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Spectrophotometric determination of promazine with an oxidative column in FIA manifolds*

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Abstract: A simple flow-injection spectrophotometric method for the determination of promazine is described. The two proposed procedures are based on the oxidation of analyte with a manganese dioxide column. Concentrations of promazine in the ranges 2–20 and 1–6 are determined with a relative standard deviation of 1.0%. The injection rates are 62 and 80 samples h^{-1}, respectively. The influence of foreign species and the determination of promazine in a pharmaceutical formulation are also reported.

Keywords: *Flow-injection analysis; promazine; oxidation reaction.*

Introduction

N-substituted phenothiazine derivatives are widely used as psychotropic drugs [1]. The importance of these drugs prompted the development of many methods for determination of phenothiazines. Since the introduction of flow-injection analysis (FIA) [2], a few flow procedures have been described for determination of phenothiazines. Koupparis and Barcuhova [3] have proposed a method based on the oxidation of phenothiazines with iron perchlorate in a strong acid medium with $HClO_4$. Another procedure with spectrophotometric detection was based on oxidation using ammonium metavanadate [4]. A spectrofluorimetric method based on the photochemical reaction under ultraviolet radiation has been proposed recently [5]. Balal and Anderson [6] have used a carbon fibre array electrode as a detector for the determination of several phenothiazine derivatives. These methods were based on oxidation reactions yielding intensely coloured free radicals. Promazine hydrochloride and other phenothiazines are easily oxidized reversibly with various oxidizing agents (e.g. Ce(IV), VO_3^-, $Cr_2O_7^{2-}$, BrO_3^-, IO_3^-, IO_4^-, NO_2^-, etc.) [7]. Manganese dioxide is used for the first time in this work for oxidizing phenothiazines.

This paper describes the simple use of manganese dioxide as an oxidative column in the FIA determination of one of the phenothiazines, promazine hydrochloride. In a previous paper the application of manganese dioxide as an oxidative column in flow injection analysis was described [8]. The sample is introduced into the carrier stream passing through the solid reactor and the oxidation product is measured spectrophotometrically.

Reagents and apparatus

Spectrophotometric measurements were made using a spectrophotometer (Spekol 10, Carl Zeiss, Jena, Germany) equipped with an HPLC cuvette (Institute of Physical Chemistry of the Polish Academy of Science, Warsaw, Poland) and recorded with a TZ 4620 recorder (Laboratorni Pristroje, Czechoslovakia). The flow-injection manifolds are shown in Fig. 1 and included a home-made rotary injection valve and a multichannel pump PP2-15 (Zalimp, Poland). Manifolds used were made from Teflon tube and home-made perspex connectors. Teflon tube coils were of 1.0 mm i.d. for the oxidative column and 0.5 mm i.d. in the flow-injection manifolds.

All reagents used were of analytical grade. Hydrochloric acid, sulphuric acid, ascorbic acid, formaldehyde, methanol, calcium chloride, sodium chloride, sodium sulphite, were all supplied by POCh (Gliwice, Poland). Phenol (Wien-Fischamend) and glucose (Polfa, Poland) were also used. Suitable solutions

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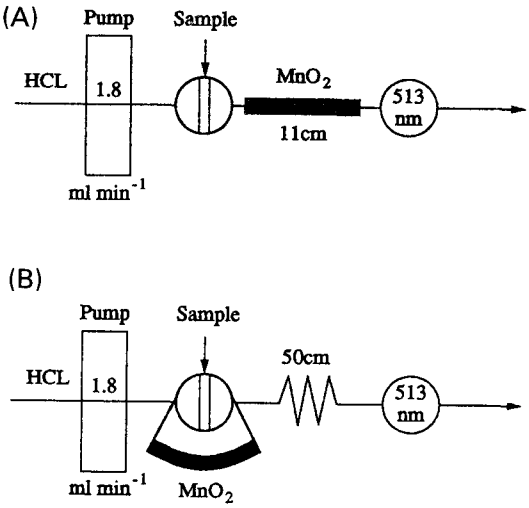

Figure 1
Manifolds with manganese dioxide column placed between sample injector and detector (A) and with the sample loop which acts as the oxidative column (B).

were prepared by dissolving in distilled water. Manganese dioxide (Matheson, Coleman and Bell) was used for preparing oxidative columns. A stock standard solution of promazine (1000 mg l^{-1}) was prepared by dissolving 100 mg of promazine hydrochloride (Polfa, Poland) in 100 ml of distilled water. The solution was kept in the dark and cold to minimize oxidation.

General procedure

Two different single channel configurations proposed for promazine determination were tested. The first manifold considered [Fig. 1(A)] was based on direct sample injection into the carrier stream (hydrochloric acid) by a loop-valve injector. The oxidative column was placed between the sample injector and detector. Figure 1(B) shows the second flow injection manifold. An aqueous solution of promazine was introduced into the sample loop, which also acted as an oxidative column. Sample injections were made every 15 s, which means about 10 s contact time between the sample and manganese dioxide, followed by direct injection into hydrochloric acid (pH 1.6). In both cases after passing through the manganese dioxide column the oxidized sample was led to the spectrophotometer flow cell and the absorbance read at 513 nm.

Oxidative columns were prepared by introducing the manganese dioxide particles into Teflon coils by suction.

In order to optimize proposed FIA methods the influence of the various experimental parameters on magnitude of the peak height and reproducibility of the results was studied. These included: flow rate, minicolumn with manganese dioxide length, injected volume and acidity of the reaction. The oxidation of promazine with manganese dioxide was observed in acidic solution. Of the various acids tested, hydrochloric acid was found to be most suitable.

Results and Discussion

Manifold with minicolumn placed between sample injector and detector

The pH of the carrier solution (HCl) was studied and the results are shown in Fig. 2. The

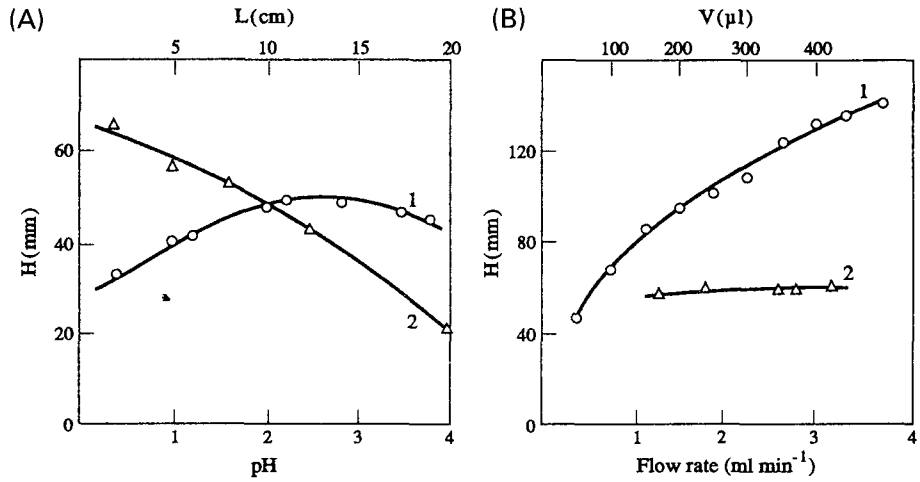

Figure 2
Effects of the manganese dioxide column length (A, curve 1), carrier stream pH (A, curve 2), injected sample volume (B, curve 1) and carrier stream flows rate (B, curve 2) on peak height for method I.

analyte peak height increased with decrease pH but the baseline noise also increased. The value pH = 1.6 was selected as a compromise. The effect of the length of the manganese dioxide column (L) was tested in the range 2–19 cm. As the column was increased in length from 2 to 10 cm (Fig. 2), the peak height also increased. The maximum peak height was obtained with 10–14 cm columns. An 11 cm long column was chosen as optimal for this manifold. The volume of sample injected was varied from 25 to 500 μl by changing the sample loop length in the injection valve. The peak height and peak width increased with increasing sample size. The volume 250 μl was a compromise between sensitivity and sample injection rate. The effect of flow rate in the sample stream was also studied. Increasing the flow rate in the range 1.3 to 3.2 ml min^{-1} was accompanied by a slight increase in the peak height. The final flow rate 1.8 ml min^{-1} was chosen.

Manifold with the sample loop which acts an oxidative column

The effect of different hydrochloric acid concentrations on the peak height were investigated. The results (Fig. 3) show an increase in peak height as the pH of carrier stream (HCl) decreased from 3 to 1.6 and then a decrease in peak height as the pH decreased to 1. The highest peak with good reproducibility was found when manganese dioxide column length was 24 cm (Fig. 3) and the distance between sample injector and detector was 50 cm. The peak heights were independent of flow rate. A flow rate of 0.8 ml min^{-1} was selected as a compromise between reproducibility and injection rate.

Validation and application

Typical calibration peaks for promazine hydrochloride obtained under optimized conditions are shown in Fig. 4. The calibration graphs obtained from these results were linear over the range 2–20 mg l^{-1} (method I) and 1–6 mg l^{-1} promazine hydrochloride (method II) with regression coefficients of 0.9978 and 0.9993, respectively. The detection limit defined as three times the baseline noise were 0.1 mg l^{-1} (method I) and 0.03 mg l^{-1} (method II). The relative standard deviations (RSD) obtained for a concentration of 10 mg l^{-1} (method I) and 5 mg l^{-1} (method II) were each 1.0%. Sampling throughput were 62 and 80 h^{-1}, respectively. Important features of the

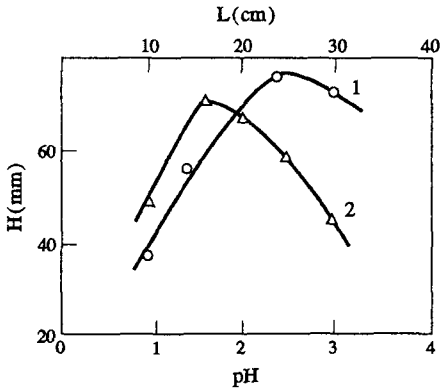

Figure 3
Effects of manganese dioxide column length (curve 1) and carrier stream pH (curve 2) on the peak height for method II.

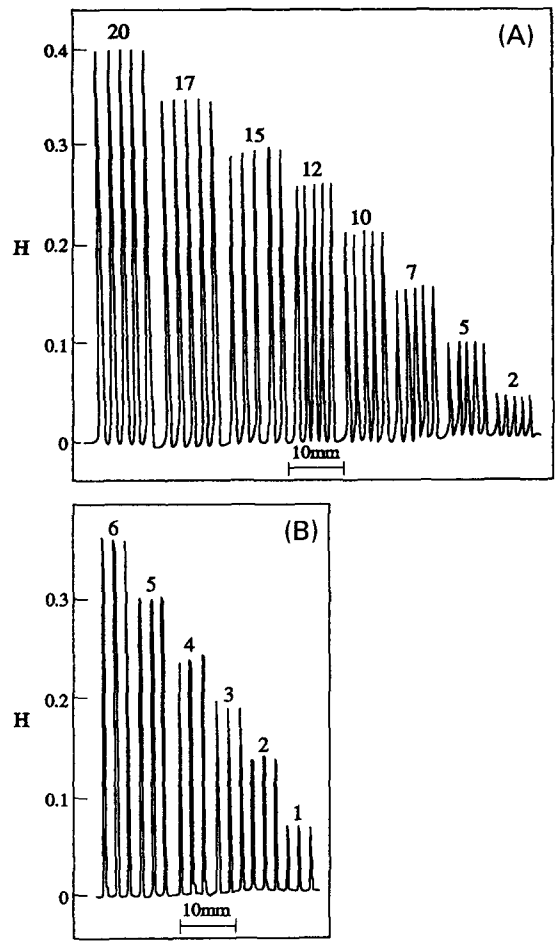

Figure 4
Typical recordings for calibration of the flow systems: (A) with column placed between sample injector and detector; (B) with the sample loop which acts as the oxidative column. Numbers on peaks refer to mg l^{-1}. Peak heights are given as absorbance readings.

Table 1
Analytical features of the proposed methods

Parameter	Method I	Method II
Linear range (mg l^{-1})	2–20	1–6
Regression coefficient	0.9978	0.9993
Detection limit (mg l^{-1})	0.1	0.03
Reproducibility (% RSD)	1.0	1.0
Sample throughput (samples h^{-1})	62	80

proposed methods for the determination of promazine hydrochloride are summarized in Table 1.

Stability of the column was checked using the manifold with the sample loop which acts an oxidative column. The carrier solution contained 2.0 mg l^{-1} of promazine hydrochloride and flowed continuously through the column. No injections were performed up to 1.5 h. Measurements were read every 180 s. The mean height (30 values) of the plateau was 21.4 mm with an RSD of 1.6%.

The manifold with minicolumn placed between sample injector and detector was used in testing the influence of foreign compounds, which can be found in pharmaceutical formulations containing promazine. The experiment was performed by preparing solutions of 2.0 mg l^{-1} promazine hydrocholoride with different amounts of potential interfering compounds. Errors were calculated by comparing the peak height with that obtained by injecting an aqueous solution of pure promazine hydrochloride. The tolerated level was taken as the measured signal variation ±5%. The results are summarized in Table 2.

In order to confirm the applicability of the proposed method, promazine hydrochloride was determined in injections of promazine (from Polfa, Poland). The results for the determination of promazine in injections were in good agreement with the results obtained with the Blazek method [9]. The results are summarized in Table 3.

Table 2
Influence of foreign compounds on promazine hydrochloride determination (promazine concentration = 2.0 mg l^{-1})

Compound	Conc. (mg l^{-1})	Error (%)
Formaldehyde	2.5	−1.9
Ascorbic acid	1.2	+4.5
Na_2EDTA	2.6	+3.4
Na_2SO_3	1.8	−0.5
NaCl	0.4	−1.5
Glucose	1.3	−0.3

Table 3
Determination of promazine hydrochloride in injections by FIA methods and by the Blazek method

	mg Found	Relative error (%)
Blazek method	0.110	—
FIA manifold I	0.114	±3.6
FIA manifold II	0.112	±1.8

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