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Flow injection spectrophotometric determination of promazine

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Abstract

A method for the spectrophotometric determination of promazine by flow injection analysis is reported. The procedure is based on the reaction of promazine with molybdophosphoric acid. Concentrations of promazine in the range 1–25 ppm have been determined with a relative standard deviation of 1.8% at 10 ppm ($n=20$). The method was applied to the determination of promazine in injections and compared favourably with an independent reference method based on spectrophotometry.

Keywords: Flow injection analysis; Promazine hydrochloride; Molybdophosphoric acid; UV spectrophotometry; Injections

1. Introduction

Phenothiazine derivatives are used as psychotropic, neuroleptic, local anaesthetic, anti-allergic and, anti-vomiting drugs. They are used in pharmaceutical preparations such as tablets, injections and elixirs. Their wide application in medicine requires methods for determining them in drugs.

Among the methods adopted for the determination of phenothiazines are chromatographic (HPLC, GLC, GLC with MS detection), spectrophotometric, spectrofluorimetric, electrochemical and others [1]. In recent years, flow injection analysis (FIA) has found wide application in various fields of routine analysis, including pharmaceuticals.

The versatility and simplicity of the FIA technique allow it to be adopted at relatively low cost to the different requirements of analytical problems. Flow injection procedures generally involve the use of chemical [2–4] or photochemical [5–7] oxidation of phenothiazines, with photometric and fluorimetric detection of their oxidized forms. Other procedures with amperometric [8,9] and voltammetric [10,11] detection have also been used. Some flow injection methods have been reported for the determination of promazine hydrochloride [12,13], involving the use of manganese dioxide in an oxidative column and hexacyanoferrate(III), which was immobilized on an anion-exchange column.

Heterpoly acids have been used for the determination of phenothiazines [14–16]. It was found that heteropoly acids oxidize phenothiazines to coloured radical cations. The oxidation of pro-

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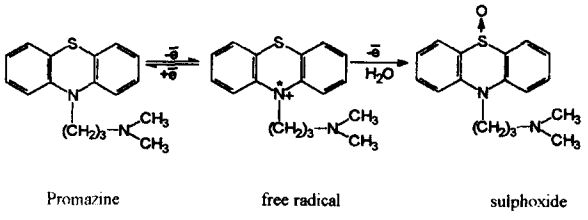
mazine takes place by a two-electron mechanism via the radical cation to the sulphoxide:



Promazine undergoes a one-electron reversible step to form the intensely coloured free radical, which is stable in acidic solution. The free radical is further oxidized irreversibly by excess of oxidant to a colourless sulphoxide [17].

Molybdophosphoric acid (MPA) is not a strong oxidizing agent and it oxidizes promazine to the free radical only. The coloured oxidation product is stable for 5 h.

This paper describes a flow injection method for the determination of promazine hydrochloride using molybdophosphoric acid.

2. Experimental

2.1. Reagents

A solution of promazine hydrochloride (PMH), 10-(3-di-methylaminopropyl)phenothiazine hydrochloride, from Polfa (Jelenia Góra, Poland) was prepared by dissolving the requisite amount of sample in distilled water. The solution was prepared fresh every day and kept in the dark and cold to minimize oxidation.

Standard molybdophosphoric acid (MPA) solution 1×10^{-2} M was prepared by dissolving 2.258 g of sample in hot water with continuous stirring, then cooling an diluting to 100 ml.

All chemicals used were of analytical grade.

2.2. Apparatus

A Spekol-10 spectrophotometer (Carl Zeiss, Jena, Germany) was used for absorbance measurements. A Hewlett-Packard Model 8452A diode-array spectrophotometer was used for spectral analysis of the coloured compound.

The flow injection assembly (Fig. 1) consisted of a two-channel manifold in which the sample solution was injected into the carrier stream and the absorbance measured spectrophotometrically at 524 nm with the Spekol-10 spectrophotometer equipped with an 18 μl flow cell (Tecator) and a TZ 4620 recorder (Laboratórní Přístrojé Prague, Czech Republic). The flow injection manifold included a laboratory-made rotary injection valve and PP2–15 multi-channel pump (Zalimp, Poland). The polyethylene tube coils used in the FIA assembly were of 0.8 mm i.d.

3. Results and discussion

Small amounts of PMH react with an excess of molybdophosphoric acid to form a soluble coloured compound. Maximum intensity of the colour is obtained instantaneously at room temperature in solutions between pH 0.9 and 2.0 and remains constant for 5 h. If the pH is below 0.9 the coloured solutions becomes turbid, whereas if it is above 2 the colour intensity decreases with time. A pH of 1.7, which is readily obtained by mixing solutions of molybdophosphoric acid and promazine hydrochloride, was selected for further studies.

The absorption spectra of molybdophosphoric acid and its coloured product with promazine hydrochloride are shown in Fig. 2. The λ_{max} of the

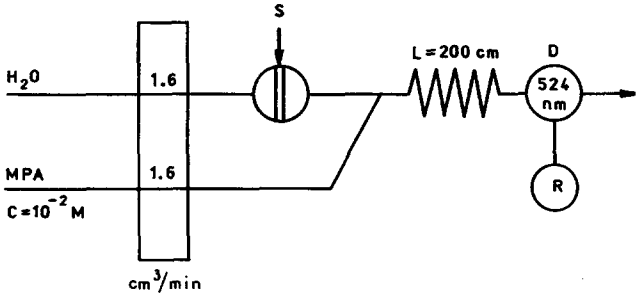


Fig. 1. Schematic diagram of the flow injection system used for determination of promazine hydrochloride (PMH): S, sample injection point; L, reaction coil; D, spectrophotometric flow-through detector; R, recorder.

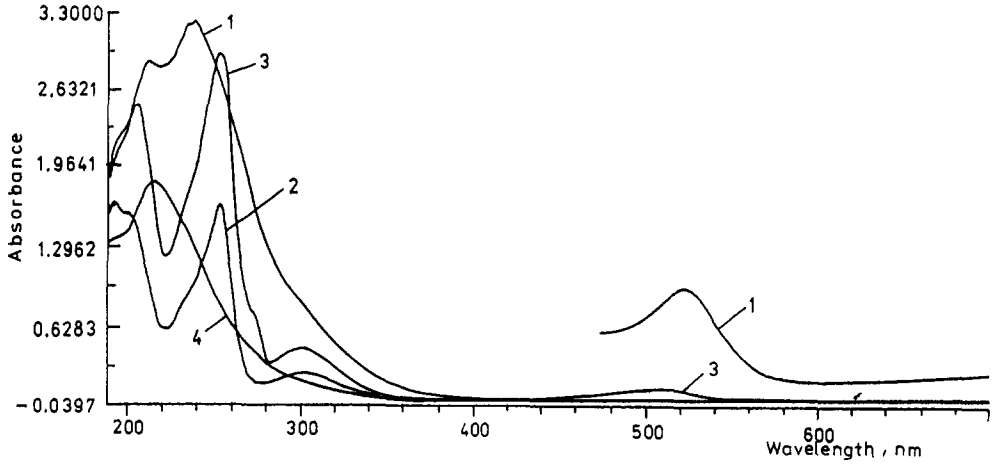


Fig. 2. Absorption spectra; 1, coloured product of PMH with MPA; 2, PMH; 3, free radical of PM obtained electrochemically; 4, molybdophosphoric acid, $C_{MPA} = 2.5 \times 10^{-5}$ M; $C_{PMH} = 5 \times 10^{-5}$ M.

coloured product was found experimentally to be 524 nm and corresponded to that reported in the literature for the free radicals formed by oxidation [18]. They agree with the λ_{max} for the free radical of promazine obtained electrochemically.

The effect of changes in the concentration of molybdophosphoric acid was studied by measuring the absorbance for solutions containing a fixed amount (2.5×10^{-5} M) of the promazine and various amounts of molybdophosphoric acid. The results are shown in Fig. 3. The rate of formation and the colour intensity of the product increased with increasing concentation of molybdophosphoric acid, but constant absorbance readings were obtained for a 20–50-fold excess of molybdophosphoric acid.

3.1. General procedure for flow injection determination of promazine

A 200 μl aliquot of promazine hydrochloride sample containing a defined amount (ppm) is injected by means of the injection valve into the carrier stream of doubly distilled water. The injected sample after mixing with the molybdophosphoric acid stream passes to the spectrophotometer flow cell and the absorbance is measured at 524 nm.

3.2. Optimization of variables

In order to optimize the proposed FIA method, the influence of various experimental parameters on the peak height and reproducibility of the results was studied. These included flow rate, reaction coil length, injection volume and concentration of molybdophosphoric acid.

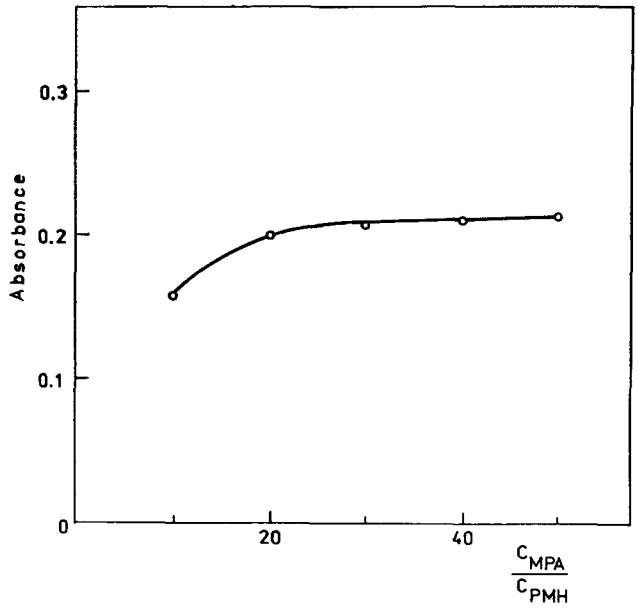


Fig. 3. Effect of the excess of molybdophosphoric acid (MPA) on absorbance of coloured product of PMH.

Flow rate and reaction coil length

Both parameters are closely related and a change of one or the other has a great influence on the peak height. The flow rate is controlled by the peristaltic pump. Increasing the flow rate in the range 1.0–3.0 ml min^{-1} was accompanied by a slight decrease in the peak height. A final flow rate of 1.6 ml min^{-1} was chosen.

The reaction coil length, which was defined as the total length of tubing from the point of sample introduction to the detector, is interchangeable with longer or shorter tubing of the same type and diameter. It was therefore decided to use a 2 m long reaction coil.

Sample volume

The sample volume was varied between 100 and 400 μl by changing the sample loop length in the injection valve. The peak height and peak width increased with increasing sample volume. The volume of 200 μl was a compromise between sensitivity and sample injection rate.

Concentration of molybdophosphoric acid

It was found that the reaction of MPA with PMH was very rapid and the coloured oxidation product formed in a few seconds.

The effect of concentration of the molybdophosphoric acid was studied in the range 0.1×10^{-2}–2×10^{-2} M. A 1×10^{-2} M concentration was chosen as the optimum for high sensitivity.

Summary of analytical parameters

Following the optimization investigations, the parameters adopted in subsequent studies were as follows: flow rate, 1.6 ml min^{-1}; reaction coil length, 2 m; sample volume, 200 μl; and MPA concentration, 1×10^{-2} M.

3.3. Analytical evaluation

Typical calibration peaks for promazine hydrochloride obtained under the optimized conditions are shown in Fig. 4.

The calibration graph obtained from these results was linear over the range 1–25 ppm with a regression coefficient of 0.9993. The detection limit (obtained as three times the baseline noise) was 0.35 ppm for 200 μl injected. The relative standard deviation (RSD) obtained for a concentration of 10 ppm was 1.8% ($n=20$). The sample throughput was about 89 h^{-1}. The regression equation was $y = 5.786x - 3.23$ (where y = peak height in mm and x = ppm of PMH).

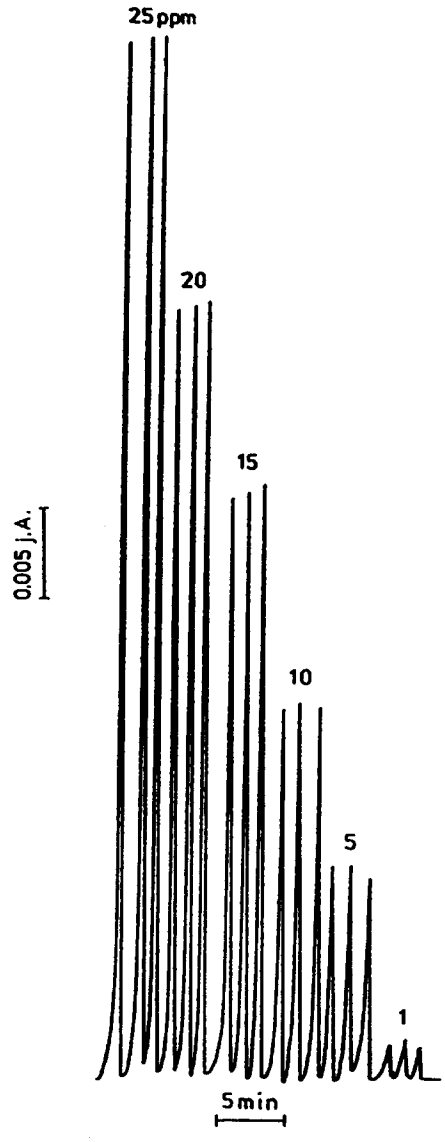


Fig. 4. Typical recordings for calibration of the flow injection system.

Effect of interferences

In order to evaluate the selectivity of the developed method for the analysis of pharmaceutical preparations, the effect of the presence of several species which can occur in real samples with promazine was investigated.

A level of interferent was considered to be acceptable if the error was not larger than 5%. Many associated materials such as glucose, lactose, sodium chloride, formaldehyde and *p*-hydroxybenzoic acid did not interfere. The most significant interferences were from ascorbic acid and sodium sulphite at concentrations of 10 ppm. However, they do not occur at such high concentrations in commercial preparations. As indicated above, the presence of sulphoxide would not be expected to intefere with this particular chromogenic reaction.

3.4. Flow injection determination promazine hydrochloride in pharmaceutical preparations

In order to confirm the applicability of the proposed method, promazine hydrochloride was determined in injections of promazine (from Polfa). The declared concentration was 100 mg in 2 ml of solution and 20 different samples were analysed. The appropriate volume of sample was transferred into a 100 ml calibrated flask and made up to the mark with distilled water, 1:5 with water. The promazine hydrochloride content in the diluted solution was determined as described above using the flow injection method. The results obtained were compared with those given by a spectrophotometric reference method of Blažek and Kracmar [19] based on absorption measurements at 254 nm in methanol solutions of appropriate concentration.

The proposed method was successfully applied to the determination of promazine hydrochloride in injections. The results of the FIA assay injections compared favourably with those obtained using Blažek and Kracmar's [19]: for a declared content of 100 mg, the FIA method gave a mean result $\pm$RSD of 101.75 mg $\pm$ 0.56% and Blažek and Kracmar's method 102.26 mg $\pm$ 0.65 ($n = 20$), the relative error of the FIA method with respect to Blažek and Kracmar's method being 0.49%. The proposed method is superior to other conventional methods in that it is fast and simple.

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