VOLTAMMETRIC STUDY OF PERPHENAZINE

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Abstract

The electrochemical oxidation of perphenazine was studied using a glassy-carbon electrode in different buffer solutions having verified that the peak potential is practically independent of pH. It was shown that using a pH 1.9 buffer solution at which the perphenazine peak is maximal there was no interference from the other active substance, amitriptyline, which is also present in current pharmaceutical preparations available in the Portuguese market. The results obtained for the electrochemical quantification of perphenazine in four pharmaceutical preparations are in good agreement with the results from the reference method (HPLC).

Key words: Perphenazine, amitriptyline, pharmaceutical preparations, voltammetry

Introduction

Since the introduction of phenothiazines and their derivatives as anti-psychotic agents in the late 1950s, several analytical methods have been used for their determination. Official methods are based on non-aqueous titration [1,2] and on high performance liquid chromatography (HPLC) [3]. Among the methods adopted for the determination of phenothiazines are spectrofluorimetry [4], colorimetry [5], gas-liquid chromatography [6] and potentiometry [7].

A phenothiazine derivative currently much used in Portugal owing to its profound cataleptic action is perphenazine and the available pharmaceutical preparations contain another active principle, amitriptyline.

For the estimation of perphenazine methods have already been described based on stripping voltammetry using carbon paste electrodes [8] and glassy-carbon electrodes coated with cellulose acetate [9]. Also described is a flow injection analysis system (FIA), with amperometric detection using a carbon fibre electrode, for the estimation of several phenothiazines in drugs [10].

Nevertheless, none of these works refers the influence of amitriptyline in the determinations. The majority of papers concerning the determination of perphenazine in preparations containing amitriptyline used spectrophotometric detection [11]. The reference method for the estimation of perphenazine in preparations containing amitriptyline use HPLC [3].

This work presents a voltammetric study using a glassy carbon electrode for the evaluation of perphenazine concentration in pharmaceutical preparations in the presence of amitriptyline and attempts to optimize the analytical conditions.

Experimental

Reagents and Solutions

All the reagents used were of pro-analysis (p.a.) quality or similar and were used without further purification. In the preparation of solutions high quality water was used, having a conductivity less than 0.1 µS/cm.

Standard solutions of perphenazine (Sigma) and of amitriptyline (Sigma) were prepared by dissolving weighed quantities of the drugs in ethanol.

The buffer solutions used were in the pH range 1.2-12.8. Quantitative determinations were carried out in a 0.2 M HCl/KCl buffer of pH=1.9.

For chromatographic HPLC comparative method all reagents were of HPLC grade. The separation was carried out at room temperature using as mobile phase a filtered and degassed mixture of water, acetonitrile, methanol and methanesulfonic acid (490:310:200:2).

Samples preparation

The determination of perphenazine was made from commercial tablets available in Portugal. Perphenazine appears in these pharmaceutical preparations in two different dosages, 2 mg/tablet (Mutabon®-M and Mutabon®-D) and 4 mg/tablet (Mutabon®-A and Mutabon®-F). Thus, ten tablets were powdered and a suitable quantity of the sample was accurately weighed and dissolved in ethanol. The solubility was increased by using an ultrasonic bath.

Instrumentation and electrodes

All experiments were performed using a 663 VA Metrohm system containing a glassy carbon working electrode, a glassy carbon rod counter electrode and an AgCl/Ag reference electrode attached to a Autolab PSTAT 10 potentiostat/galvanostat running with model GPES version 3 software (Ecochimie).

The pH measurements were obtained with a pH-meter from Anatron Instruments, model pH 300 with a combined glass electrode.

HPLC experiments for the official method were carried out using a HPLC Sykan system, model A1210, equipped with a 3200 UV wavelenght detector set at 254 nm, and connected with a computing integrator model chromatography data station PRIME version 2.2.6. For chromatographic separation a Nucleosil 100-10 C18 (250×4 mm, 10µm particle size, Macherey-Nagel, Düren, Germany) was employed. The flow rate used was 1 mL per minute.

Results and Discussion

The electrochemical behaviour of perphenazine was studied with a glassy carbon electrode over a wide range of pH values, between 1.2 and 12.8, using differential pulse voltammetry. Plots of Ep vs pH for 1×10^{-4} M solutions of perphenazine show that the peak potential is practically independent of pH. However, the peak current intensity was shown to be highest at pH 1.9. In the same way, the electrochemical behaviour of amitriptyline was investigated and a well-defined oxidation peak was only detected between pH values 7 and 11. It was confirmed that there was no oxidation peak for amitriptyline at pH 1.9 at which the perphenazine oxidation peak was maximal. Therefore, a HCl/KCl pH 1.9 buffer was used for subsequent studies.

A cyclic voltammogram (Fig. 1) was performed on a solution of perphenazine in buffer pH 1.9 and an oxidation peak at a potential of 0.70V vs AgCl/Ag was observed. Also observed was an inverse peak at a potential of 0.63V for scan rates of 100 mV/s.

A plot of I vs $\nu^{1/2}$ is a straight line passing through the origin, indicating that the oxidation is a diffusion-controlled process.

A square wave voltammetry electroanalytical method has been developed for the determination of perphenazine in several pharmaceutical preparations that contains perphenazine and amitriptyline as active principles. The effect on the square wave frequency, f, pulse amplitude,

Es, and ionic strength, I, was assessed aiming the optimization of the experimental conditions. The optimal parameters found were f = 50 Hz, Es = 50 mV and I = 0.2 M.

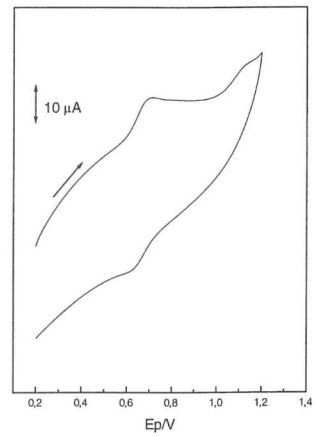

Fig. 1. Cyclic voltammogram of perphenazine, 1.0×10^{-4} M, in 0.2 M HCl/KCl buffer of pH 1.9. Scan rate 100 mVs^{-1}, pulse amplitude 50 mV.

The samples and calibration standards were prepared according to previous description. Calibration curve was constructed using standard solutions of perphenazine in the range $1.0x10^{-5}$ and $5.0x10^{-5}$ M. A linear relationship was obtained with a correlation coefficient of 0.999. Results obtained for the electrochemical quantification of perphenazine in four preparations available in Portugal are presented in Table 1.

Table 1. Results obtained for pharmaceutical preparations containing perphenazine and amitriptyline† by voltammetry and by the reference method (HPLC).

Name	Claimed (mg/tablet)	Voltammetry (mg/tablet)‡	HPLC (mg/tablet) ‡	RD(%)
Mutabon®-M	2	1,9 ± 0,06	1,9 ± 0,08	0
Mutabon®-D	2	2,0 ± 0,12	2,1 ± 0,05	- 4,8
Mutabon®-A	4	3,8 ± 0,06	3,9 ± 0,04	- 2,6
Mutabon®-F	4	4,1 ± 0,15	4,0 ± 0,13	2,5

† *Mutabon®-M* and *–A* have 10 mg/tablet of amitriptyline; *Mutabon®-D* and *–F* have 25 mg/tablet of amitriptyline

‡ Mean and standard deviation for 3 determinations of the same sample

The quality of the results was evaluated by comparing the results obtained by voltammetry (CV) and the reference method (CR) for 4 pharmaceutical preparations; the relative deviation (RD%) was, in general, less than 5%. The relationship between the methods was found to be a straight line with the following equation: $CV = 6.7\times10^{-3} + 0.973CR$. The correlation coefficient (r) was 0.999, which demonstrates excellent agreement between the methods.

Using square wave voltammetry under the experimental conditions described, a detection limit of 3×10^{-7} M estimated according to IUPAC recommendations was found [12].

Final Comments

The electrochemical method is convenient for the study and quantification of perphenazine in pharmaceutical preparations commonly found in Portugal. It was possible to show that the presence of amitriptyline in perphenazine preparations had no effect on the estimation of perphenazine when using a pH 1.9 buffer.

The sample preparation procedure is very simple and accuracy and precision of the results is accomplished.

The results obtained with this technique promise that perphenazine should be able to be determined in samples containing amitriptyline.

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SELF-ASSEMBLED MONOLAYERS OF FERROCENYLTHIOLS ON GOLD. AN ELECTROCHEMICAL AND OPTICAL CHARACTERISATION

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Abstract

Short chain ferrocenyalkylthiols, $(C_5H_5)Fe(C_5H_4)CO(CH_2)_nSH$ (n= 3, 5 and 7), were self-assembled on gold (111). The influence of the chain length and adsorption time on stability, surface coverage and order of the monolayers were assessed electrochemically and by the use of optical ellipsometry. The redox behaviour and structure of the SAMs were strongly dependent on the chain length. Long adsorption times were required to obtain ordered monolayers with high surface coverage. Ellipsometry indicated that the thicknesses of the layers were dependent on the surface concentration of the ferrocene derivatives. The thickness of the monolayer with the longer alkyl chain was estimated to be 2.9 nm with a complex refractive index $\hat{n}$= 1.472-0.076i. Imaging Ellipsometry allowed the visualisation of the lateral thickness distribution of a monolayer deposited on gold.

Keywords: Self-Assembled Monolayers, Au, Ferrocenyalkylthiols, Voltammetry, Ellipsometry.

Introduction

Self-Assembled Monolayers (SAMs) are prepared by the spontaneous adsorption of organic molecules onto a substrate from homogeneous solution. Versatility, ease of preparation, stability and organisation contributed to the great popularity of self-assembly in the last two decades [1].
Alkanethiols used in the formation of SAMs generally contain three important parts [2]: (i) the surface active head group, which binds strongly to the substrate, (ii) the alkyl chain, responsible for the stability and order of the layer due to van der Waals chain interaction, and (iii) functionality. The latter plays a paramount role in controlling the redox behaviour of the monolayer and can be tailor-made to create the desired interfacial microenvironment. Self-assembly of thiol derivatives on gold is believed to occur in two stages [1-3]. Physisorption of the thiol, which after a short time on the surface, forms a strong covalent bond with the substrate via the formation of a thiolate,