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Electrochemical determination of cephalosporins using a bare boron-doped diamond electrode

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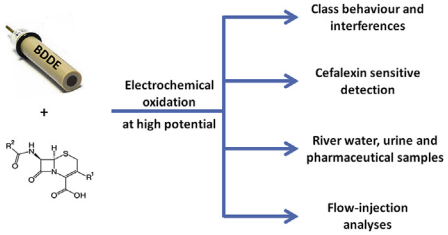
HIGHLIGHTS

- The electrochemical oxidation at BDDE of seven cephalosporins was evaluated at high potential.
- The influence on the analytical response of the cephalosporin side chains was investigated.
- A simple and sensitive method was developed for the electrochemical detection of cefalexin by DPV.
- Successful cefalexin detection from real environmental, biomedical and pharmaceutical samples.
- The anodic oxidation of cephalosporins was successfully adapted for flow injection analyses.

GRAPHICAL ABSTRACT



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ABSTRACT

The electrochemical oxidation of seven cephalosporins (ceftriaxone, cefotaxime, ceftazidime, cefadroxil, cefuroxime, cefaclor, cefalexin) was evaluated at high potential, using a bare boron-doped diamond electrode and the influence on the analytical response of the side chains was investigated. Based on the anodic oxidation of the cephalosporin nucleus, a simple and sensitive method was developed for the electrochemical detection of cefalexin by differential pulse voltammetry. After the optimization of the experimental conditions, a linear correlation was obtained between the peak height and the molar concentration of cefalexin in the range of 0.5 μM–700 μM, with a limit of detection of 34.74 ng mL^{-1}. The anodic peak for cefalexin was evaluated in the presence of other cephalosporin molecules and of other common interferents. The developed method was applied to detection of cefalexin from real environmental, biomedical and pharmaceutical samples, with good results. The electrochemical oxidation of cephalosporins was successfully adapted for flow injection analyses, with sensitive and reproducible successive analyses of cefalexin, in different concentrations. The flow analyses allowed also the determination of the total amount of cephalosporins found in the sample.

1. Introduction

Antibacterial resistance is one of the most concerning health issues nowadays and represents a considerable medical challenge for the clinicians [1]. Antibiotics are extensively used in humans and animals, for prophylactic and treatment purposes, and in

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agriculture, to promote crops growth. Unfortunately, the overuse of this therapeutic class leads to environmental contamination, which together with antibiotics from the food chain assures a constant, uncontrolled exposure to antibiotics increasing the risk of allergies and resistance to broad-spectrum antibacterial drugs, with significant impact on economy and health. Therefore, World Health Organization (WHO) elaborated a surveillance campaign aimed to evaluate the current status of the antibiotic resistance and it has been proven that cephalosporins, fluoroquinolones, carbapenems and penicillins are the most common drugs that have developed bacterial resistance so far [2]. Because of this concerning situation there is a tremendous need for new, rapid detection methods capable to detect selectively low concentrations of antibiotics from different matrices.

Cephalosporins (Fig. 1) are β-lactam antibiotics used to treat Gram-positive and Gram-negative bacterial diseases [3]. They are usually prescribed as an alternative to penicillins in case of allergic reactions or resistance. Their mechanism of action is common with the other β–lactams, they interrupt the biosynthesis of the bacterial cell wall [4]. For this reason, the bacteria present cross-resistance to antibiotics from the same class and a simple method allowing the detection of the total amount of cephalosporins would be a useful tool in the fight against antibiotic resistance. Cefalexin is a first-generation cephalosporin, widely used as therapy for upper respiratory infections, uncomplicated pneumonia or soft-tissue infections produced by *Staphylococcus* sp., *Streptococcus* sp., *Klebsiella, Escherichia coli* or *Proteus mirabilis* [4,5].

Over the past years, the detection of cefalexin has been achieved by many analytical methods, applied on food, pharmaceuticals and biological samples. These techniques present different difficulty, accessibility, cost, limit of detection or analysis time and can be divided into four main groups: microbiological tests, instrumental methods, biosensors and electrochemical techniques [6].

Microbiological tests have been applied for the detection of various antibacterial agents from milk samples using the *Bacillus stearothermophilus* var. *calidolactis* growth inhibition [7–9]. The main disadvantage of the method is the lack of specificity, since it can also be applied for the detection of other antibacterial drugs, such as sulphonamides, tetracyclines, aminoglycosides, macrolides, and quinolones.

Several instrumental methods have been described for the quantitative detection of cefalexin or other cephalosporins including spectrophotometry [10], high performance liquid chromatography (HPLC) with ultraviolet absorption [11–14] or electrochemical detection [15], molecularly imprinted solid phase extraction (MISPE) [16] with mass spectrometry (MS) [17], thin-layer chromatography (TLC) [18], capillary electrophoresis (CE) [19], CE with electrospray ionization and MS (CE-ESI-MS) and liquid chromatography with mass spectrometry (LC-MS) [20]. Unfortunately, all these methods are laborious, time-consuming, require complex analytical equipment, and very qualified staff.

The detection of cefalexin and other cephalosporins was conducted using different biosensors [21], like optical sensors [22], surface plasmon resonance-based biosensors [23] and immunoassays [24,25].

The electrochemical analyses represent a more attractive option since they are simple, reproducible and provide very sensitive and fast analytical responses. Moreover, they do not require expensive equipment and give the possibility of *in situ* and flow analyses. The electrochemical direct or indirect detection of cefalexin has been evaluated, using different electrode materials and different electrochemical techniques [26–29].

The boron-doped diamond electrode (BDDE) has been used for the detection of a plethora of drugs [30–32], presenting high chemical and mechanical stability, wide potential window, resistance to a large variety of electrolytes and low background currents [33,34].

The boron-doped diamond electrode, as a thin-film of diamond

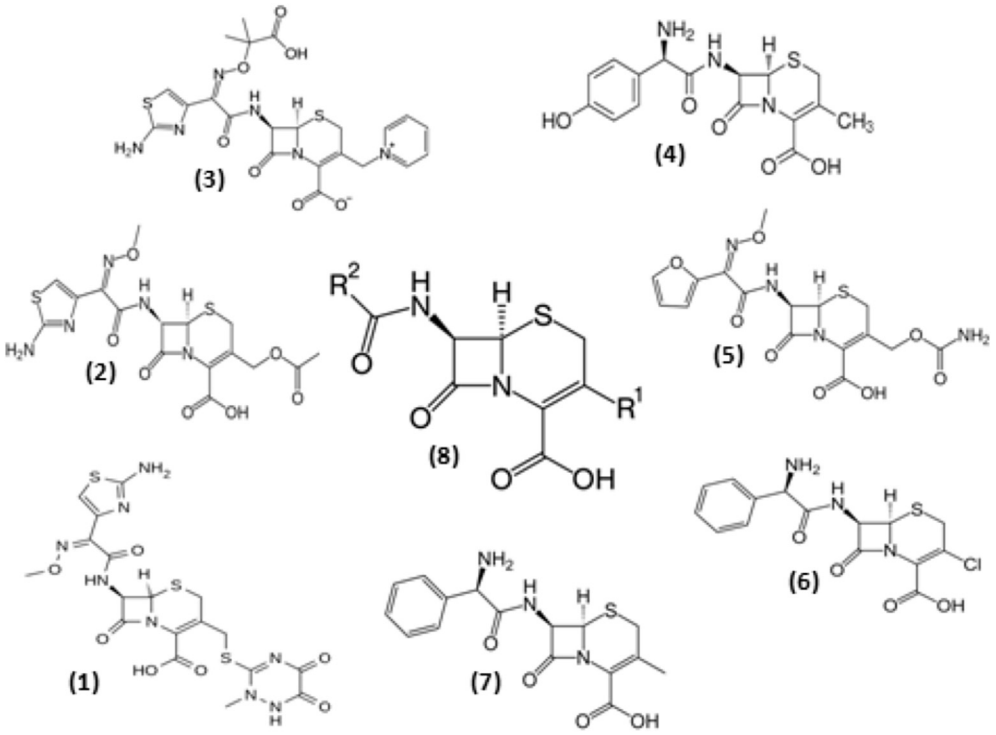

Fig. 1. The chemical structures of (1) ceftriaxone, (2) cefotaxime, (3) ceftazidime, (4) cefadroxil, (5) cefuroxime, (6) cefaclor, (7) cefalexin, and (8) the core structure of cephalosporins.