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DEVELOPMENT AND VALIDATION OF DIFFERENTIAL SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF PANTOPRAZOLE IN TABLET DOSAGE FORM

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ABSTRACT

A simple, rapid and sensitive difference spectrophotometric method was used for the determination of Pantoprazole in pharmaceutical dosage forms. The method is based on the induced spectral changes upon changing the pH of the medium that differ in their UVspectra. Difference spectrum, obtained by keeping Pantoprazole in 0.1N H_2SO_4 in reference cell and Pantoprazole in 0.1N KOH in sample cell, showed two characteristic peaks at 296 nm and 314 nm with positive and negative absorbance respectively. Difference of absorbance between these two maxima was calculated to find out the amplitude, which was plotted against concentration. The calibration curve is linear over the concentration range of 5-25 µg/ml (r^2= 0.996), with a detection limit of 0.0954µg/ml. The method was successfully applied to the commercial pharmaceutical drug without interference from common ingredient accompanying the drug. The result statistically compared with those obtained by the reference method. The proposed methods were successfully applied to the assay of Pantoprazole in pure and tablet dosage form. No interference was found from tablet excipients at the selected wavelengths and assay conditions. The data were compared with those obtained from the spectrophotometric method given in the literature and no difference was found statistically.

KEY WORDS

Difference Spectroscopy, Pantoprazole sodium and Tablet.

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INTRODUCTION

Pantoprazole Sodium Sesquihydrate (Figure No.1), (*RS*)-6-(difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1*H*-benzo[*d*]imidazole[1-4] is a proton pump inhibitor. It accumulates in the acidic compartment of parietal cells and is converted to the active form, a sulfanilamide, which binds to hydrogen-potassium-ATP-ase at the secretory

surface of gastric parietal cells. Inhibition of hydrogen-potassium-ATP-ase blocks the final step of gastric acid production, leading to inhibition of both basal and stimulated acid secretion. The duration of inhibition of acid secretion does not correlate with the much shorter elimination half-life of PTZ.

It is used to treat gastro esophageal reflux disease (GERD), a condition in which backward flow of acid from the stomach causes heartburn and possible injury of the esophagus. It is used to treat the symptoms of GERD, allow the esophagus to heal, and prevent further damage to the esophagus. It is also used to treat conditions where the stomach produces too much acid, such as Zollinger-Ellison syndrome. It works by decreasing the amount of acid made in the stomach. The stability of the compound in aqueous solution is pH-dependent. The rate of degradation increases with decreasing pH. The main purpose of the present study was to establish a relatively simple, single-step, sensitive, validated and inexpensive spectrophotometric method for the determination of PTZ in pure form and in pharmaceutical dosage form, since most of the previous methods have been found to be relatively complicated and expensive, such as HPLC and CE. The literature survey shows that UV spectroscopic method [5-7], RP-HPLC [8-11] method and HPTLC [12] method reported for PTZ. The developed methods were relatively more sensitive and the limit of detection (LOD) and limit of quantitation (LOQ) values for proposed methods were lower than the UV spectrophotometric method in the literature.

EXPERIMENTAL CONDITION

Materials and Methods

A Lab India UV-VIS Spectrophotometer 3000^+ with 1.0 cm matched quartz cells was used. PTZ bulk drug was obtained from Cipla Pvt. Ltd, India, Pantosec tablet (40mg) were obtained from the market, manufactured by Cipla Ltd., Roorkee, Haridwar, India. Sulfuric acid and Potassium hydroxide (0.1N Solution), Water was always double distilled.

PROCEDURE

Calibration

Stock PTZ solution was prepared by dissolving 100 mg of working standard in 100ml of Distilled Water. Working standard solutions with concentration ranging from 5-25 µg/ml in methanol were prepared by transferring appropriate volume of stock solution to 25 ml volumetric flask in duplicate. The volume was then adjusted with 0.1N H_2SO_4 and 0.1N KOH to give a series of equimolar solutions of PTZ in different pH medium. Difference spectra were obtained by keeping acidic form (in 0.1N H_2SO_4) in reference cell and basic form (in 0.1N KOH) in sample cell. Difference of absorbance between 296 nm and 314 nm was calculated to find out the amplitude (Table No.1).

Calibration plot

A plot of difference absorbance Vs. PTZ concentration was seen to be linear over the concentration range 5-25 µg/ml (r^2 =0.996) with a slop of 0.037 and intercept of 0.0024 (Figure No.2). The limit of detection (LOD) was determined by establishing the minimum level at which the analyte can be detected. The LOD was found to be 0.0954µg/ml and LOQ was also found to be0.2891 µg/ml.

Procedure for the assay of Pantoprazole Sodium in tablet

The average mass of 10 tablets was determined and was ground in a mortar. An amount of powder (accurately weighed) equivalent to 250 mg Pantoprazole was transferred in 100ml volumetric flask and made up to the mark with KOH and H_2SO_4. The content of the flask was sonicated for 10min and then the solution was filtered through Whatmann no-1 filter paper. The flask gradually was shaken and then solution was made up to the mark. The volume was then adjusted with 0.1N H_2SO_4 and 0.1 N KOH. The Absorbance Difference (ΔA) between the acidic solution and basic solution was measured at 314nm and 296nm by placing acidic solution as reference and basic solution as sample. The content of the tablet is calculated from the calibration curve or using the corresponding regression equation in (Table No.2).

INTERFERENCE STUDIES

The effect of foreign substances, inactive excipient material that commonly accompanying the drug in pharmaceutical formulation such as tablets (starch, mannitol, cellulose, PVP, magnesium stearate, titanium dioxide) was studied by Comparision of the absorption spectra of PTZ in standard solution and in solution at some extract (for example: Pantosec 40 mg). The obtained absorption spectra are identical. Figure No.3 confirmed that tablet excipient have no interference effect on the measurement of ΔA values.

RESULTS AND DISCUSSION

This work describes a simple pH induced difference spectrophotometric method for the determination Pantoprazole in tablets (in the presence of excipients).The absorbance spectra of equimolar solutions of Pantoprazole in 0.1N H_2SO_4 (pH 1) and 0.1N KOH (pH 11), are shown in Figure No.3.

Figure No.3 shows the difference absorption spectrum of Pantoprazole solution. It is generated by measure the absorbance of equimolar Pantoprazole solution at pH 11 (in 0.1N KOH) in sample cell against the Pantoprazole at pH 1 (in 0.1N H_2SO_4) form in reference cell.

The proposed method was validated with respect to linearity, precision and accuracy according to ICH guidelines[13]. The accuracy of the proposed method was evaluated by recovery studies (standard addition method) at three different levels. The results of the recovery studies are given in Table No.2. For precision of method, six standard solutions were evaluated at same day as well as at different days.

Where σ = The Standard deviation of the response

S = Slope of calibration curve.

The LOD and LOQ of the method were calculated by using equation no.1 and no.2.

Summary of all the validation parameters are given in Table No.2.

Analysis of commercial tablets

Difference spectrophotometric method was applied to brand of Pantoprazole tablet well known in the market (Figure No.4). The result of analysis is reported in Table No.2. The reproducibility of the method was checked by five replicate determinations and then the Relative standard deviation (RSD) is calculated.

Table No.1: Concentration and Absorbance of PTZ in Acidic and alkaline medium (Amplitude)

S.No	Concentration (mcg/ml)	Absorbance		Amplitude
		296nm	314nm	(Difference)
1	05	0.022	-0.130	0.152
2	10	0.228	-0.091	0.319
3	15	0.494	-0.040	0.534
4	20	0.666	-0.030	0.699
5	25	0.899	-0.024	0.923

Table No.2: Regression analysis and Validation Parameter

S.No	Linearity Range	5-25mcg/ml
1	Precision (% RSD)	0.5-0.9
2	Intraday %	1.0-1.7
3	Interday %	1.0-1.8
4	SD	0.002
5	LOD	0.0954
6	Correlation Coefficient	0.997
7	% Recovery (Tablets)	99.06%

(LOD is limit of detection, LOQ is limit of quanification, %RSD is percentage relative standard deviation)

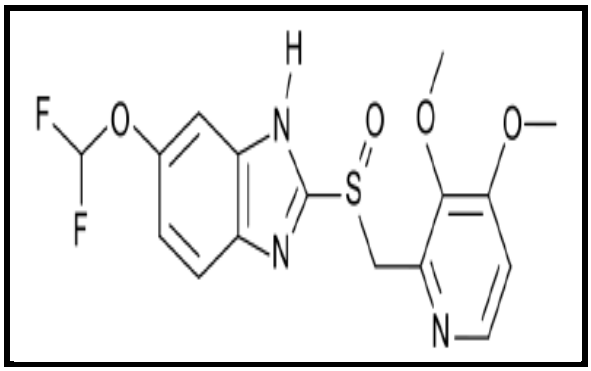

Figure No.1: Structure of PTZ

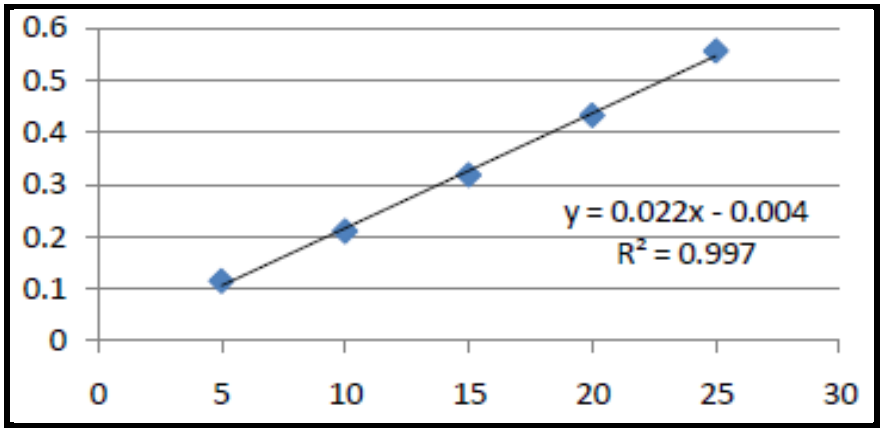

Figure No.2: The Difference Absorption Calibration Curve of Pantoprazole in 0.1N KOH and 0.1N Hcl. The Linear regression equation is y = 0.022x-0.004, r^2 = 0.996

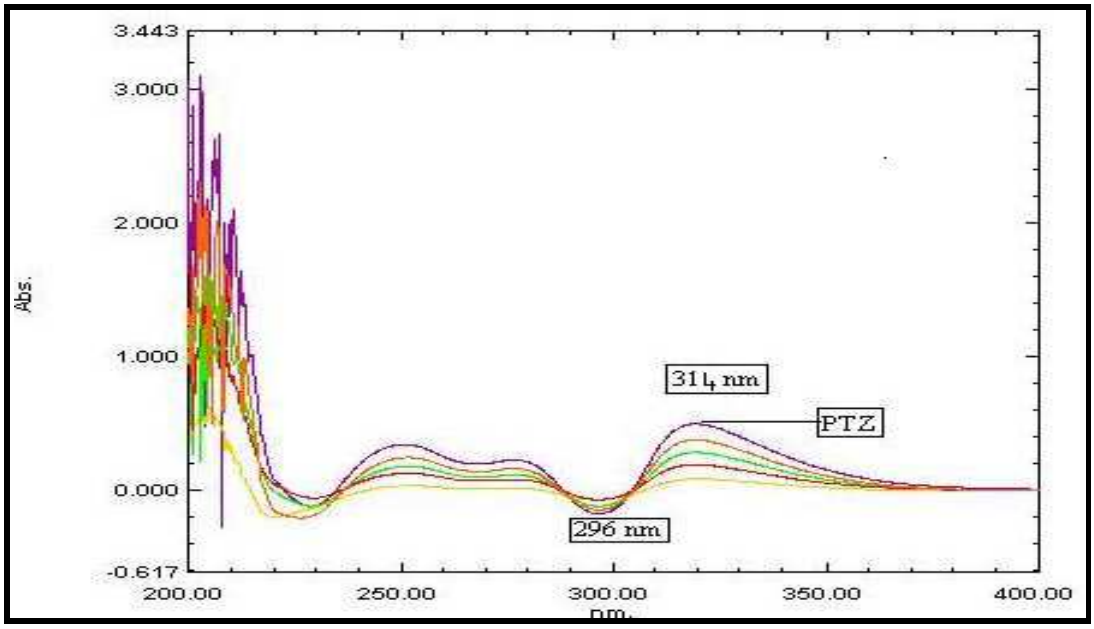

Figure No.3: Overlain spectra for Pantoprazole Sodium in Acidic and Alkaline medium

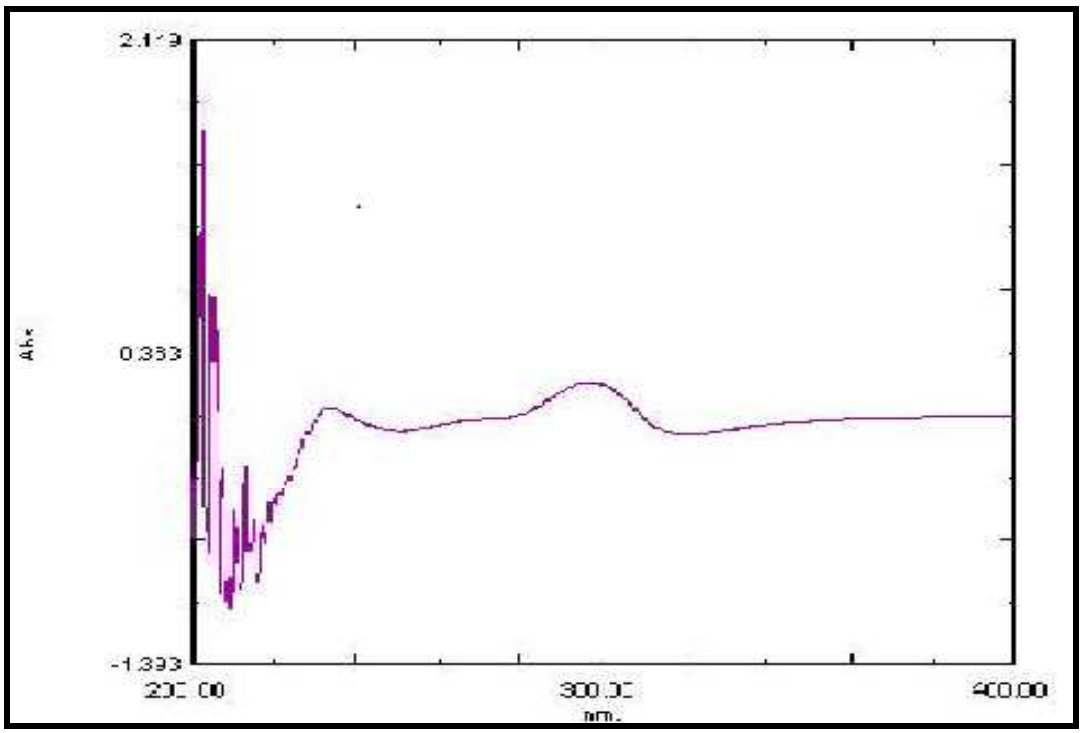

Figure No.4: Assay curve for market formulation (PTZ tablets)

CONCLUSION

The method is found to be simple, economical, selective and sensitive. The low value of relative standard deviation for repeated measurement indicates that the method is precise. The statistical parameters clearly indicate the reproducibility and accuracy of the method. Analysis of Pantoprazole in its dosage forms showed no interference from the common excipients and additives. Difference Spectrophotometry by indicating pH of the medium may be recommended for routine and quality control analysis of the investigated drug in tablets.

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