibiotics; Complexes; Cyclic voltammetry; Osteryoung square wave voltammetry

1. Introduction

Cephalosporins are the second major group of β-lactam antibiotics [1], they are classified into four generations. The biological activity of these antibiotics is the β-lactam ring [2]. The possible interaction that may occur between metal ions and these antibiotics is of importance as this may affect the drug absorption through the human membrane [3]. This may help in understanding what is going in vivo when administrating an antibiotic. Since metal ions are known to accelerate the rates of chemical reactions [4], it may also "mask" a nucleophile and thus prevent an otherwise likely side reaction [4]. Metal ions also act as Lewis acid catalysts especially the transition ones like Zn, Fe, Mn and Cu because they have empty d electron orbitals that can act as electron sinks [5]. The functioning of a metal as a Lewis acid requires chelate formations with a ligand such as that occur with the enzymes in vivo [5]. Antibiotics also can behave as ligands [6–11]. Although few reports exist in the literature concerning this topic area, some are cited either using voltammetry [6–8] or other methods, e.g. spectrophotometry [9–11].

Various electroanalytical techniques have been used to study the polarographic activity [12–17], degradation products, and the electrode reaction of cephalosporins [18,19]. The electrochemical behavior of cephalexin has been studied by Li and Chen [20]. The electrochemical behaviors of cephalexin and cephapirin have been determined using differential pulse polarography in Britton–Robinson buffer (pH 7.3) by Fredrik et al. [21]. Bernacca et al. [22] have investigated a polarographic behavior of the β-lactam antibiotic cefuroxime and study of the reduction mechanism in acidic media. The electrochemical behavior and analysis of cefotaxime sodium have been studied by Raghavan et al. [23]. Cathodic

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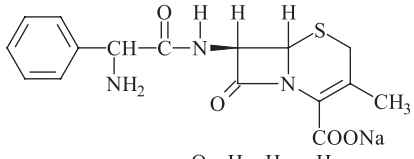
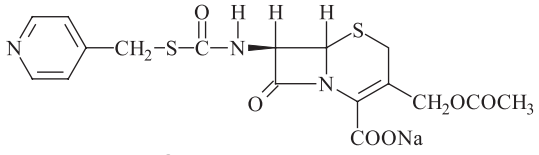
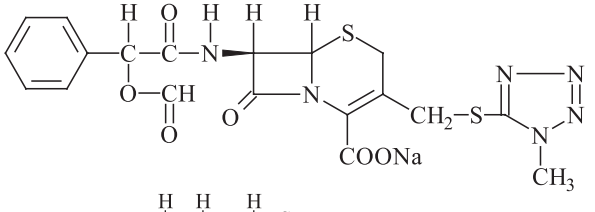
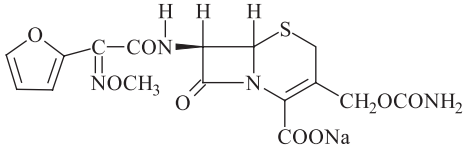
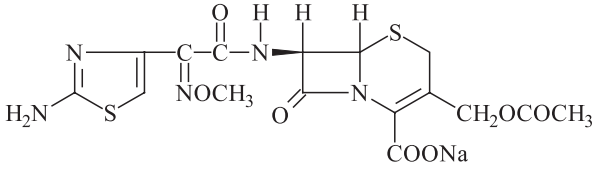
stripping voltammetric method has been described for determining cephalosporin antibiotic ceftriaxone by Abo El Maali et al. [12].

Cefotaxime and cefuroxime in Britton–Robinson or Clark–Lubs buffer solution as supporting electrolyte have been examined by d.c., sampled-d.c. and differential pulse polarography and cyclic voltammetry [24]. Cefotaxime and cefuroxime each gave two reduction waves ($E_{1/2}$=−0.6–0.8 V vs. Ag–AgCl). Each drug could be determined at weakly acid pH by Zhang et al. [25] have studied the voltammetric behavior of cefotaxime sodium and its determination by single-sweep oscillopolarography. Interference caused by Fe (II), Cu (II), Zn (II), and Cd (II) can be avoided by addition of 0.3 ml of 5% EDTA.

A differential pulse polarographic method has been described for determining ceftazidime in urine samples with and without prior extraction [26]. Ceftazidime also has been determined by cathodic-stripping voltammetry [27] in a supporting electrode containing 0.45 μg/ml poly-L-lysine in Britton–Robinson buffer of pH 10. Various types of electrodes have been utilized [28] for an electrochemical study of ceftazidime in aqueous and biological media.

Few reports are found in the literature concerning the identification and isolation of the metal ions–cephalosporin complexes [29]. The aim of the present work is to utilize our previous publications [30,31] for studying the electrochemical behavior of the isolated solid Cu (II), Cd (II) and Zn (II) cephalosporin antibiotics namely: Cephalexin (CEX), Cephapirin (CEP), Cefamandole (CML), Cefuroxime (CRX), Cefotaxime (CTX) and Ceftazidime (CFZ), with their use for quantifying either the antibiotic or the metal ions using the adsorptive stripping voltammetric method of analysis.

Table 1
Structure, name, generation, and notation of the antibiotics under investigation

Name	Generation	Notation	Structure
Cephalexin	First	CEX	
Cephapirin	First	CEP	
Cefamandole	Second	CML	
Cefuroxime	Second	CRX	
Cefotaxime	Third	CTX	
Ceftazidime	Third	CFZ