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Spectro Photometric Determination of Promethazine using Sodium Nitroprusside

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A simple, accurate and rapid method for the quantitative determination of promethazine in either pure form or in pharmaceutical formulations is proposed. The method is based on the formation of red product with sodium nitroprusside in sulphuric acid medium having maximum absorption at 515 nm.

PROMETHAZINE hydrochloride, 10-[2-(dimethylamino) Propyl] phenothiazine hydrochloride, is a drug used as an anthistamine. It has also some anticholinergic, antiserotoninergic and marked local anaesthetic properties[1].

The determination of promethazine has been achieved by different procedures, e.g., by forming ion-association complex[2], and spectrophotometry[3] using N-bromophthalimide, fluorimetry[4], partition column chromatography[5] and ion-exchange chromatography[6].

Gas Chromatography has been used to separate promethazine from other phenothiazines[7] and for its determination in the presence of paracetamol[8]. Titrimetric procedures including thermometric titrimetry[9] have been widely used. Low levels of promethazine have been determined by anodic stripping voltammetry[10] and flow-injection analysis (FIA) procedures[11,12].

In the present work, a simple, accurate and rapid spectrophotometric method for the determination of promethazine using sodium nitroprusside in sulphuric acid medium is proposed.

Absorbance measurements were carried out using an Elico model CL- 27 Digital spectrophotometer, provided with 1cm matching cells.

Table - 1 : Determination of promethazine hydrochloride in commercial formulations using the proposed method

Formulation	Drug content, mg			Relative difference %
	Label claim, per tablet or ml.	Proposed* method	Official+ method	
Tablets				
Phenergan	10	10.3±0.5	10.3±0.5	2.0
(Rhoˆne-Poulenc)	25	24.5±0.4	24.1±0.5	1.6
Phena	10	10.1±0.1	10.2±0.2	-1.0
(Ind-Swift)	25	24.3±0.3	24.6±0.5	-1.2
Injections				
Phenergan (Rhoˆne-Poulenc)	25	24.5±0.2	24.2±0.4	1.2
Promethazine (Jogsonpal)	1	1.04±0.03	1.05±0.04	-1.0
Elixir				
Phenergan (Rhoˆne-Puolenc)	1	1.03±0.03	1.06±0.02	-3.0
Phenzee (Shaskspharm)	1	1.01±0.02	1.02±0.03	-1.0

* Average of five determination ± standard deviation.
+ Average of three determinations ± standard deviation.

All solutions were prepared in distilled water from analytical reagent-grade materials. Pure promethazine hydrochloride was obtained from British pharmaceuticals Ltd., Vapi and formulations from local commercial sources.

A 1000 μgml^{-1} stock solution of promethazine hydrochloride was prepared and stored in amber coloured bottle in a refrigerator. Working standard solutions were prepared by appropriate dilution of stock solution.

A 0.4% (m/v) sodium nitroprusside solution was prepared.

A 10M solution was prepared by dilution of Analar concentrated sulphuric acid.

Various aliquots containing 8-40 μgml^{-1} of promethazine hydrochloride solution were combined with 5 ml of 10M sulphuric acid and 5 ml of 0.04% sodium nitroprusside solution in 25 ml calibrated flasks, diluted to the mark with distilled water, mixed well and absorbance of the coloured solution was recorded after 10 min at 515 nm against the reagent blank. The colour was stable for at least 30 min.

The graph of absorbance against concentration was straight line over the concentration range 8-40 μgml^{-1}.

A known number of tablets were weighed and ground into a fine powder. A portion of the powder containing about 10 mg of promethazine hydrochloride was transferred into a 100 ml beaker and extracted three times with 10 ml portion of distilled water, filtered into 50 ml calibrated flasks and diluted to get 200 μgml^{-1} drug solution. In the case of injections, the contents of ampoules were appropriately diluted so that the promethazine concentration was 200 μgml^{-1}. In respect of elixir, 10 ml equivalent to 10 mg of drug were transferred into 250 ml separator. The sample was rendered alkaline to litmus paper with 6N ammonia solution and 1 ml in excess was added. The mixture was then extracted with 3 x 15 ml portions of chloroform, the chloroform extracts were evaporated to dryness and the residue was dissolved in 0.1 N hydrochloric acid and made up to 50 ml with distilled water. An aliquot of this solution was treated as described above. The samples were also assayed by the BP method[13] for comparison, and the results are given in table 1.

Of the several oxidising agents used for the oxidation of pehnothiazines, e.g., iron (iii) salts, cerium (iv) salts, persulphate, hydrogen peroxide and others,[14] it was found that nitroprusside in sulphuric acid medium oxidises promethazine to a red coloured product with maximum absorption wavelength at 515 nm and apparent molar abosrptivity 4.24 x 10^3 l. mol^{cm-1} and Sandell's senstivity 7.568 ng/cm^2. The red colour produced is due to the oxidation of promethazine to the semiquinonoid radical[15].

Common excipients and other additives coexisting in formulations were tested for possible interference. No interference was observed.

Accuracy of the proposed method was examined by performing recovery experiments in solutions prepared from promethazine formulations. A mean recovery of 99.95 was found (range 96.0 - 104.0 %).

The proposed method is simple and rapid and shows good precision and accuracy. The method is more sensitive compared to other colorimetric[3,16,17] and Fia[18,19] procedures. The coloured species is more stable compared to the one produced by other reaction[20,21]. These advantages make the method suitable for routine quality control.

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Formulation and Evaluation of Lincomycin HCl Gels

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Lincomycin is an antibiotic active against most common gram positive and several anaerobic organisms. It has proved to be excellent for the treatment of skin conditions such as furunculosis, abscesses, carbuncles, cellulities, erysipelas, impetigo, infection burns and wounds. Gels were prepared using different gel forming agents such as carbopol-940, HPC, HPMC and PEG 6000 in different proportions. The formulations were evaluated for drug content, viscosity, pH, extrudability, homogenity, irritation test, spreadability and skin permeation studies through rat skin using kashery chein cell. Formulation F5 with carbopol 940 (1.5%) as the gel forming agent was found to be the best.

LYNCOMYCIN HCl is an antibiotic belonging to the group of lincosamides. It has proved to be excellent for the treatment of skin conditions such as furunculosis, abscesses, carbuncles, cellulities, erysipelas, impetigo, infected burns and wounds[1]. It is presently available as capsules and injections and no topical preparation is available. As topical application of the drug at the affected site offers potential advantage of delivering the drug directly to the site of action, preparation and evaluation of lincomycin HCl gels was taken up in the present study.

*For correspondence

Five different gel formulations were prepared using the formulae as shown in table 1. The gel forming agents (carbopol-940, HPMC, HPC, PEG 6000) were soaked in water and warmed if necessary. The drug was added to this followed by other ingredients and stirred to obtain the gels.

The drug content in the gels was determined by dissolving 1 g of the gel in water and estimating the drug by U.V. Spectroscopy at 194 nm. Viscosity of the gels was determined using a Brookefield's viscometer.

The extrudability of the formulations from the collapsible tubes was determined. Spreadability[2]