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The qualitative electrochemical determination of clarithromycin and spectroscopic detection of its structural changes at gold electrode

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Abstract

The aim of the present study was the qualitative determination of the pure clarithromycin using a gold electrode in neutral electrolyte by cyclic linear sweep voltammetry. It was shown that in the range of −1.2 V to 1.0 V vs. SCE in 0.05 M $NaHCO_3$, a gold electrode is successfully employed for the qualitative determination of clarithromycin by detection of the reproductive four anodic and one cathodic peaks. After the potentiostatic measurements at the potential values corresponded to current peaks, the bulk electrolyte was analyzed by FTIR spectroscopy to show the changes in molecular structure of clarithromycin. FTIR analysis of the bulk electrolyte after 4 h of holding the potential at −0.61 V vs. SCE (cathodic peak) showed the apparent changes in clarithromycin molecule structure: in the ester bond of the lactone and in ethers and acetal bonds.

Keywords: Clarithromycin; Qualitative determination; Gold electrode; Cyclic voltammetry; FTIR spectroscopy

1. Introduction

Erythromycin is a natural compound metabolized by a strain of *Streptomyces erythreus.* It has proved invaluable for the treatment of bacterial infections in patients with β-lactam hypersensitivity. From this parent macrolide, several derivatives have been synthesized. If the 6-hydroxy group is methylated, clarithromycin is obtained, which has an improved pharmacokinetic profile compared to the parent molecule. Azithromycin has a methylated nitrogen atom at position number nine on the macrolide lactone ring, and clarithromycin has a methyloxyl substitution at position number six of the macrolide ring (Fig. 1). Azithromycin and clarithromycin present several clinical advantages over erythromycin, including enhanced spectrum activity, higher tissue concentrations, and improved tolerability [1–3]. Clarithromycin is widely used for the eradication of *Helicobacter pylori* that causes gastritis and gastric ulcers [4–7]. Quantitative methods using high performance liquid chromatography (HPLC) procedures for the analysis of azithromycin and clarithromycin have been widely applied [8–11]. Some information on clarithromycin voltammetry (Klaricid® tablets, obtained from Glaxowellcome, S. Korea) was presented in the literature related to electrochemical detection in HPLC procedures [12]. It is reported that amperometric detector with glassy carbon working electrode was used in a condition of hydrodynamic voltammetry after column-switching HPLC preparation of human plasma containing metabolized Klaricid® tablets. The data concerning the only electrochemical identification of not metabolized tablets, their content and its influence on the detection comparing to pure clarithromycin are not provided [12].

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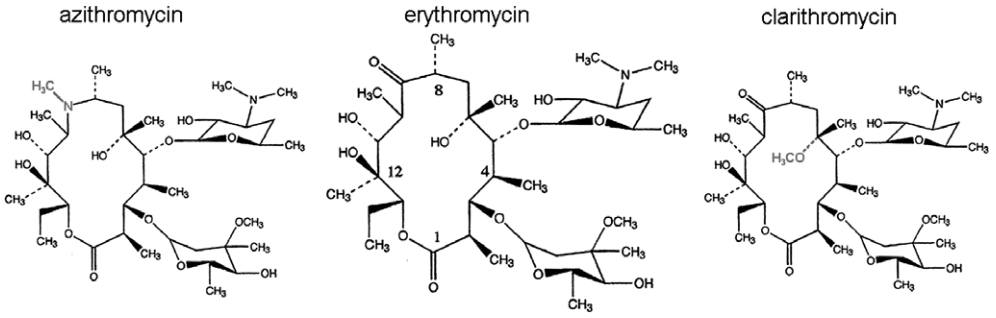

Fig. 1. Chemical structures of azithromycin, erythromycin and clarithromycin.

The electrochemical methods are cheaper and faster. Hitherto, voltammetric determinations of azithromycin [13,14] have been published. We previously reported the oxidative behavior and qualitative and quantitative determination of azithromycin at a gold electrode [15]. As in the case of azithromycin, gold electrode is selected as the best one for the examination of the next member of macrolide antibiotics family [15]. The aim of the present study was the qualitative determination of the pure clarithromycin using its reactivity at a gold electrode in neutral electrolyte by cyclic linear sweep voltammetry. After the potentiostatic measurements, the bulk electrolyte was analyzed by FTIR spectroscopy to detect the changes in the structure of clarithromycin molecule. It was also analyzed by HPLC.

2. Experimental

Clarithromycin, provided by pharmaceutical company, Hemofarm, was used as a pure substance. It was added directly into the electrolyte, which was purged with nitrogen for 20 min before each measurement, in the concentrations in the range of 0.235–0.588 mg cm^{-3}. $NaHCO_3$ used for the supporting electrolyte were of analytical grade (Merck). The solutions were prepared with 18 MΩ water. Standard equipment and a three electrode electrochemical cell were used for the cyclic voltammetry measurements, as previously described in detail [15–19].

Polycrystalline gold (surface area 0.500 cm^2), which served as the working electrode, was prepared by polishing with diamond paste, and cleaning with a mixture of 18 MΩ water and sulfuric acid. Platinum wire was used as the counter electrode and a saturated calomel electrode as the reference electrode. Prior to the control of the electrode surface, which was performed by cyclic voltammetry before each experiment, the electrolyte was purged with nitrogen. All the experiments were performed at temperature of 20 °C, and all the potential values are given vs. saturated calomel electrode.

The pH of the electrolyte before and after addition of clarithromycin was measured using PHM 93 reference pH meter, Radiometer Copenhagen. The characteristics of the HPLC instrument are as follows: HPLC Instrument GBC, pump LC 1120, UV VIS detector LC 1205, manual injector RHEODYNE 7725i, column Asahipak ODP-50 (250 × 4 mm), stationary phase L21 (USP-a rigid, spherical styrene–divinyl copolymer, 5 μm), mobile phase 0.002 M diammonium hydrogen phosphate, propanol-2, acetonitrile (pH 9.5, flow rate 1.0 ml/min), wave length 215 nm.

The IR spectra were obtained using a FTIR BOMEM MB 100 Hartmann Braun FTIR spectrometer. The samples were analyzed in the form of KBr pellets after removal of the liquid under high vacuum at low temperature.

3. Results and discussion

A polycrystalline gold electrode was already selected as the optimal working electrode for the examination of different organic molecules including azithromycin [15,18,19]. As in a case of azithromycin, for clarithromycin, our choice was 0.05 M $NaHCO_3$ as the supporting electrolyte [15]. The solubility of clarithromycin in water is very poor, and it is slightly soluble in methanol [20]. The

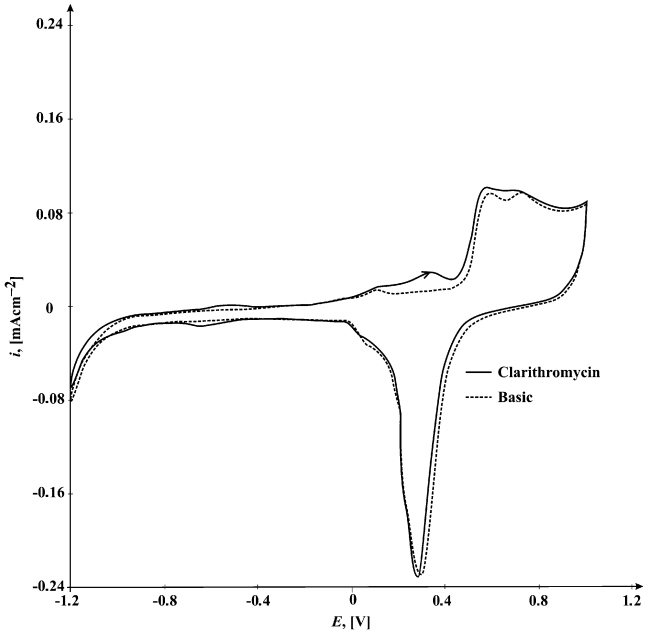

Fig. 2. Cyclic voltammogram of the Au electrode in 0.05 M $NaHCO_3$ (——) and with the addition of 0.4 mg cm^{-3} of pure clarithromycin, third sweep, (full line), sweep rate: 50 mV/s.