

Spectrofluorimetric Determination of Diethazine and Promethazine in Pharmaceutical Preparations

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A simple, sensitive and accurate spectrofluorimetric method is described for the quantitative determination of diethazine and promethazine either in the pure form or in its pharmaceuticals. The method is based on the formation of red fluorescent product of these drugs with Au(III). A linear calibration graph is obtained over the range 0.05–100 p.p.m. of diethazine and promethazine. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

The phenothiazines are one of the most important groups of pharmaceuticals, used as antihistamines, tranquilizers, antiemetics and anti-Parkinsons drugs and, therefore, their determination in pharmaceutical formulations is of considerable importance. On the other hand, phenothiazines exhibit certain interesting analytical properties owing to their characteristic structure, the presence of chemically active nitrogen and sulphur atoms and substituents. It is important to point out the lability to oxidation by means of many oxidants with formation of coloured or fluorescent oxidation products (Ortiz *et al.*, 1993; Ruiz *et al.*, 1993; Kojlo and Calatayud, 1995; Catalayud and Mateo, 1992; Ragland and Wright, 1964). The oxidation involves a series of one-electron steps providing free radicals and cations (Hanson and Norman, 1973; Mottola and Hauna, 1978; Nemcova and Rychlovsky, 1990). Phenothiazines have been shown to complex with Fe(III), Co(III), Mn(III), Au(III), Co(II) and Pd(II) to produce rose-red coloured solutions and the complexes have been used to determine phenothiazines by spectrophotometry (Borg and Cotzias, 1962; Barbe and Hurwic, 1973; Ryan, 1959; Fossoul, 1950).

The aim of the present work was to provide a simple and sensitive method for the estimation of phenothiazine in formulations. We found that diethazine and promethazine with Au(III) produce an intensive red fluorescent product in alcoholic and weakly acidic media and that the reaction can be utilized for determination of these drugs.

EXPERIMENTAL

Apparatus. Fluorescence measurements were made with a Hitachi 650–60 spectrofluorimeter (Tokyo, Japan).

Reagents. All materials were analytical reagent grade and were used as received. Pharmaceuticals were obtained from EGIS

Pharmaceutical Works, Budapest, Hungary. Ethanol was double distilled. A 0.001 M H₂AuCl₄ solution was prepared by dissolving the gold compound in ethanol.

Procedure for calibration curves. We prepared solution series of 10⁻³–10⁻⁷ g/mL concentration from pure diethazine and promethazine with ethanol. From each solution 1 mL was taken and transferred to a 10 mL measuring flask and 1 mL 0.001 M H₂AuCl₄ was added to it before diluting to the mark with ethanol. The flask was left at room temperature for 10–15 min, then the developed fluorescence was measured at excitation 373 nm and emission 636 nm. The fluorescence intensity plotted against the phenothiazine concentration showed a linear connection over the range 0.05–100 p.p.m. of drugs.

Determination of diethazine and promethazine in pharmaceutical formulations. Twenty tablets were massed and powdered. Powder equivalent to 50 mg of active ingredient was transferred to a 100 mL volumetric flask and dissolved in 100 mL of twice distilled water and filtered. This solution was further diluted with ethanol so that the final solution contained about 50 µg/mL of drug. One millilitre of the resulting solution was used for reaction with H₂AuCl₄. The amount of drug in these tablets was calculated using the observed fluorescence intensity, the mass of the powdered sample and the dilution factor.

For the determination of drugs in an injection dosage form, the mass of drug per mL was determined. Results are shown in Table 1.

Table 1. Analysis of phenothiazine derivations in various formulations

Sample	Found (mg/tab or mg/mL)		
	Nominal value/mg	Reference method ^a	Proposed method
Diethazine, HCl			
Tablet	25	24.87 (99.36%)	24.90 (98.84%)
Injection	25	24.69 (98.55%)	24.78 (99.70%)
Promethazine, HCl			
Tablet	25	24.79 (99.18%)	24.71 (100.24%)
Injection	25	24.60 (98.72%)	24.78 (97.84%)

^a Hungarian Pharmacopoea, Edition VII. Tomus II., 1986.

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Table 2. Recovery of diethazine and promethazine from pharmaceutical preparation

Sample	Added (mg/mL)	Found ^a (mg/mL)	Recovery (%)
Diethazine	Tablet	0.50	0.52 ± 0.03
		1.00	1.02 ± 0.05
		1.50	1.46 ± 0.06
	Injection	0.50	0.51 ± 0.04
		1.00	0.99 ± 0.03
		1.50	1.45 ± 0.06
Promethazine	Tablet	0.50	0.49 ± 0.03
		1.00	1.01 ± 0.06
		1.50	1.47 ± 0.05
	Injection	0.50	0.51 ± 0.04
		1.00	1.47 ± 0.06
		1.50	1.46 ± 0.06

^aAverage of three determinations ± SD.

Recovery experiment. To determine the precision and accuracy of the above method, recovery experiments were performed using the method of additions. A fixed volume sample of solution was added to one of three different concentrations of the standard drug solution. The results are shown in Table 2.

RESULTS AND DISCUSSION

The reaction mechanism of phenothiazines with Au(III) is not entirely clear. According to the paper cited, Hanson and Norman, 1973, the red fluorescent product is based on the

oxidation of phenothiazine and the cation radical forms a complex with HAuCl_4 .

The complex ratio was measured by the Job (Job, 1928) method. The continuous variations and the molar ratio method yielded the stoichiometric ratio of the product components, phenothiazine: Au 1:1, confirming the proposed structure. The red fluorescent product appeared immediately after the reactants were mixed, and it remained stable at room temperature in both ethanol and water solutions. In ethanol the fluorescence intensity was about twice that in aqueous solution.

The excitation and emission spectra of the red fluorescent product of diethazine and promethazine are shown in Fig. 1. The excitation and emission spectra have maxima at 290, 372, 522 and 638 nm, respectively. A significant advantage of the proposed method is that it can be applied to the determination of individual compounds in multicomponent mixtures since those phenothiazine drugs which contain different group in benzene ring, e.g. Cl, CF_3 and OCH_3 do not show the above fluorescent reaction e.g. chlorpromazine, perphenazine, trifluoperazine, fluophenazine and levopromazine.

This aspect of spectrofluorimetric analysis is of major interest in analytical pharmacy since it offers distinct possibilities in the assay of a particular component in a complex dosage formulation.

The results of the proposed method showed good agreement when compared with the official method. Additives used in the formulation did not interfere with the proposed method. These results indicate that the proposed method is simple, rapid and accurate and offers advantages in that only a small amount of drug or dosage formulation is required for analysis.

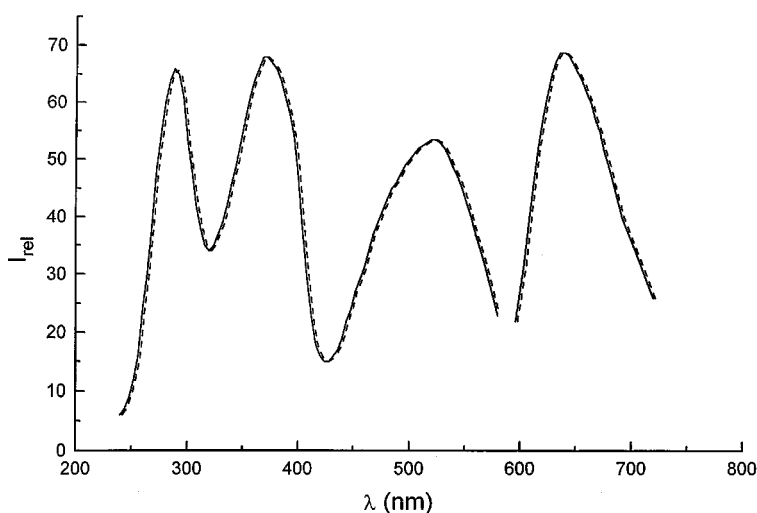


Figure 1. Excitation and emission spectra of diethazine and promethazine with HAuCl_4 in ethanol solution.

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