

STUDY OF THE ELECTROCHEMICAL OXIDATION OF AZITROMYCIN

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Azithromycin is the first member of a class of macrolide antibiotics called azalides [1]. It is an effective therapeutic agent for oral treatment of sexually transmitted diseases, upper and lower respiratory tract infections, and skin and skin structure infections. Azithromycin (Fig 1) has a methyl-substituted nitrogen at position 9a in the lactone ring to create a fifteen-membered macrolide. This modification produces an enhanced spectrum and potency against bacteria compared with others macrolides [2] and superior stability in an acid environment [3]. Azithromycin also has greater oral bioavailability, longer elimination half-lives and high tissue concentrations.

Due to the electrochemical activity of azithromycin, Electrochemical Detection (ED) has been the preferred method for chromatographic determination of azithromycin in several biological samples [4-5]. The electrochemical response of azithromycin has been attributed to oxidation of both tertiary amino groups, however, the overall oxidation mechanism had not been well studied. In this work, we discuss the electrochemical oxidation of azithromycin using voltammetry and *in situ* FTIR spectroscopy to obtain mechanistic information about the overall process of azithromycin oxidation on platinum in acetonitrile.

Fig 2. shows the voltammetric response for azithromycin oxidation on platinum in acetonitrile at several scan rates; the graph set displays the normalized function current against de scan rate (v), showing the typical behavior of an E.C mechanism. A separate electron controlled potential electrolyzes show that overall electron number transferred for the azithromycin oxidation at 800 mV vs Ag/AgNO₃ was $n=4$. This is consistent with a process involving the simultaneous oxidation of the two tertiary amino groups in which one hydrogen atom from its methyl groups are removed to generate protons; this assumption is confirmed by *in situ* FTIR spectroscopy. Fig. 3 shows the SNIFTIR spectra for 0.05 M azithromycin oxidation at Pt electrode in acetonitrile / 1 M tetrabutylammonium hexafluorophosphate (TBAHFP), the salient features are negative going downward band at 3500 cm⁻¹ attributed to the formation of -OH group due to the hydrolysis of azithromycin, positive going upward band at around 2700 cm⁻¹ due to the loose of -CH₃ vibration and a bipolar band centered at 1700 cm⁻¹ that can be attributed to the displacement of the carbonyl absorption frequency. There are several bands between 1700 and 1000 cm⁻¹ whose nature is discussed. With these results we are able to propose a general mechanism for azithromycin oxidation that include electrochemical step followed by chemical reaction.

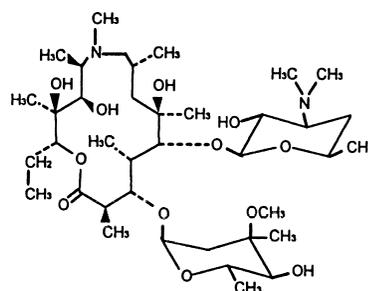


Figure 1.-Structure of Azithromycin

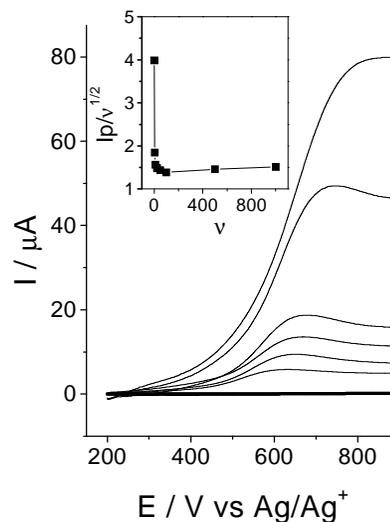


Figure 2.- Cyclic voltammetric response for the azithromycin oxidation at Pt electrode at various scan rates

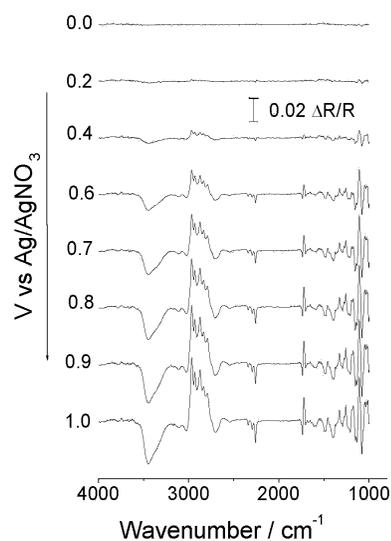


Fig. 3.- In situ FTIR spectra for azithromycin oxidation

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