An electrochemical sensor for dipyrone determination based on nickel-salen film modified electrode

Marcos F. S. Teixeira*, Tony R. L. Dadamos

Department of Physics, Chemistry and Biology, Faculty of Sciences and Technology, University of State of Sao Paulo (UNESP) Presidente Prudente – SP – Brazil.

Abstract

An amperometric dipyrone sensor based on a polymeric nickel-salen (salen = N,N’-ethylenebis(salicylideneiminato)) film coated platinum electrode was developed. The sensor was constructed by electropolymerization of nickel-salen complex at a platinum electrode in acetonitrile/tetrabuthylammonium perchlorate by cyclic voltammetry. After cycling the modified electrode in a 0.50 mol L\(^{-1}\) KCl solution, the estimated surface concentration was found to be equal to 1.29 x 10\(^{-9}\) mol cm\(^{-2}\). This is a typical behavior of an electrode surface immobilized with a redox couple that can usually be considered as a reversible single-electron reduction/oxidation of the nickel(II)/nickel(III) couple. A plot of the anodic current versus the dipyrone concentration for chronoamperometry (potential fixed = +0.50 V) at the sensor was linear in the 4.7 x 10\(^{-6}\) to 1.1 x 10\(^{-4}\) mol L\(^{-1}\) concentration range and the concentration limit was 1.2 x 10\(^{-6}\) mol L\(^{-1}\). The proposed electrode is useful for the quality control and routine analysis of dipyrone in pharmaceutical formulations.

Keywords: modified electrode, nickel-salen polymer, amperometric detection, dipyrone analysis

1. Introduction

Dipyrone (analgin, metamizol) is a pyrazolone derivative with a strong analgesic, antipyretic and spasmylytic activity. The biotransformation of the dipyrone takes place at the hepatic level, and the duration of its effect is approximately 4-6 h, and its elimination is at renal level [1]. The drug can cause occasional or rare reactions as transitory disturbances and inflammation of the renal tissue, mainly in patients with renal disease history or in cases of overdose. Dipyrone form the main active constituent of several pharmaceutical preparations and determination in this formulation is therefore very important.

The application of chemically modified electrodes as sensors has received considerable attention. Recent years, the increased use of sensors based on metallic complexes for electroanalytical measurements of a variety of organic species of biological and pharmaceutical importance has been reported [2]. Transition metal–salen complexes (salen = N,N-ethylenebis(salicylideneiminato)) are functional mimics of metalloproteins in dioxygen binding and oxidation of olefins and aromatic compounds. Characterization of metal salen-based electroactive polymers is an active field.

* Corresponding author. Tel.: +55-18-3229-5355; fax: +55-18-3221-5682.
E-mail address: funcao@fct.unesp.br.

1876-6196/09 © 2009 Published by Elsevier B.V. Open access under CC BY-NC-ND license. doi:10.1016/j.proche.2009.07.074
of research due to their potential application as electrocatalysts and chemical sensors. The preparation of metal-salen based modified electrodes is obtained via oxidative electropolymerization of the monomers (salen) on bare electrodes using cyclic voltammetry or constant-potential electrolysis in weak donor organic solvents deoxygenated [3]. The incorporation of metal salen complexes into a polymeric system offered some advantages in certain applications such as: the possibility of thickness control; good membrane-forming properties; the film should permit amperometric measurements to be carried out in aqueous media and easy preparation of the modified electrodes. In the present work, the preparation, properties and application of an amperometric sensor based on a polymeric nickel-salen film coated platinum electrode for amperometric determination of dipyrone in pharmaceutical formulations is reported.

2. Experimental

The sensor was constructed by electropolymerization of nickel-salen complex at a platinum electrode (surface = 0.071 cm²) in acetonitrile/ 0.1 mol L⁻¹ tetrabuthylamonium perchlorate by cyclic voltammetry between 0 to 1.4 V vs. SCE. The resulting polymer exhibited stable and reversible redox process when submitted to voltammetry repeated scans, whatevever the nature of the metal or the structure of the ligand. Amperometric measurements were performed using this sensor, a saturated calomel reference electrode (SCE) and a Pt auxiliary electrode. All measurements were made in a deaerated 0.5 mol L⁻¹ KCl solution. Pharmaceutical formulations containing dipyrone were obtained from local drugstores.

3. Results and discussion

3.1. Electrochemical studies of the nickel-salen thin film electrode

The voltammetric behavior of the modified electrode was investigated in a 0.5 mol L⁻¹ KCl solution (pH = 6). The typical cyclic voltammogram of the sensor shows two peaks at +0.48 V (anodic) and +0.46 V (cathodic) vs. SCE at a potential scan rate of 25 mV s⁻¹, and that remained stable after the third cycle. These processes are usually assumed to be reversible single-electron reduction/oxidation of the Ni²⁺(salen)/Ni³⁺(salen) couple on the electrode surface. During successive cycles (50 cycles) in supporting electrolyte, the peak currents decreased by less 2%. The ratio of cathodic to anodic peak currents at various scan rates was almost unity. The reduction and oxidation peak currents for entrapped Ni²⁺/Ni³⁺ were found to linearly increase with potential scan rates between 5 and 70 mV s⁻¹. The linear correlation of the peak current with the scan rate shows that the system is similar to a surface-controlled process. These results suggest that all the electroactive Ni(II) in the film has been converted in Ni(III) during the reverse scan. Additionally, the difference in potential between the anodic peak and the cathodic peak (ΔE_p = 20 mV) was practically constant over the range of studied scan rates. Such behavior may be due to a good interaction between the electrode and the site of activation of the polymer (metallic cation).

The method by Sharp et al. was used to roughly estimate the surface coverage of the electrode by background-corrected electric charge (Q) [4]. The average surface coverage was found to be 1.29 x 10⁻⁹ mol cm⁻². To obtain an ultrathin membrane bound to the electrode surface, four cycles of potential scans were performed during the electropolymerization. Assuming that the film density (ρ) of the nickel-salen polymer is equal to 1 g cm⁻³ [3], the film thickness (h) can be estimated by:

$$ h = \frac{WQ}{nFA\rho} \quad (1) $$

where W (324.04 g mol⁻¹) is the molecular weight of the Ni-salen polymer fragment, Q (C) is calculated by integrating relevant waves of voltammograms, n represents number of electrons transferred (assume =1), F (96485.3 C mol⁻¹) is the Faraday constant, and A is the surface area of the electrode. The background-corrected electric charge (Q) was calculated by integrating the anodic peak of the cyclic voltammogram (ν = 25 mV s⁻¹) in solution aqueous of KCl. Under the electropolymerization conditions described above, Q is about 8.84 x 10⁻⁶ C, and the thickness of the resulted membrane is about 4.18 nm.
3.2. Voltammetric determination of dipyrone

At the unmodified electrode the electrochemical oxidation of dipyrone is represented by irreversible peaks at 0.54 V (peak 1), 0.68 V (peak 2) and 0.9 V (peak 3) vs. SCE in KCl solution 0.5 mol L\(^{-1}\) (pH = 6) as shown in Fig. 1A. The magnitude of peak currents decreased with increasing of the number of cycles.

In Figure 1B shows the obtained cyclic voltammograms for the sensor based on the nickel-salen film in a 0.5 mol L\(^{-1}\) KCl solution (pH = 6.0) in the absence (curve 1) and in the presence (curve 2) of dipyrone. With the addition of dipyrone to the solution, the anodic peak current (at 0.48 vs. SCE) of the modified electrode increased significantly. This result shows that the nickel-salen film on the surface of the electrode promotes the oxidation of dipyrone. The observed increase can be explained by the fact that dipyrone diffuses up to the electrode surface and reduces the Ni(III) electrochemically produced. The overall reaction scheme can be represented by an initial electrochemical step (Eq. 2) followed by a chemical step (Eq. 3):

\[
\text{Ni(II)-salen}_{(\text{electrode})} \rightarrow \text{Ni(III)-salen}_{(\text{electrode})} + e^- \quad (2)
\]

\[
2\text{Ni(III)-salen}_{(\text{electrode})} + \text{Dipyrone}_{(\text{red})} \rightarrow 2\text{Ni(II)-salen}_{(\text{electrode})} + \text{Dipyrone}_{(\text{ox})} \quad (3)
\]

The reaction can be brought about electrochemically wherein the nickel(II) complex is first oxidized to a nickel(III) complex at the electrode surface. The nickel(III) complex then undergoes a catalytic reduction by the dipyrone in solution back to the nickel(II) complex, which can then be electrochemically reoxidized to produce an enhancement of the oxidation current.

3.3. Amperometric measurement of dipyrone

In order to evaluate the performance of the sensor as an amperometric sensor for dipyrone in a KCl medium, experiments involving chronoamperometry at different applied potentials (0.2 – 0.8 V versus SCE) with modified electrodes were performed to determine the best potential for the amperometric determination of dipyrone. The highest amperometric response for dipyrone was obtained at 0.50 V (versus SCE) with modified electrodes. A typical hydrodynamic chronoamperometric response (Fig. 2) was obtained by the progressive addition of dipyrone to 25 mL of a 0.5 mol L\(^{-1}\) KCl solution under continuous stirring at 300 rpm. The electrode response time was fast for the different dipyrone concentrations, presenting stable currents in a few seconds (± 20 seconds). The anodic currents for the different concentrations of dipyrone were recorded in order to obtain the typical analytical curve. In this curve (illustrated in Fig. 2) the anodic current at the sensor ranged from \(4.7 \times 10^{-6}\) to \(1.1 \times 10^{-4}\) mol L\(^{-1}\) with a detection limit of \(1.2 \times 10^{-6}\) mol L\(^{-1}\).
Fig. 2. Chronomperometric response of the sensor in KCl 0.1 mol L⁻¹ solution for successive additions of dipyrone. (1) 0; (2) 1.2 x 10⁻⁶; (3) 4.7 x 10⁻⁶; (4) 3.1 x 10⁻⁵; (5) 6.0 x 10⁻⁵; (6) 8.3 x 10⁻⁵ and (7) 1.1 x 10⁻⁴ mol L⁻¹. Applied working potential = 0.50 V vs. SCE. Stirring rate = 300 rpm. The inset is the relationship of the current response of the sensor with the dipyrone concentration.

The results obtained for the determination of dipyrone in pharmaceutical formulations are in good agreement with those obtained by pharmacopoeia method (r=0.9995). The proposed amperometric procedure was applied for the determination of dipyrone in pharmaceutical formulations (see Table 1). The dipyrone content was determined by the standard addition method and compared with that obtained by official method (iodimetric titration) [5]. The results obtained, confirming that there are no significant differences between the results obtained by both procedures confirming the importance of the proposed amperometric determination presented in this work.

Table 1. Mean results obtained for the determination of dipyrone in pharmaceutical formulations by amperometric procedure (n=3) in comparison with the iodometric method (n=3) [5].

<table>
<thead>
<tr>
<th>Samples</th>
<th>sensor (mg)</th>
<th>iodometric (mg)</th>
<th>Relative error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>460</td>
<td>491</td>
<td>-6.3</td>
</tr>
<tr>
<td>2</td>
<td>472</td>
<td>500</td>
<td>-5.6</td>
</tr>
<tr>
<td>3</td>
<td>944</td>
<td>960</td>
<td>-1.7</td>
</tr>
<tr>
<td>4</td>
<td>250</td>
<td>253</td>
<td>-1.2</td>
</tr>
<tr>
<td>5</td>
<td>298</td>
<td>295</td>
<td>+1.0</td>
</tr>
</tbody>
</table>

Acknowledgements

The scholarship granted by FAPESP (08/00910-9) to T.R.L.D. and research support (05/01296-4) is gratefully acknowledged. The authors thank SJT.

References