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Electrochemical sensor for ranitidine determination based on carbon paste electrode modified with oxovanadium (IV) salen complex

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ABSTRACT

The preparation and electrochemical characterization of a carbon paste electrode modified with the *N*,*N*-ethylene-*bis*(salicyllideneiminato)oxovanadium (IV) complex ([VO(salen)]) as well as its application for ranitidine determination are described. The electrochemical behavior of the modified electrode for the electroreduction of ranitidine was investigated using cyclic voltammetry, and analytical curves were obtained for ranitidine using linear sweep voltammetry (LSV) under optimized conditions. The best voltammetric response was obtained for an electrode composition of 20% (m/m) [VO(salen)] in the paste, 0.10 mol L^{-1} of KCl solution (pH 5.5 adjusted with HCl) as supporting electrolyte and scan rate of 25 mV s^{-1}. A sensitive linear voltammetric response for ranitidine was obtained in the concentration range from 9.9×10^{-5} to 1.0×10^{-3} mol L^{-1}, with a detection limit of 6.6×10^{-5} mol L^{-1} using linear sweep voltammetry. These results demonstrated the viability of this modified electrode as a sensor for determination, quality control and routine analysis of ranitidine in pharmaceutical formulations.

1. Introduction

Ranitidine, RNH (Fig. 1), is an H2 receptor antagonist widely used in the treatment of duodenal and gastric ulceration associated with *Helicobacter pylori* infection, gastroesophageal reflux disease, conditions of elevated gastric acidity and the treatment of photogenic gastrointestinal hypersecretory condition such as the Zollinger–Ellison syndrome [1].

Several analytical methods have been reported for ranitidine determination in pharmaceutical and biological fluids, including high-performance liquid chromatography with spectrophotometric [2], fluorimetric [3] or electrochemical [4] detection as well as other methodologies such as capillary electrophoresis [5], mass spectrometry [6], spectrofluorimetry [7], near infrared reflectance spectroscopy [8] and indirect UV-Vis spectrophotometry [9]. However, most of these techniques are time consuming, involve the use of large volumes of organic solvents and specific reagents or require expensive and sophisticated instruments. In addition, some of these methods involve several manipulation steps before the final result of the analysis.

In recent years, the development of electrochemical sensors has attracted tremendous research interest [10–15]. Its main attraction is the low cost of instrumentation and the possibility of construction of electrochemical sensors from various types of material [16–18]. Furthermore, the ability to add different chemical species to the electrode surface in order to change the physico-chemical nature of the electrode–solution interface has helped to improve the selectivity and sensitivity of these devices.

The operation mechanism of such chemically modified carbon paste electrodes depends on the properties of the modifier materials used to promote selectivity and sensitivity towards the target species [19,20]. In this way, the use of vanadium complex has also been recently intensified, mainly due to its participation in many biochemical processes in human body. Transition metal–salen complexes (salen = *N*,*N*-ethylene-*bis*(salicyllideneiminato)) are functional mimics of metalloproteins in dioxygen binding and oxidation of olefins and aromatic compounds [21,22]. The salen complexes are conformationally flexible and adopt a variety of geometries to generate several active site environments allowing different oxidation reactions [23,24].

Electrochemical methods have been also applied for ranitidine determination including voltammetry [25], potentiometry [26] and polarography [27], but there are few reports about the use of chemically modified electrodes for its determination.

In our research group, we have been developed carbon paste electrodes modified with vanadyl complexes with Schiff bases as well as other compounds as modifier for determination of pharmaceuticals with satisfactory results [28–32]. The major advantage of these

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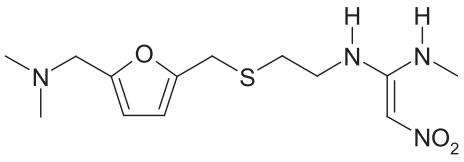

Fig. 1. Structure of ranitidine.

electrodes is the decrease in the over-potential and/or increase in the sensibility for the oxidation of these analytes.

In the present work, the preparation, properties and application of a carbon paste electrode modified with the *N,N*-ethylene-*bis* (salicyllideneiminato)oxovanadium (IV) complex ([VO(salen)]) were proposed for voltammetric determination of ranitidine in pharmaceutical samples. The influence of several parameters such as pH, potential scan rate and several concomitants as potential interferents on the electrode voltammetric profile is also presented.

2. Experimental

2.1. Apparatus

All voltammetric measurements were carried out in a 20-mL thermostated glass cell at 25 °C, with a three-electrode configuration: a modified carbon paste electrode as the working electrode, an Ag/AgCl (3 mol L^{-1} KCl) as reference and a platinum auxiliary electrode. During the measurements, the solution in the cell was neither stirred nor deaerated. Cyclic voltammetric and linear sweep voltammetry (LSV) measurements were performed with an Autolab/PGSTAT-30 (Eco Chemie) potentiostat/galvanostat connected to a microcomputer that was controlled by the software GPES2 version 4.9.

2.2. Reagents and solutions

All solutions were prepared using water purified with a Millipore Milli-Q system (Bedford, MA, USA) model UV plus ultra-low organics water. All chemicals were purchased from Sigma and Merck, with analytical grade and used without further purification. The supporting electrolyte used for all experiments was a 0.10-mol L^{-1} KCl solution at pH 5.5 adjusted with hydrochloridric acid. A 0.010-mol L^{-1} ranitidine stock solution was freshly prepared by dissolution of an appropriate amount of this reagent in 50 mL of above supporting electrolyte solution. Graphite powder (1–2 μm particle size, Aldrich) and mineral oil (Aldrich) of high purity were used in the preparation of the carbon paste.

2.3. Synthesis of *N,N*-ethylene-bis(salicyllideneiminato)oxovanadium (IV) complex ([VO(salen)])

The Schiff base (salen) was prepared according to a previously described procedure [29]. The ligand was used without further purification. The *N,N*-ethylene*bis*(salicylideneiminato)oxovanadium (IV) complex ([$VO^{(IV)}$(salen)]; Fig. 2) was prepared from oxovanadium (IV) sulfate and the ligand salen, using the method described by Zamian and Dockal [33]. The complex was purified by Soxhlet extraction using MeCN. No precautions were taken to exclude air from the reaction system, since the complex is stable in the air. The purified complex (green crystals) was dried under vacuum at room temperature for 72 h.

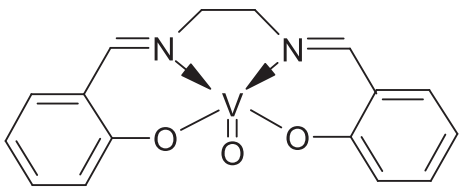

Fig. 2. Molecular structure of the *N,N*-ethylene*bis*(salicylideneiminato)oxovanadium (IV).

2.4. Carbon paste electrode construction

The modified carbon paste electrode was prepared by mixing 0.100 g of *N,N*-ethylene*bis*(salicylideneiminato)oxovanadium (IV) complex ([$VO^{(IV)}$(salen)]) with 0.300 g of graphite powder and subsequently adding 0.100 g of mineral oil. This mixture was homogenized by magnetic stirring in a 50-mL beacker containing 20 mL of hexane. The final paste was obtained after the solvent evaporation. The modified carbon paste was packed into an electrode body, consisting of a plastic cylindrical tube (o.d. 8 mm, i.d. 6 mm) equipped with a stainless steel rod serving as an external electric contact. Appropriate packing was achieved by pressing the electrode surface against a glass plate.

2.5. Preparation and analysis of pharmaceutical samples

Solid samples of pharmaceutical formulations (Ranitidina (Hexal), Ulcerit® (Hexal) and Label® (Aché) containing ranitidine were ground in an agate mortar and a known amount of powder was dissolved in appropriate volume of supporting electrolyte solution (pH 5.5) by sonication during 20 min. Insoluble excipients were filtered off with a filter paper. The filtrate was transferred to a 10.0-mL volumetric flask, and this volume completed with the same solution. For liquid formulations of ranitidine, an aliquot of 500 μL was diluted to 50.0 mL with supporting electrolyte solution. No other treatment of the sample was required. The content of ranitidine in these samples was determined by the standard addition method and compared with a Brazilian Pharmacopoeia method (spectrophotometric method) [34].

3. Results and discussion

3.1. Electrochemical behavior of the MCPE

The voltammetric behavior of the modified electrode was investigated in three different supporting electrolytes (phosphate buffer, KNO_3 and KCl). In phosphate buffer, the voltammetric response was unstable, and no redox peaks were observed with respect to the couple [VO^{II}(salen)]/[VO^{III}(salen)]. That behavior is a well-known inhibition effect observed for many phosphate-metabolizing enzymes [35,36] and can be explained by the vanadyl(IV) cation interaction with phosphate ions at the electrode surface since its pK_{sp} is 25.1 [37]. For voltammetric measurements using KNO_3 and KCl solutions, the voltammetric profiles show up very similar and stable analytical response.

Fig. 3 presents a typical cyclic voltammogram with two peaks at 0.84 V (anodic) and 0.38 V (cathodic) vs. Ag/AgCl at potential scan

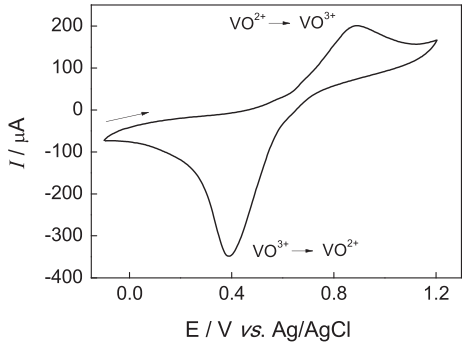

Fig. 3. Cyclic voltammograms obtained for the MCPE with 20% (m/m) of the [VO(salen)] complex in 0.1 mol L^{-1} KCl solution (pH 5.5).