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Differential-pulse polarographic determination of Metopimazine in tablets through treatment with Oxone

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Introduction. Metopimazine (MPZ) is a phenothiazine dopamine antagonist with an antiemetic action. It is used in the treatment of nausea and vomiting, including that associated with cancer chemotherapy [1]. Chemically it is 1-[3-[2-(methylsulfonyl)-10H-phenothiazin-10-yl]propyl]-4-piperidinecarboxamide [2]. The official method for the assay of MPZ in bulk form is a non-aqueous titration method [3]. No official methods are available for MPZ pharmaceutical formulations. Few methods have been reported for the MPZ determination including: HPTLC [4], TLC [5] and Spectrofluorimetry [6]. MPZ in Vogalene® syrup was assayed using a difference spectrophotometric technique based on measuring the ΔA at 358 nm after the addition of a solution of peroxyacetic acid [7,8]. Finally, only single analytical procedure is available in the literature for analysis of Metopimazine by differential pulse voltammetric method [9]. No attempts have yet been made to determine either metopimazine by any other electrochemical method. An alternative is derivatization polarography, that is, the transformation of a polarographically inactive compound into an active one, which is carried out with the help of chemical reactions [10]. Work from our laboratory revealed the successful application of this approach in the assay of several pharmaceutical compounds [11, 12].

The aim of the study. Explore the opportunity the use of Potassium caroate ($KHSO_5$) in form Oxone to obtain a polarographically active form from MPZ, namely the corresponding MPZ sulfoxide derivative (MPZO) and the development of a simple and sensitive method for its assay by the cathodic voltammetric method.

Materials and methods. Vogalene Lyoc 7.5 mg Metopimazine Oral sugar-free-lyophilizate № B/16 (Teva Sante, France). Composition of lyophilizate for preparation of oral solution: micronized Metopimazine (*active ingredient*) 7.5 mg. *Excipients:* xanthan gum (Rodigel 23), aspartame, sodium docusate, dextran 70, mannitol. We used Oxone® for MPZ oxidation to its S-oxide. The active ingredient of Oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) is $KHSO_5$. The differential-pulse cathodic voltammetric measurement on the hanging mercury drop electrode (HMDE).

The results obtained. The MPZO is formed quickly (300 s) and quantitatively at room temperature by adding $KHSO_5$ solution. Well defined cathodic waves were obtained for MPZO in 0.02 mol L^{-1} HCl using the differential-pulse mode at the HMDE. Factors affecting the peak current were studied and optimized. Calibration curve is linear in the concentration range of 0.4 to 2.7 $\mu g.mL^{-1}$. Using calibration curve a LOQ was estimated to be 0.40 $\mu g \cdot mL^{-1}$. RSD for Vogalene Lyoc tablets, 7,5 mg, was ≤1.63%. The trueness of the measurement method was investigated by comparing the accepted reference value (μ) with the level of the results given by the measurement method : $|(\bar{X}-\mu)100\% / \mu| < t\alpha(0.95, n=7) \times RSD / \sqrt{n}$. The method is simple, sensitive and do not require expensive and relatively toxic solvents.

Conclusions. The use of Caro's acid, for the derivatization has some distinct advantages over peroxy acetic acid which is toxic with bad suffocating odour. In addition, Caro's acid in form Oxone is a more stable oxidizing agent compared with peroxy acetic acid, therefore, the proposed method is more specific, more safe and more simple than other methods.

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