

Rapid Spectrophotometric Determination of Some Phenothiazine Drugs with 1, 2 - Naphthaquinone-4-sulphonic Acid

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A sensitive method is described for the rapid spectrophotometric determination of some phenothiazine drugs based on the formation of coloured oxidation species with 1,2-naphthaquinone-4-sulphonic acid (NQSA) in hydrochloric acid medium. Usual excipients do not interfere with this method when applied to pharmaceutical preparations.

PHENOTHIAZINE drugs are known to act on a wide range of receptors in the nervous system and have been found to be versatile anticholinergic and antihistamine compounds.¹ Various methods are reported for the determination of phenothiazine class of drugs as reviewed by Blazek et al² and Fairbrother.³ Eriochrome blue black R⁴, phenol red and Alizarinviridin⁵ and modified Dragandoff's reagents⁶ have been reported for colorimetric determination of phenothiazines. Other methods include spectrophotometry^{7,8,9,10} chromatography^{11,12}, oxidometric^{13,14,15} gravimetric¹⁶ and polarographic.¹⁷ In a preliminary investigation on the reaction of phenothiazines with NQSA, coloured species are formed instantaneously with promethazine hydrochloride¹⁸ (PH), chlorpromazine hydrochloride (CPH), methiomepazine hydrochloride (MMH), fluphenazine dihydrochloride¹⁸ (FPH), diethazine hydrochloride (DH) and mepazine hydrochloride (MH). In the present study, these phenothiazine drugs or pharmaceutical preparations are determined spectrophotometrically with NQSA.

EXPERIMENTAL

Apparatus

All spectral measurements were carried out with Beckmann Model DB Spectrophotometer.

Materials and Reagents

Stock solutions of phenothiazines were prepared by dissolving an appropriate amount of the sample in water and then standardised by cerium (IV) solution. Working solutions were prepared as required by dilution.

A 0.025% freshly prepared aqueous solution of NQSA was used. A 10M solution of hydrochloride acid was used.

Pure phenothiazine drugs

An aliquot of phenothiazine solution is transferred into a 25ml standard flask containing 10 M HCl acid (15 ml). 0.025% NQSA (1ml) solution is added and the solution is diluted up to the mark with distilled water. The solution is shaken well and the absorbance is measured against a reagent blank.

Pharmaceutical preparations

Twenty tablets are weighed and pulverised. A portion of the powder equivalent to about 25mg of phenothiazine drug is accurately weighed and shaken with distilled water. The solution is filtered using a G-4 sintered glass filter. The residue is

Table 1: Spectrophotometric Study of Phenothiazine Drugs with NQSA

Phenothiazine drug*	Colour formed	Stability of the coloured species (~ hrs)	λ max (nm)	calibration range (ppm)	Molar absorptivity $\times 10^{-3}$ ($\text{mol}^{-1} \text{cm}^{-1}$)
PH	Pink	5	520	2-20	5.86
CPH	Pink	3	530	2-25	5.15
MMH	Blue	2	652	2-25	3.25
FPH	Orange-red	5	508	5-28	4.06
DH	Pink	6	515	2-20	6.00
MH	Orange-red	6	510	2-30	5.94

Overall acid concentration: 6M for all except CPH (5M)

*Abbreviation explained in Text.

Table 2: Assay of Phenothiazines in Pure and Dosage Forms

Sample	Labelled amount	Amount (mg) found* Proposed	by method B.P. '73
PH Powder	20 mg	19.80 \pm 0.5	19.55 \pm 0.4
Tablets	25 mg/tab	24.55 \pm 0.4	24.60 \pm 0.3
Ampoules	25 mg/ml	24.02 \pm 0.6	23.90 \pm 0.5
CPH Powder	25 mg	24.2 \pm 0.2	24.10 \pm 0.2
Tablets	25 mg/tab	24.7 \pm 0.2	24.55 \pm 0.3
Ampoules	25 mg/ml	23.95 \pm 0.6	23.92 \pm 0.7
MMH Powder	25 mg	25.10 \pm 0.2	—
FPH Powder	20 mg	19.85 \pm 0.2	19.80 \pm 0.3
DH Powder	20 mg	19.89 \pm 0.2	19.75 \pm 0.4

Marketed by : a - May and Baker b - Sandoz and c - Sarabhai

*Five determinations \pm standard deviation

washed with distilled water. The filtrate and washings are collected into a 100ml volumetric flask and diluted to the mark and analysed as described in the procedure.

For the analysis of injection solution, an appropriate amount of the sample is diluted with distilled water and analysed as above.

RESULTS AND DISCUSSION

When dilute solutions of phenothiazines and NQSA are mixed in hydrochloric acid medium, coloured oxidation species of phenothiazines are formed instantaneously. Different media were tried for this reaction, but the coloured species were found to be unstable. Hence HCl was prepared and the acid range was fixed at 5-6M. Also, it was found that a 0.5-2.0 ml of 0.025% NQSA was necessary for the maximum colour intensity. The experimental data of the spectrophotometric study of all the phenothiazines with NQSA is given (Table 1).

The results of the assay of pure phenothiazine drugs and also in the tablets and injections are presented (Table 2), compare favourably with the labelled values and with those obtained by the official method of the British Pharmacopoeia.¹⁹ Usual excipients which occur in pharmaceutical preparations do not interfere. However, compounds like amino acids, vitamins, hydrazine derivatives interfere seriously in the determination.

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