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Flow injection spectrophotometric determination of promazine hydrochloride and thioridazine hydrochloride

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A flow injection method has been proposed for the determination of the promazine hydrochloride and thioridazine hydrochloride. The method is based on the oxidation of phenothiazines by potassium dichromate in hydrochloric acid medium. Linear calibration graphs have been obtained in the range of 10-200 ppm and 10-110 ppm for promazine and thioridazine respectively with a sampling rate of 80 samples/h. The present method has been applied to determination of promazine and thioridazine in pharmaceuticals.

Thioridazine hydrochloride and promazine hydrochloride are known to be neuroleptic tranquil-lisers and are commonly used as sedatives, antie-metics and anaesthetics. They are widely used in the treatment of care of mental illness. A number of analytical procedures have been reported for determination of phenothiazines in pure form, in pharmaceuticals or in biological fluids. The British Pharmacopoeia[1] recommends the titration method for evaluation of these compounds in their dosage forms. Other reported methods include spectrophotometric[2], fluorimetric[3], electrochemical[4] and chromatographic techniques[5].

Flow injection analysis (FIA)[6] is a continuous flow analysis that involves injection of reproducible sample volume into a continuously flowing unsegmented carrier stream. Due to its speed, simplicity and use of small amounts of the sample, the technique has found application in pharmaceutical, clinical, environmental and agricultural analysis.

The present note reports the estimation of phenothiazine derivatives (promazine and thioridazine) by studying their reaction with potassium dichromate in hydrochloric acid media in a flow injection system. The method is sensitive and reproducible and has been applied to the determination of the investigated compounds in their dosage forms.

Experimental

All reagents used were of analytical grade.

Aqueous (1000 ppm) stock solutions of promazine hydrochloride and thioridazine hydrochloride were prepared from the pure product (EGYT, Budapest) by dissolving 1 g of compound in 1 litre of distilled water and stored in a refrigerator. Working solutions of 50 ppm were prepared fresh daily by appropriate dillution of stock solution with distilled water.

Solutions (1000 ppm) of thioridazines were prepared by dissolving crushed and powdered tablets equivalent to the required amount of thioridazine in water and filtrated. The volume was made up to the mark in a 50 ml calibrated flask. Working solutions were obtained by appropriate dilution. Working solutions of promazine injection fluid were prepared by appropriate dilution of the fluid without any further treatment. A solution of potassium dichromate solution (10^{-2} *M*) (Gliwice POCH, Poland) was prepared from the pure product by dissolving an appropriate amount in 1 litre of water. The working solutions were prepared by stock solution diluting the appropriately. An appropriate concentration of hydrochloric acid solution was prepared by diluting the concentrated hydrochloric acid (Gliwice POCH, Poland).

Flow system

A schematic diagram of the flow system is shown in Fig. 1 (ref 14) A multichannel peristaltic pump (model Ismatec MS-4-Reglo/100) and rotary injection valve Rheodyne (model 5041) with exchangeable sample loops were used. The Spekol

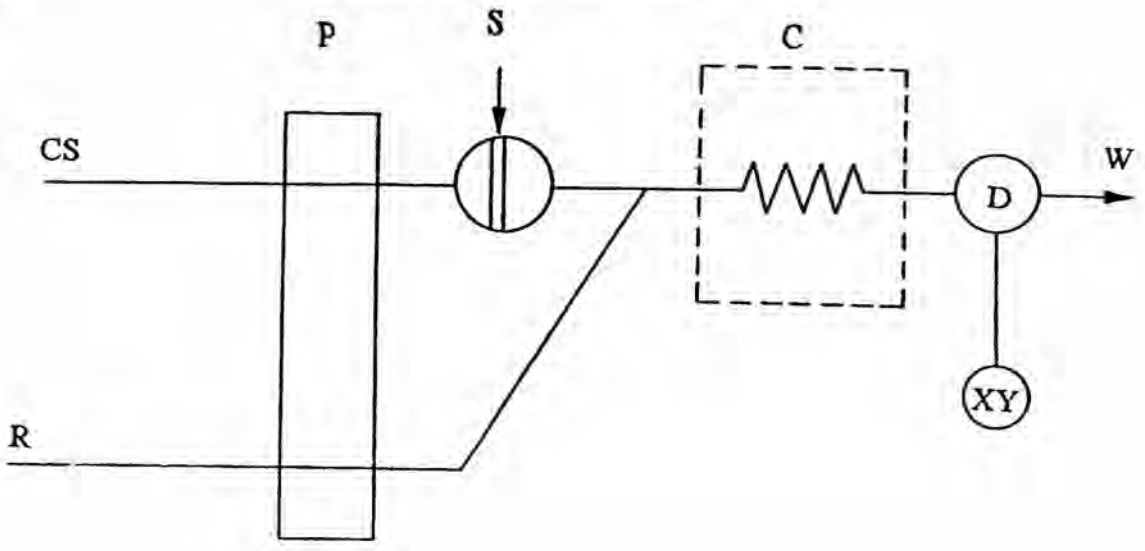


Fig. 1 - Schematic diagram of the FI system used for the assay of phenothiazines; [R - potassium dichromate solution; CS - water; P - peristaltic pump; S - sample injector; C - reactor; D - spectrophotometer; XY - recorder; and W - waste

11 (Carl Zeis, Jena) was connected to a model TZ 4620 strip-chart recorder (Laboratorni Pristroje, Praha). The PCV tubing used (i. d. 0.7 mm) was joined with perspex connectors.

General procedure

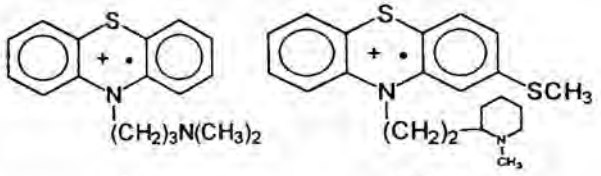
Among many available flow systems[7], the double-channel manifold was chosen. Such a system ensured stable base line and minimised random errors connected with changes of reagents concentration. Distilled water was used as carrier stream and was supplied by one of the lines while through the second channel the potassium dichromate in hydrochloric acid solution was pumped. Sample 50 ppm of promazine or thioridazine solution) was injected into the water stream and carried into the reactor. The reaction between phenothiazine derivative potassium dichromate takes place in the reactor and the coloured products were transferred into the flow cell of spectrophotometer. The absorbance was read at 512 nm for promazine hydrochloride and at 630 nm for thioridazine hydrochloride. Optimum conditions of flow analysis were studied by investigating the influence of parameters such as flow rate, length of reactor, volume of injected sample, concentration of reagent and acidity of reaction on the peak high and reproducibility, using 50 ppm sample injection.

Results and discussion

The proposed method is based on oxidation of the investigated substances by potassium dichromate in hydrochloric acid media. The oxidation process of phenothiazine derivatives proceeds via coloured free radical to colourless sulphoxide[8]. This reaction is strongly depended on acidity of reaction medium, the concentration and the oxidative potential of the oxidant.

Promazine hydrochloride and thioridazine hydrochloride react with potassium dichromate to give coloured products (I) and (II) that absorbs at 512 and 630 nm respectively. The colour is attributed to the radical cation of the oxidised form of phenothiazine. The described reaction is fast and the coloured products (pink for promazine and blue for thioridazine) are unstable and quickly transform into colourless products.

The effect of flow rate on the peak height and travel time (t_a) was investigated. An increase in flow



(I) (II)

Table 1 - Optimum conditions for the estimation of promazine and thioridazine.

Compound	λ_{max}	Range (ppm)	Calibration equation*	r	RSD (%)	Detection limit (ppm)	Flow rate (ml/min)	Sampling frequency (samples/h)
Promazine	512	10-200	H=0.75x - 19	0.999	0.5	0.7	1.2	80
Thioridazine	630	10-110	H-1.22x + 0.3	0.999	0.6	1.3	1.2	80

*H is the peak height in millimetres and (x) is expressed in ppm

Table 2 - Determination of promazine and thioridazine in pharmaceuticals

Sample	Certified value	Found (g)		Relative error*
		FIA method + std.dev.	Standard pharmacopoeic method	(%)
Promazin injections liquid Source: Polfa, Jelenia, Gora, Poland.	0.10	0.108+0.001	0.1090	-0.5
Thioridazin (tablets) Source : Polfa, Jelenia, Gora, Poland	0.01	0.0098+0.0001	0.0099	-0.6

*versus standard pharmacopoeic method

rate resulted in a decrease in absorption and travel time (the signals appeared faster). The optimum flow rate involves a compromise between sensitivity and sampling rate and a flow rate 1.2 ml/min was chosen. The sampling throughput was 80 samples h^{-1} for both phenothiazine derivatives.

The reactor length varying from 100-400 cm was tested. An increase in coil length resulted in an increase in peak height. However, at larger reactor size, a decrease of reproducibility was observed. A 200 cm reactor length was selected as this provided the greatest reproducibility.

The influence of the sample volume was studied from 50 to 400 µl of 50 ppm solution injected. The peak height increases as the sample volume increases with the maximum at 200 µl of the injected sample.

The composition of the dichromate stream has a strong influence on the peak height. Three acids, HNO_3, HCl and H_2SO_4, were tested to determine the most suitable media. The best results were obtained in hydrochloric acid medium.

The influence of hydrochloric acid concentration in the range 0.2-3 mol/dm^3 on the peak absorbance was investigated. The optimum concentration was found to be 0.6 mol/dm^3.

The influence of potassium dichromate concentration was studied in the range 1×10^{-4}-1×10^{-3} mol/dm^3. The maximum values for peak heights were obtained with a reagent concentration of 6×10^{-4} mol/dm^3. Experimental conditions are given in Table 1.

Determination of promazine hydrochloride and thioridazine hydrochloride

Under the optimum experimental conditions described above (6×10^{-4} mol/dm^3 $K_2Cr_2O_7$, 0.6 mol/dm^3 HCl), calibration graphs in the range 10-200 ppm for promazine and 10-110 ppm for thioridazine were obtained. Series of standard solutions were run in triplicate for both compounds. A typical plot is shown in Fig.2. The statistical parameters of described method are given in Table 1. The detection limits were taken as three times of noise level.

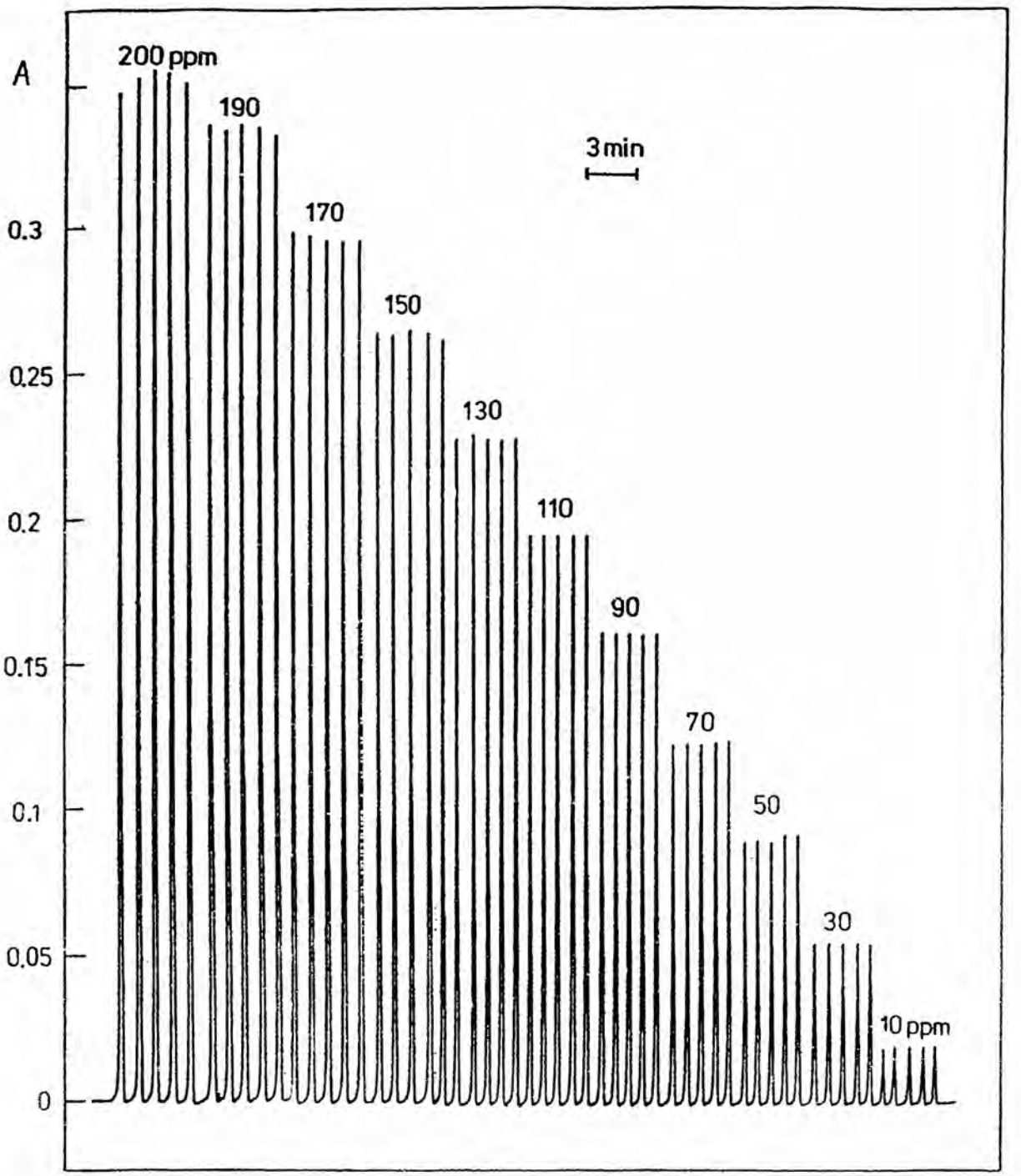


Fig. 2. Typical FIA plots (n=5) for promazine standard solutions

Drugs containing promazine hydrochloride (injection liquid Promazin) and thioridazine hydrochloride (tablets Thioridazin) were analysed by the above method (Table 2). Samples were also analysed by the BP method and relative error was calculated. The results obtained reveal that a similar degree of accuracy is afforded by both methods. Excipients such as glucose, starch and other drug components do not interfere.

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