JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Development and Validation of Differential Spectrophotometric method for Determination of Pantoprazole in Tablet Dosage Form

Jigar Pandya* , Mr. Sagar Solanki, Dr. Mandev Patel

Department of Quality Assurance, K. B. Raval College of Pharmacy, Gandhinagar, Gujarat, India.

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 HCl in reference cell and Pantoprazole in 0.1N NaOH in sample cell, showed two characteristic peaks at 296 nm and 319 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= 0.997), with a detection limit of 0.15µg/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, Tablet.

Article history:
Received 11 Jan 2012
Revised 23 Jan 2012
Accepted 01 Feb 2012
Available online 13 Feb 2012

For Correspondence:

Jigar Pandya

Department of Quality Assurance, K. B. Raval College of Pharmacy, Gandhinagar, Gujarat, India

Email: jigar114_pandya@yahoo.com

INTRODUCTION:

Pantoprazole Sodium Sesquihydrate, (*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 gastroesophageal 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

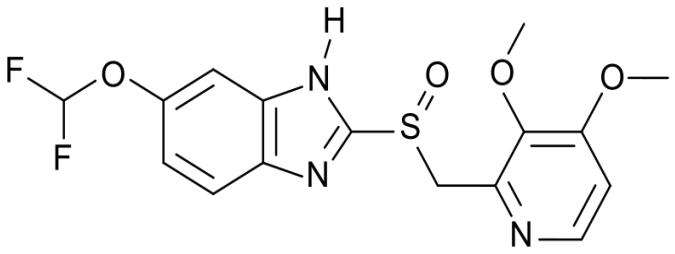

Figure 1 Structure of PTZ.

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 & Methods-

A Shimadzu UV-VIS Spectrophotometer 1800 with 1.0 cm matched quartz cells was used. PTZ bulk drug was obtained from Torrent Research Centre, Ahmedabad, India, Pantosec tablet (40mg) were obtained from the market, manufactured by Cipla Ltd., Roorkee, Haridwar, India. Sodium hydroxide and Hydrochloric Acid (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 HCl and 0.1N NaOH to give a series of equimolar solutions of PTZ in different pH medium. Difference spectra were obtained by keeping acidic form (in 0.1N HCl) in reference cell and basic form (in 0.1N NaOH) in sample cell. Difference of absorbance between 296 nm and 319 nm was calculated to find out the amplitude (Table1).

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 =0.997) with a slop of 0.022 and intercept of 0.004 (Figure 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 0.09543 µg/ml and LOQ was also found to be0.2891 µg/ml.

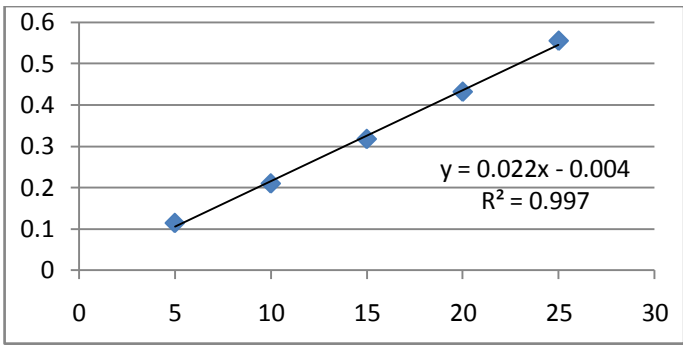

Figure 2 (The Difference Absorption Calibration Curve of Pantoprazole in 0.1 N NaOH and 0.1 N HCl.The Linear regerssion equation is y = 0.022x-0.004, r^2 = 0.997)

Table 1 Concentration and Absorbance of PTZ in Acidic and alkaline medium (Amplitude)

Concentration (mcg/ml)	Absorbance		Amplitude
	296nm	319nm	(Difference)
5	0.0718	-0.0435	0.1153
10	0.0726	-0.138	0.2106
15	0.1467	-0.1712	0.3179
20	0.199	-0.2329	0.4319
25	0.2497	-0.3052	0.5549

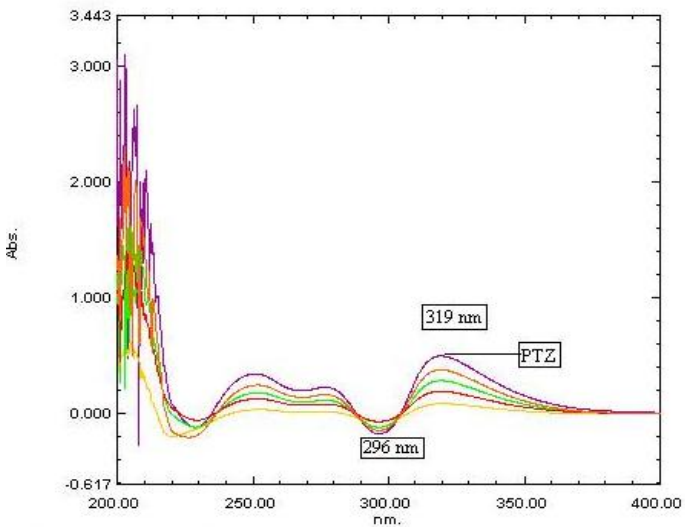

Figure 3 Overlain spectra for Pantoprazole Sodium in Acidic & Alkaline medium

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 40 mg PTZ was transferred in 100ml volumetric flask and made up to the mark with NaOH and HCl. 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

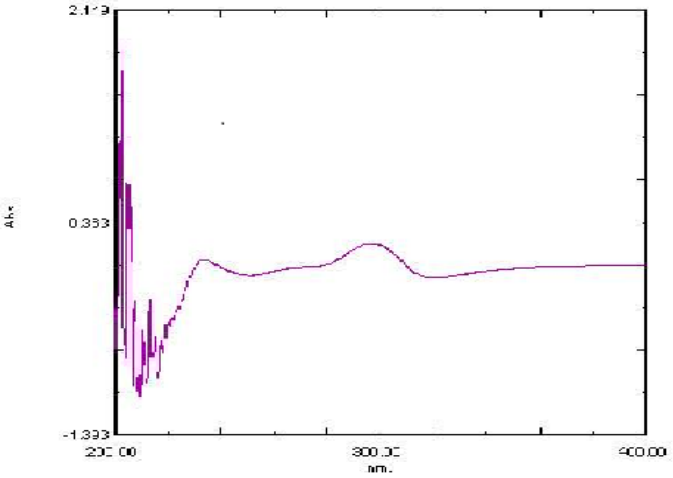

Figure- 4 Assay curve for market formulation (PTZ tablets)

Table 2 Regression analysis and Validation Parameter

Linearity Range	5-25mcg/ml
Precision (RSD)%	0.5-0.9
Intraday%	1.0-1.7
Interday%	1.0-1.8
SD	0.002
LOD	0.0954
LOQ	0.2891
Correlation Coeffecient	0.997
% Recovery(Tablets)	99.06%

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

the mark. The volume was then adjusted with 0.1N HCl and 0.1 N NaOH. The Absorbance Difference (ΔA) between the acidic solution and basic solution was measured at 296nm and 319nm 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-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- 4 confirmed that tablet excipient have no interference effect on the measurement of ΔA values.

RESULT AND DISCUSSION:

This work describes a simple pH induced difference spectrophotometric method for the determination PTZ in tablets (in the presence of excipients).The absorbance spectra of equimolar solutions of PTZ in 0.1N HCl (pH 1) and 0.1N NaOH (pH 11), are shown in Figure 3.

Figure 4 shows the difference absorption spectrum of PTZ solution. It is generated by measure the absorbance of equimolar PTZ solution at pH 11 (in 0.1N NaOH) in sample cell against the PTZ at pH 1 (in 0.1N HCl) form in reference cell.

The proposed method was validated with respect to linearity, limit of detection (LOD), limit of quantification (LOQ), 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 2. For precision of method, six standard solutions were evaluated at same day as well as at different days.

Limit of Detection (LOD): $3.3 \times \sigma/S$ – **Equation (1)**

Limt of Quantification (LOQ): $10 \times \sigma /S$ – **Equation (2)**

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 & no.-2.

Summary of all the validation parameters are given in Table 2.

Analysis of commercial tablets:

Difference spectrophotometric method was applied to brand of PTZ tablet well known in the market. The result of analysis is reported in table 2. The reproducibility of the method was checked by five replicate determinations and then the Relative standard deviation (RSD) is calculated.

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 PTZ 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.

REFERENCES

1.) Indian Pharmacopoiea, 6th Edition, Ministry of Health and Family welfare, published by The Indian Pharmacopoiea Commission, Ghaziabad, vol-II, (2010), 1856-57.

2.) British Pharmacopoiea. 6th Edition (6.1-6.5), vol-II, (2010), 1607.

3.) European Pharmacopoeia Supplement 6.1 6th Edition, Council of Europe Strasbourg; (2007), 3518-19.

4.) The Merck Index - an encyclopedia of chemicals, drugs and biologicals, 14th edition, (7014), 1209.

5.) Basavaiah, K., Anil kumar U.R., Kalsang T, Spectrophotometric Determination of Pantoprazole Sodium in Pharmaceuticals Using N-Bromosuccinimide, Methyl Orange and Indigo Carmine as Reagents, Iran. J. Chem. Chem. Eng. 2009, Vol. 28 No. 1.

6.) Ravi Kumar P. ,Bhanu Prakash P., Murali Krishna M., Santha Yadav M and Asha C., Simultaneous Estimation of Domperidone and Pantoprazole in Solid Dosage Form by UV Spectrophotometry, E-Journal of Chemistry, July 2006, Vol. 3, No.12, 142-145.

7.) Rajnish K., Harinder S. and Pinderjit S., Development of UV Spectrophotometric method for estimation of Pantoprazole in pharmaceutical dosage forms, Journal of Chemical and Pharmaceutical Research, *2011, 3(2):113-117.*

8.) Birajdar AS, Meyyanathan SN, Bojraj S, Application of UV-Spectrophotometry and RP-HPLC for Simultaneous Determination of Rabrprazole (Internal standard Pantoprazole) and Domperidone in Pharmaceutical Dosage Form." Pelagia Res. Lib. Der Pharmacia Sinica. **2010**, 1(3), 69-78.

9.) Prasanna Reddy.B, Mathsa.J. , Kotta.S., Jyothesh Kumar G., and Surendranath R., Determination of Pantoprazole sodium and Omeprazole in individual dosage form tablets by RP-HPLC using single mobile phase. Int. J. of Applied Biology and Pharma. Tech. **2010**, 1(2), 45-49.

10.) Kumar R, Singh P and Singh H, Development and validation of RP-HPLC method for simultaneous estimation of Naproxen and Pantoprazole in Pharmaceutical dosage form. Int. J. of Pharma. Res. and Development. 2011, 12, 12-14.

11.) Sivakumar T, Manavalan R and Valliappan K, Development and Validation of a Reversed-phase HPLC method for simultaneous determination of Domperidone and Pantoprazole in pharmaceutical dosage forms. ACTA Chromatographica, 2007, 18, 30-32.

12.) Patel GH, Prajapati ST and Patel CN, HPTLC Method Development and Validation for simultaneous Determination of Cinitapride and Pantoprazole in Capsule Dosage Form. Res. J. of Pharm. and Tech. 2011, 4(9), 1428-1431.

13.) International Conference on Harmonization (ICH) Topic Q2A, Validation of Analytical Procedures; Methodology, CPMP / ICH /281, 1995.