Determination of Pantoprazole Sodium by Complexation method: Hyphenated techniques

Ganta Deepthi[1] Nemani Archana[2] G. Bhagat[3]

[1]*Assistant professor, Dept.of Chemistry, Siddhartha Institute of Engineering & Technology, Ibrahimpatnam, Hyderabad, Telangana, India.*

[2]*Associate professor, Dept.of Chemistry, Siddhartha Institute of Engineering & Technology, Ibrahimpatnam, Hyderabad, Telangana, India.*

[3]*Assistant professor, Dept.of Chemistry, Siddhartha Institute of Engineering & Technology, Ibrahimpatnam, Hyderabad, Telangana, India.*

Abstract: Derivative spectroscopy offers a useful approach for the analysis of drugs in multi-component mixtures. In this study a first-derivative spectroscopic method was used for the simultaneous determination of diclofenac and pantoprazole in combined capsule dosage form using the zero-crossing technique. A simple and sensitive extractive spectrophometric method has been described for the assay of Mianserin hydrochloride (M-HCl) either in pure form or in pharmaceutical solid dosage form. The developed method involves formation of colored chloroform extractable ion-association complex of Mianserin hydrochloride (M-HCl) with Picric acid (PA), Chlorophenol red (ClPR), Bromthymol blue (BrTB), Bromcresol purple (BrCP) reagents. The extracted complexes showed absorbance maxima at 428 nm. Beer's law is obeyed in the concentration range of 10-50 μg mL^{-1}. Correlation coefficient was found to be 0.9997. The proposed method is useful for the routine estimation of pantoprazole sodium in bulk and tablet dosage form. Results of analysis were validated statistically. The excipients present in the formulations do not interfere with the assay procedure.

Keywords: Spectrophotometry; Pantoprazole sodium, Bromothymol blue, Ion-association complex

I. INTRODUCTION

Pantoprazole sodium sesquihydrate (PPS) is chemically known as sodium 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl] sulfinyl]1H-benzimidazole sesquihydrate. It is used as an antiulcerative agent by inhibiting the gastric acid secretion. Pantoprazole sodium sesquihydrate is immensely used for the cure of erosion and ulceration of esophagus caused by a gastroesophageal reflux disease [1-2]. The literature survey reveals that only few methods are available for the determination of PPS in dosage forms and biological materials includes spectrophotometric determination, high performance liquid chromatography (HPLC) and capillary electrophoresis[15-16]. No reports have appeared dealing with the extractive spectrophotometric method for the determination of PPS in drug forms so far. Therefore, this paper proposes a simple and sensitive extractive spectrophotometric method for the assay of PPS. This method is based on ion-pair complexes of drug with bromothymol blue and extraction into chloroform under reaction conditions used [3-5].

II. EXPERIMENTAL Apparatus

The spectrophotometric measurements were carried out using An Elico UV/Visible double beam spectrophotometer SL-164 with 1 cm matched quartz cells [6-7]. A calibrated digital pH meter was used for pH measurements.

Reagents

All chemicals were of analytical reagent grade of E.Merck unless otherwise specified. Doubly distilled water was used to prepare all solutions. Freshly prepared solutions were always employed. Potassium hydrogen phthalate buffer solution of pH-4 was also prepared. 0.12% (w/v) Bromothymol blue was prepared. Pure sample of pantoprazole sodium sesquihydrate was used [8-9].

Standard solution of the drug

A stock standard solution of 100 mg mL^{-1} was prepared by dissolving PPS in doubly distilled water. Working standard solution was then prepared by suitable dilution of the stock standard solution with doubly distilled water.

Procedure for the assay of bulk sample

From the 100 μg mL^{-1} solution, 1, 2, 3, 4 and 5 mL was transferred to a series of separating funnels and 2 mL of pH-4 buffer was added to each and then 1mL of 0.12 % w/v bromothymol blue was added and shaken well and 10 mL of chloroform was added to each and shaken well and kept for few minutes [10-12]. The chloroform layer was separated and treated with anhydrous sodium sulphate and the absorbance of the solution at 428 nm was measured against reagent blank. Final concentrations of analysed solutions were 10 μg mL^{-1} to

50 µg mL^{-1}. The standard calibration plot was prepared to calculate the amount of the PPS in unknown samples.

Procedure for formulations

Twenty tablets containing PPS were weighed and finely powdered. An accurately weighed portion of the powder equivalent to 50 mg of PPS was dissolved in a 50 ml of doubly distilled water and shaken well for about 5 minutes and filtered through a Whatman filter paper No.40. Convenient aliquots from this solution were taken for the determination of PSS in the range 10 to 50 µg mL^{-1}.

III. RESULTS AND DISCUSSION

Anionic dye like BTB form ion-association complex with the positively charged drug. The drug-dye stoichiometric ratio as calculated by the continuous variation and moleratio method is found to be 1:1 with BTB. The drug-dye complex, with two oppositely charged ions, behaves as a single unit held together by an electrostatic force of attraction.

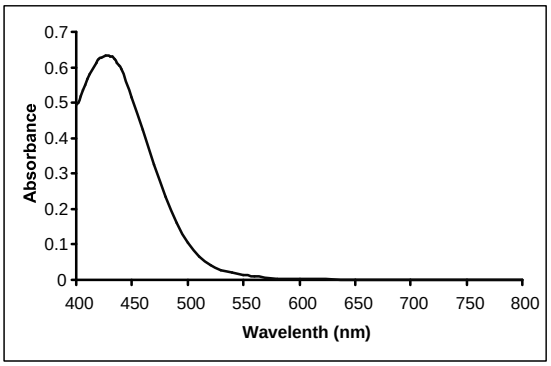

Fig. 1: Absorption spectra of PPS-BTB complex extracted into 10 mL chloroform

Optimization of variables

Optimum conditions necessary for rapid and quantitative formation of colored ion-pair complexes with maximum stability and sensitivity were established by a number of preliminary experiments. Potassium hydrogen phthalate buffer was found to be suitable for this method. Chloroform was preferred to other solvents (carbon tetrachloride, dichloromethane and ether) for this method for its selective and quantitative extraction. Optimum conditions were fixed by varying one parameter at a time while keeping other parameters constant and observing its effect on the absorbance at 428 nm for BTB. A maximal absorbance was observed at the pH 4.0 and using 2 mL of buffer. A volume of 1mL of 0.12% (w/v) BTB was found to be optimal for complete complexation.

Spectral characteristics

Absorption spectra of the yellow drug-BTB ion-pair complex with its lmax at 428 nm has been shown in the Figure 1. The colorless blank is practically negligible absorbance.

Table 1: It shows optical characteristics of proposed method

Parameters	Values
λ_{max} (nm)	428
Beer's law limit (µg mL^{-1})	10 - 50
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)	0.0812
Molar absorptivity (L mol^{-1} cm^{-1})	8.0426×10^3
Limit of detection, µg mL^{-1}	1.2261
Limit of quantification, µg mL^{-1}	3.7157
Regression equation (Y = a + bc)	
Slope (b)	0.0122
Intercept(a)	0.0021
Correlation coefficient (r^2)	0.9997

Linearity and range

Beer's law range, molar absorptivity, Sandell's sensitivity, reg ressionequation, and correlation coefficient determined for thi s method are given in Table 1. A linear relationship was obtained in the concentration range of 10 to 50 µg mL1. Regression analysis of the Beer's law plots reveals a good correlation. The graphs show negligible intercept and are described by the regression equati on, Y = mX + C (where Y is the absorbance of 1 cm layer, m i s the slope, C is the intercept and X is the concentration of the measured solution in µg mL1. The high molar absorptivities o f the resulting complexes
indicate the high sensitivity of this method.

Validation of the method

Samples of pure PPS were prepared and testd at four levels of drugusing the proposed procedure. The complete
set of validation assaywas performed for drug, determined by t he opposed methods. The results obtained for formulation are given ITable 2. The precisionand accuracy of t his method were tested by analysing six replicates of the drug. The standard deviation, relative standard deviation, recovery and were determined from the calibration curve, as recorded in Table 2. The accuracy of the method is indicated b y theexcellent recovery (99.96 – 100.21%) and theprecision is supported by the low standard deviation <0.09.

Table 2: It shows assay results of PPS in tablets

Drug	Label Claim (mg per tablet)	Amount found, mg*	% Recovery* ± % R.S.D
Sample I	40	40.19	100.01 ± 0.4457
Sample II	40	39.98	100.03 ± 0.4402

Tablets analysis

The proposed method was applied to the determination of PPS in commercial tablets. Satisfactory results were obtained for drug and were in a good agreement with the label claims (Table 2). The results were reproducible with low R.S.D. values. The average percent recoveries obtained were quantitative (9.96-100.21%), indicating good accuracy of this method. The results of analysis of the commercial tablets and the recovery study of drug suggested that there is no interference from any excipients present in tabl ets.

IV. CONCLUSION

The proposed method is simple, sensitive, rapid, precise and accurate for determination of PPS in pharmaceutical preparations when compared with the other methods, especially with HLPC. The proposed method may be applied for routine analysis and in quality control laboratories for the quantitative determination of the PPS in pharmaceutical preparations.

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