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Potentiometric determination of pantoprazole using an ion-selective sensor based on polypyrrole doped films

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ABSTRACT

The present work reports for the first time the use of polypyrrole (PPy) doped film for development of a potentiometric disposable sensor for determination of pantoprazole (PTZ), a drug used for ulcer treatment. Selective potentiometric response has been found by using a membrane of PPy doped with PTZ anions prepared under galvanostatic conditions at graphite pencil electrode (GPEM/PPy-PTZ) surface. Potentiometric response has been influenced for conditions adopted in polymerization and measurement step. After optimization of experimental (e.g. pH and time of conditioning) and instrumental parameters (e.g. current density and electrical charge) a linear analytical curve from 1.0×10^{-5} to 1.1×10^{-2} mol L^{-1} with a slope of calibration of the 57.6 mV dec^{-1} and limit of detection (LOD) of 6.9×10^{-6} mol L^{-1} was obtained. The determination of the PTZ content in pharmaceutical samples using the proposed methodology and official method recommended by Brazilian Pharmacopeia are in agreement at the 95% confidence level and within an acceptable range of error.

1. Introduction

Several aspects related to contemporary lifestyle like stress or prolonged use of medications such as non-steroidal anti-inflammatory [1] could promote development of lesions in the gastric mucous membranes or in the duodenum. These lesions are called ulcers and the principal form to combat it is the administration of proton pump inhibitor drugs, among which are the highlighted ones omeprazole [2], rabeprazole [3] and pantoprazole (PTZ) [4]. PTZ (sodium of 5-(difluoromethoxy)-2-{[(3,4-dimethoxy-2-pyridyl)methyl]sulfinyl}-1H-benzimidazole hydrate (2:2:3)) was introduced as an alternative to the use of anti-histamines, since these have more side effects when administered for the treatment of gastrointestinal ulcers [5].

In order to have a quantification of PTZ some methods were developed including mainly separation techniques as the high performance liquid chromatographic (HPLC) methods [6]. Spectrophotometric approaches [7] and titration procedures [8] have also been reported. The official methods for PTZ determination recommended by the Brazilian Pharmacopeia [8] are potentiometric titration and HPLC. The potentiometric method consists in titration in ethanol medium using hydrochloric acid as the titrant. This method requires testing in the absence and presence of the analyte in order to make necessary corrections. Chromatographic method has high sensitivity, selectivity and precision, however, it requires pre-treatment of the sample, time-consuming extraction steps in testing commercial samples, and it is a technique that requires high investment in equipment.

Electroanalytical methods described in the literature for PTZ determination have demonstrated success in exploring mostly voltammetric techniques [9–12]. Radi [9] reported a procedure based on adsorptive stripping by differential pulse voltammetry using a carbon paste electrode. A linear dependence between current peak and concentration in the range from 1.0×10^{-7} to 1.0×10^{-5} mol L^{-1} was found and a detection limit of 2.0×10^{-8} mol L^{-1} was calculated. The method was applied for PTZ determination in pharmaceutical formulations and human blood plasma. A similar procedure was proposed by the same author [10] based on previous adsorption of PTZ at a hanging mercury electrode followed by its electrochemical reduction under square-wave voltammetry conditions. A detection limit of 5.0×10^{-10} mol L^{-1} was reported. Recently, the determination of PTZ using an antimony film electrode (SbFE) under square-wave voltammetric (SWV) conditions was described by Nigovic and Hocevar [11]. After optimization of experimental parameters the voltammetric signal was linear for concentration range of 9.0×10^{-6} and 2.0×10^{-4} mol L^{-1}.Although cited works have demonstrated good performance for voltammetric PTZ determination, the use of ion-selective electrodes (ISE) for PTZ determination is still poorly explored. This approach allows the development of devices that could be commercially available with high sensitive and selective and low cost in comparison with other instrumental methods. In addition, they could be used as detectors in systems such as liquid chromatography (HPLC) and/or flow injection analysis (FIA) [13].

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In the recent years there is a growing demand for potentiometric sensors with rapid response, reliable and inexpensive. In this way, the use of polypyrrole (conductive polymer) has attracted attention due its similar characteristic to a model for molecular imprinted polymer (MIP) [14,15]. During electrochemical preparation of polypyrrole films thereoccurs a phenomenon of intercalation of anions to keep the electroneutrality of the polymeric structure. When a specific anion is present in the solution, it could be trapped into the polymer chain and confers a selective potentiometric response to the electrode. The incorporation of anions in the polypyrrole films allowed the development of ISE for several inorganic species such as nitrate, chlorite, and iodide ions among others [16–19]. Nowadays, research has been focused on the development of sensors for organic species. Bindewald et al. [14] prepared a graphite electrode modified by PPy doped with dipyrone for its determination in pharmaceutical formulations and synthetic urine. A linear dynamic range was verified for concentration from 1.0×10^{-4} to 1.0×10^{-2} mol L^{-1}, detection limit of 7.2×10^{-5} mol L^{-1} and a sensitivity of 27.6 mV dec^{-1}. Alvarez-Romero et al. [15] have developed a saccharin ion selective electrode using a film of polypyrrole doped with saccharinate anion on a substrate of stainless steel. The sensor that was applied in the determination of saccharin in diet products obtained agood concordance compared to a chromatographic method witha detection limit of 3.6×10^{-4} mol L^{-1}.

Thus, the present study is aimed at the construction and evaluation of a disposable potentiometric sensor for PTZ determination based on polypyrrole doped films. The proposed ISE presented low cost, practice response and a reliable strategy to determining the analyte in commercial pharmaceutical samples.

2. Experimental

2.1. Apparatus

Galvanostatic procedures for polymerization and potentiometric measurements for the evaluation of electrode response were carried out using a microAutolab Type III (Eco Chemie) under computer control managed by GPES 4.9 software. The potentiometric measurements were performed in a two-electrode cell using a graphite pencil electrode modified (GPEM) with pantoprazole-doped polypyrrole film (PPy-PTZ) as an indicator electrode and Ag/AgCl (KCl 3.0 mol L^{-1}) as reference electrode. The measurements of the potential differences between the indicator (GPEM) and reference electrodes were performed using chronopotentiometry (zero current), and were recorded 1 min after pantoprazole addition.

2.2. Reagents and solutions

All solutions were prepared using ultrapurified water obtained from Millipore (Milli-Q) system employing analytical reagent grade. Pyrrole was distilled to insure better reproducibility in formation of polypyrrole film. All others chemicals were used without previous purification. Pantoprazole solutions were prepared daily by dissolving of adequate amount of solid standard (Merck) in ammonium sulfate solution. Potentiometric measurements were performed in solution with strength ionic adjusted using 1.0×10^{-2} mol L^{-1} solution of ammonium sulfate.

2.3. Electrochemical procedures

Electrodes were prepared using commercial graphite pencil (soft lead (HB) with 2.0 mm diameter).Graphite rods were used after polishing with an abrasive sheet P200 and directly connected to the potentiostat by cable, no additional pretreatment was required. Polymerization step was conducted using a delimited area of 0.659 cm^2 with parafilm® tape and the electrode was immersed in the polymerization solution containing 1.0 mol L^{-1} of pyrrole and 1.0×10^{-1} mol L^{-1} of pantoprazole. The preparation of polypyrrole film was realized using a galvanostatic procedure based on controlled current (anodic) in solution above cited. PPy doped preparation was carried out in a 10 mL cell, with a three-electrode conventional system; a graphite pencil electrode was used as the working electrode, a Ag/AgCl (KCl 3.0 mol L^{-1}) electrode was used as the reference electrode, and a platinum plate electrode was used as the auxiliary electrode. Electrochemical parameters were used running electric current densities varying from 0.2 to 2.0 mA cm^{-2} and electrical charge from 50 to 1000 mC. After the polymerization, the GPME was submitted in the conditioning time in a solution containing 1.0×10^{-2} mol L^{-1} of PTZ.

2.4. Sample preparation

The test solutions were obtained directly by dissolving of sample commercials in an ammonium sulfate 1.0×10^{-2} mol L^{-1} solution at pH 5.0 after pulverization using mortar and pistil. No additional pretreatment of the samples was required. The content of pantoprazole in these samples was determined by the standard addition method and the values found were compared those obtained using Brazilian Pharmacopeia's official method [8].

3. Results and discussion

3.1. Electropolymerization of polypyrrole films and potentiometric behavior of the sensor

Galvanostatic procedure was adopted in this work based on good results for film preparation using this methodology previously [14,20]. These results might be attributed to a constant rate of conversion at the electrode surface promoting stable films. Polypyrrole films (PPy) can be obtained through several methods, one feature is that of electrochemical methods that allow deposition over different surfaces and simultaneous oxidation, making this polymer film with cationic charge. The advantage of producing PPy in oxidized form is the incorporation of anions for reaching electroneutrality of films, thus they can be applied as membrane selective to anion dopant. A mechanism of electropolymerization of pyrrole proposed for the preparation of graphite pencil electrode modified with polypyrrole doped films (GPEM/PPy-PTZ) is showed in Scheme 1.

After the selective polymeric membrane is prepared its potentiometric response was characterized in order to evaluate the effective incorporation of PTZ into the polypyrrole film. A GPME was prepared using chloride ions in polymerization step; this strategy is similarlyadopted for not imprinted polymer (NIP), and a PPy membrane not doped with PTZ. The GPME/PPy-PTZ has shown a slope of 15 mV dec^{-1} for PTZ concentration while no significant response was observed for GPME prepared in the absence of PTZ. From this result it is possible to suggest a mechanism of response based on ion transport inside the polymer film. When the doped PPY film is exposed to a PTZ solution, the PTZ anion is moved from high concentration sites to a region of low concentration (or vice-versa) and it will promote the appearing of potential difference across the interface membrane/solution which may be explained using an equation $E = constant - \beta * (59.16\ mV) \log C^{PTZ}{}_{OUT}$[21], where β is the electromotive efficiency and $C^{PTZ}{}_{OUT}$is the PTZ concentration in solution (out of PPY doped membrane). These results suggest not only the incorporation of PTZ into the PPy film but also the conferring of a selective potentiometric response for the sensor.

3.2. Sensor optimization: effect of experimental parameters

In order to optimize the potentiometric response of the proposed electrode the influence of experimental and instrumental parameters related to polymerization (different times (electric charge) and electric current) and measurement steps (electrolyte, conditioning time and pH)was evaluated. At the first time, the electric current density was studied in the range of 0.2 mA cm^{-2} to 2.0 mA cm^{-2}. Using lower