INDIRECT POLAROGRAPHIC DETERMINATION OF PROCHLORPERAZINE IN TABLETS USING HYDROGEN PEROXOMONOSULFATE

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Prochlorperazine maleate (PM), a member of the piperazine subclass of phenothiazines, chemically dihydrogen maleate of 2-chloro-10-[3-(4-methyl piperazine-1-yl) propyl] phenothiazine (Fig. 1), is a well-known antipsychotic and antiemetic with a weak sedative activity [1]. It is official in the European Pharmacopoeia (EP) and United States Pharmacopoeia (USP). The USP [2] describes the liquid chromatographic method for the estimation of Prochlorperazine in tablets, while BP [3] and EP [4] describe the potentiometric method for assay.

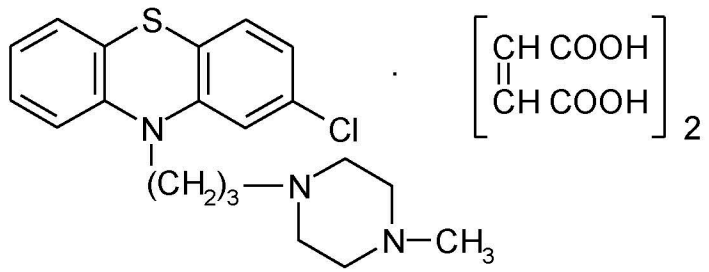

Fig. 1. Chemical structure of Prochlorperazine maleate

Several methods have been published for the determination of Prochlorperazine in bulk or in different pharmaceutical formulations, as well as in biological fluids. These methods include titrimetric, spectrophotometric, kinetic, fluorometric, electrochemical, liquid chromatographic with liquid-liquid or solid-phase extraction and different detector methods. The procedures proposed required intensive isolation and purification steps in the case of the assay of phenothiazines in their pharmaceutical formulations.

Among the methods, the electrochemical ones are very useful for the determination of drugs. A powerful hyphenated technique for the determination of phenothiazines based on peroxoacidic oxidation, and different detection methods of the oxidation products formed have been developed [5]. The oxidation of phenothiazine leads to the formation of the corresponding sulfoxides that can be detected electrochemically. The basic phenothiazine derivatives are converted into polarographic active sulfoxides. This offers possibilities to quantify phenothiazines at very low limits of detection in the nano- and micromolar range using the polarographic detection with a simple, robust, and readily available instrumentation and avoiding laborous derivatization procedures. An electrolytic reduction of phenothiazine sulphoxides is less liable to electrochemical interferences from other ingredients of pharmaceuticals. The methods described offer advantages in their simplicity, rapidity and common access to instrumentation. There are only a few methods based on the electrolytic reduction of S-oxide phenothiazines for their determination. These methods may be recommended as alternatives to the official methods.

The oxidation of PM to its corresponding sulphoxide by means of $KHSO_5$ (in form a potassium triple salt) was used to develop a new method for the polarographic determination of the drug.

The scheme of the oxidation process of prochlorperazine with potassium hydrogen peroxomonosulphate into the corresponding sulfoxide has the form (Fig. 2).

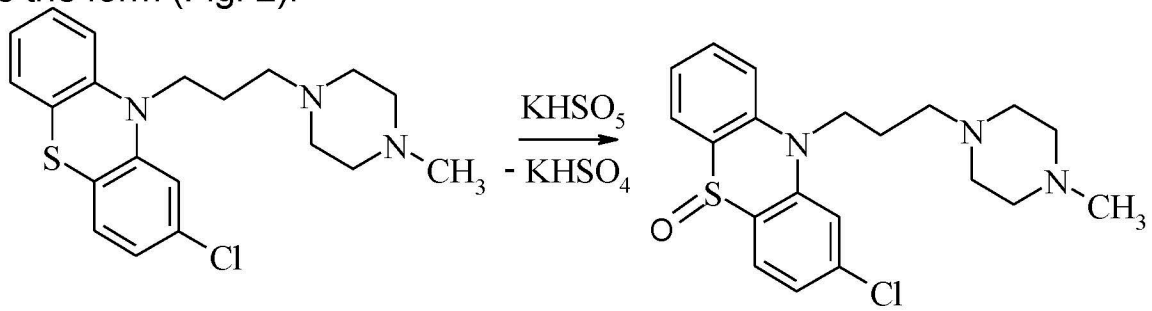

Fig. 2. Scheme of the oxidation reaction of prochlorperazine with potassium hydrogen peroxomonosulphate to S-oxide Prochlorperazine

The subject of the test was Vertinex® tablets. The following API were used: PM; 1 tablet containing 5 mg of PM; Excipients were Lactose monohydrate, Microcrystalline Cellulose, Maize Starch, Croscarmellose sodium, Sodium Lauryl Sulfate, Magnesium Stearate, Colloidal anhydrous Silica. A potassium triple salt containing $KHSO_5$, $KHSO_4$, and K_2SO_4 in the molar ratio of 2:1:1 was used. This product is sold under the trade name Oxone®. Moreover, it is considered as a “green” oxidizing agent since it has no toxic effects.

The aim of this study is to establish the experimental conditions needed to investigate the determination of Proclorperazine in tablets using differential pulse voltammetry (DPV) method was applied for the first time for the determination of studied phenothiazine derivative in the form of the corresponding of sulphoxide.

All the electrochemical experiments were conducted in a three electrode single compartment glass cell. An Ag/AgCl (3.0 mol/L KCl) electrode was used as reference electrode and auxiliary electrode was a Pt electrode. The working electrode was a hanging mercury drop. The polarographic measurements were carried out using Metrohm 797 VA Computrace system (Metrohm AG Ltd., Switzerland).

The calibration graph is linear in the concentration range of 0.05–4.0 μg/ml ($I = (2.65 \pm 0.10) \cdot 10^4 \times C + (3.49 \pm 0.90)$ ($r = 0.999$) (Fig 3). LOQ (10S) is 0.2 μg/ml.

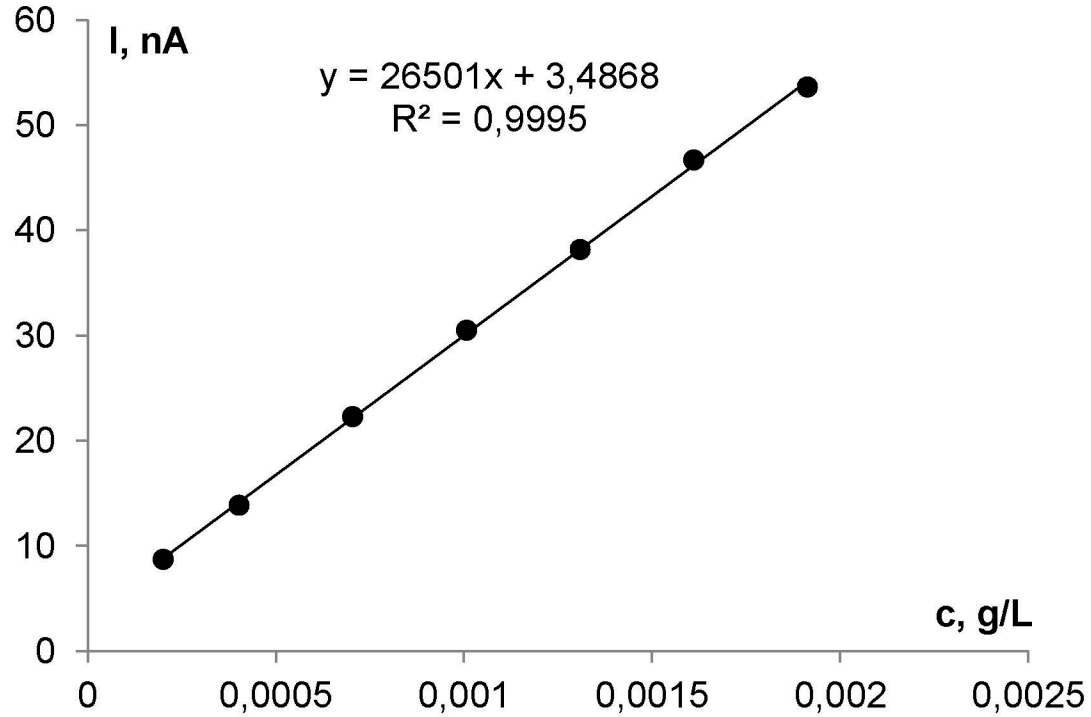

Fig. 3. Dependence of the peak current of electrochemical reduction of the oxidation product of Prochlorperazine on the concentration of Prochlorperazine

The possibility of the quantitative determination of PM in Vertinex® tablets, 5 mg, (manufactured by KUSUM HEALTHCARE PVT LTD. (Alwar (Rajasthan), India) by the polarographic method developed has been shown (RSD <2.1%; $(\overline{X} - \mu)100\%/\mu$ <1.3%) (Tabl.1). (μ - Certificate data).

Tabl. 1. The results of quantitative determination of Prochlorperazine in tablets

Taken for analysis	Found content, mg	Metrological characteristics, p = 0.95
0.3000 g (4.92 mg / tablet ± 5%) powder Vertinex® tablets, 5 mg, (manufactured by KUSUM HEALTHCARE PVT LTD. (Alwar (Rajasthan), India) serial number VE7003 (dilution 200)	5,04 4,84 5,01 4,92 5,05	$\overline{X}$ =4.97 $S_{\bar{x}}$=0.040 $\Delta\bar{x}$=0.112 RSD=1.80% $(\overline{X}-\mu)100\%/\mu$ =+1.1%
0.3000 g (4.92 mg / tablet ± 5%) powder Vertinex® tablets, 5 mg, (manufactured by KUSUM HEALTHCARE PVT LTD. (Alwar (Rajasthan), India) serial number VE7003 (dilution 133)	4,91 5,07 4,85 5,10 5,00	$\overline{X}$ =4.99 $S_{\bar{x}}$=0.106 $\Delta\bar{x}$=0.131 RSD=2.1% $(\overline{X}-\mu)100\%/\mu$ =+1.3%

The results are in good agreement with the findings of the study of PM in Vertinex® tablets in the dose of 5 mg in accordance with the recommendations of the E Ph.

References

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