Spectrophotometric Determination of Secnidazole in Tablets

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An extractive spectrophotometric method was established for the determination of secnidazole in pure and tablets using bromothymol blue as an analytical reagent. The method is based on the formation of a chloroform-extractable yellow colored ion-associated complex (bromothymol blue cation-secnidazole anion) through the reaction of secnidazole with an excess of bromothymol blue at pH 4.4. Beer's law was obeyed in the range of 2.0-40.0 µg/ml. The method is simple, precise and accurate for pure analyte with recovery (98.0-102.0%) and also, this does not require any separation of soluble excipients in tablets.

Secnidazole, 1-(2-hydroxy propyl)-2-methyl-5-nitro imidazole is an antiprotozoal and antiameobic agent[1]. Only a few methods for the determination of secnidazole have been reported. These include spectrophotometry[2-4], titrimetry[5,6], gas liquid chromatography[7] and high speed liquid chromatography[8]. The aim of the present work was to develop an improved extractive and spectrophotometric method with greater precision, accuracy and sensitivity for the determination of secnidazole in bulk and tablets.

Pure sencidazole was obtained from Cadila Pharmaceutical Ltd., Ahmedabad. All other chemicals were of analytical reagent grade. A Systronics UV Spectrophotometer type-150 with 10 mm glass cell was used for the absorbance measurements. pH measurements were made using a Systronic 361 pH-meter.

Stock solution of pure secnidazole was prepared by dissolving 100 mg of the drug in 100 ml of methanol. The bromothymol blue (0.1%) was prepared in double-distilled water and stored at 4°. The neutralized phthalate buffer solutions having pH range of 4.0-5.0 were prepared by placing 50.0 ml of 0.2 M potassium hydrogen phthalate in a 200 ml volumetric flask and adjusting the pH with different volume of 0.2 M sodium hydroxide.

Aliquots of secnidazole solutions in the concentration range of 2.0-40.0 µg/ml were prepared by sequential dilution of the standard stock solution. In a series of 125 ml separating funnels, 4.0 ml of different drug solutions representing 2.0-40.0 µg/ml, 4.0 ml of bromothymol blue solution and 2.0 ml of neutralized phthalate buffer pH 4.4 were mixed together. The ionic strength (µ) now produced by the buffer was 0.2 M. After adding 10 ml volume of chloroform to it the contents were shaken for 5 min. The separated chloroform layer was collected in a 25 ml volumetric flask, Fresh 10 ml portion of chloroform was added and shaken for 5 min. This second extract was combined with the first and then the volume was made up with chloroform. The organic layer was dried over a dehydrating agent and the absorbance was measured against a reagent blank at 431 nm.

The average weight of a tablet was determined. An amount of tablet powder equivalent to 100 mg of secnidazole was weighed accurately, thoroughly dissolved in 25 ml of methanol and finally filtered through a Whatman filter paper (No. 40) to remove residual insoluble matter. The solution was transferred, into a 100 ml volumetric flask and the volume was made up with methanol. Two different aliquots of this solution giving analyte concentrations about 10 and 30 µg/ml were obtained by sequential dilution. Each aliquot of 4.0 ml was mixed with 4.0 ml bromothymol blue solution (0.1%) and 2.0 ml of neutralized phthalate buffer (pH 4.4) and the procedure as described for pure secnidazole was followed.

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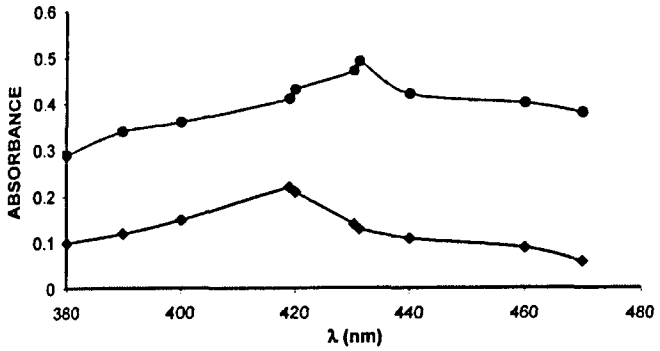

Fig. 1: The absorption spectrum of secnidazole bromothymol blue complex.

Absorption spectra of the blank reagent (-◆-) and the complex of secnidazole and bromothymol blue (-●-) formed in 0.2 M neutralized phthalate buffer containing 1 x 10^{-3} M bromothymol blue extracted with chloroform.

intensity. Hence 4.0 ml of bromothymol blue and 2.0 ml of neutralized phthalate buffer were selected.

The optimum pH where the ion-associated complex show maximum absorbance was found to be 4.4 in an experimental where the secnidazole was mixed with bromothymol blue in aqueous solutions of varying pH 4.0-5.0. The decrease in absorbance beyond pH 4.6 is due to the new ion-associated complex formation. The absorbance of reagent blank does not show any change with increasing pH. Hence a pH of 4.4 was used in all the subsequent experimental work.

The effect of temperature on the product was studied at different temperatures. The colored product was stable in the temperature range of 0.0-35°. At higher temperatures the drug concentration increased on prolonged heating due to volatile nature of chloroform. As a result the absorbance value of the colored products was increased. However, resultant product was stable for more than 48 h at 25±5°.

TABLE 1: DETERMINATION OF SECNIDAZOLE IN TABLETS USING PROPOSED METHOD.

Pharmaceutical Formulation	Label Claim (mg/tablet)	%Recovery* ± RSD	
		Proposed method	Reported method[3]
Tablet 1	500	100±0.80	100±0.53
Tablet 2	500	100±0.48	99.73±1.04
Tablet 3	1000	99.18±1.01	99.09± 1.00

*average of 5 determinations.

In aqueous alkaline medium, secnidazole form a yellow colored ion-associated complex with bromothymol blue. This complex was extractable with chloroform. The absorption spectra of these complexes are shown in fig. 1. The analytical wavelength for measuring absorption maximum for secnidazole-bromothymol blue complex was observed at 431 nm against the reagent blank. Absorption maximum at 419 nm was observed for the reagent blank when identical experimental conditions were used.

The extent of formation of ion-association secnidazole-bromothymol blue complex is governed by bromothymol blue concentration. The solute absorbances were plotted as a function of bromothymol blue concentration. The absorbance of the complexes initially increased in the concentration range of (0.02-0.10%) bromothymol blue and then attained practically a constant value in the concentration range of (0.10-0.12%) bromothymol blue. Thus it was found that 0.1% w/v concentration of bromothymol blue in the range of 3.0-5.0 ml and neutralized phthalate buffer in the range of 1.0-3.0 ml was necessary for the achievement of maximum color

The optical characters such as Beer's law limits 2.0-40.0 µg/ml, molar absorptivity 4.01/mol/cm/x10^3, Sandell's sensitivity 0.0901 µg/cm^2/0.001 absorbance unit and optimum photometric range 6.0-35.5 µg/ml were found. The precision was made by analysis of five replicate samples containing a known amount of secnidazole and the results were correlation coefficient (r) 0.9939, % relative standard deviation 1.2 and % error±0.73.

The validity of the method for the assay of tablets was determined. These results obtained by the proposed method and reported method was in good agreement (Table 1). The percentage recovery experiments revealed good accuracy of the data. There is no need for the separation of soluble excipients present in various marketed tablets as the results were always reproducible and equivalent to the labeled contents of the preparations.

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Simultaneous Determination of Phenylpropanolamine Hydrochloride, Dextromethorphan Hydrobromide and Chlorpheniramine Maleate in Formulations by Reversed-phase Liquid Chromatography

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A simple and cost effective reversed-phase high performance liquid chromatography method has been developed for the simultaneous determination of phenylpropanolamine hydrochloride, dextromethorphan hydrobromide and chlorpheniramine maleate in expectorant formulations. Water's symmetry C_{18} column (5 µ, 4.6 x 250 mm) was used with a mobile phase consisting of water, methanol and glacial acetic acid in the ratio 70:30:1, with a flow rate of 1.0 ml/min isocratically. Linearity coefficients, assay values, recovery studies showed that the method is accurate and precise.

Chlorpheniramine maleate (CPM) is official in IP[1], BP[2] and USP[3]. Dextromethorphan hydrobromide (DMH) is official in IP[4], BP[5] and USP[6], While phenylpropanolamine hydrochloride (PPH) is official in BP[7] and USP[8]. Fixed dose combinations of PPH, DMH and CPM are widely used for the symptomatic treatment of cough and cold. Many methods have been reported in the literature for the determination of similar formulations with various other drugs using HPLC[9-14], gas chromatography[15], spectrophotometry[16] and thin layer chromatography[17]. However, a method for the simultaneous determination of PPH, DMH and CPM in formulations by HPLC has not been reported. In this present work efforts have been made to develop an isocratic method using a simple mobile phase and UV detection for the simultaneous determination of the above drugs.

A high performance liquid chromatographic system from Shimadzu, consisting of LC 10 AS Pump, SPD IOA UV Detector, C-R7A Integrator was used for the analysis. Analysis was carried out using Water's symmetry C_{18} (5 µ, 4.6 x 250 mm) column with a flow rate of 1.0 ml/min. A Rheodyne 7725i injector with a 20 µl loop was used for injecting the samples. Detection was carried out at 250 nm for PPH and CPM and 280 nm for DMH.

Methanol HPLC grade (Merck), glacial acetic acid HPLC grade (Spectrochem), chloroform AR grade (Merck), and water collected from Millipore Milli Q system was used. Working reference standards of PPH, CPM and DMH were used

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