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Validation and Derivative Spectroscopy of Prasugrel HCl In Bulk and Formulation

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ABSTRACT

This study describes the development and validation for the determination of Prasugrel Hydrochloride in bulk and pharmaceutical dosage form by the first-order derivative UV spectroscopy method. The quantification was achieved by the first-order derivative spectroscopy method at 248 nm over the concentration range of 5-25 µg/ml for estimation of Prasugrel Hcl (r2=0.9993) keeping methanol as solvent in zero order derivatization and same 5-25 µg/ml for estimation of Prasugrel Hcl (r2=0.9981) in methanol upon first order derivatization. Procedure does not require prior separation of components from the sample. LOD values for Prasugrel Hclwas found to be 0.591µg/mL for zero order derivatization and upon first order derivatization 0.165 µg/mL. LOQ values for Prasugrel Hclwas found to be 1.970 µg/mL for zero order derivatization and upon first order derivatization0.55 µg/mL. The results of analysis have been validated statistically and recovery studies carried out in the range 50-150% to confirm the accuracy of the proposed method. The relative standard deviation was found to be <2.0%. The proposed method was successfully applied for the assay of drug in pharmaceutical formulations. No interference was observed from common pharmaceutical excipients. Hence, the method herein described can be successfully applied in quality control of combined pharmaceutical dosage form.

Keywords: Prasugrel Hydrochloride, first-order derivative spectroscopy, zero order derivatization, pharmaceutical dosage form.

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INTRODUCTION

Prasugrel Hcl chemically is 5-[2-cyclopropyl-1-(2-fluoro-phenyl)-2-oxoethyl]-4,5,6,7-tetra hydrothieno [3,2-c] pyridin-2-yl acetate. It is a member of the thienopyridine class of ADP receptor inhibitors, like ticlopidine and clopidogrel. These agents reduce the aggregation ("clumping") of platelets by irreversibly binding to P2Y12 receptors. Prasugrel inhibits adenosine diphosphate–induced platelet aggregation more rapidly, more consistently, and to a greater extent than do standard and higher doses of clopidogrel in healthy volunteers and in patients with coronary artery disease. A pharmacodynamic study suggests that acute coronary syndrome (ACS) patients can be safely switched from clopidogrel to prasugrel and that doing so results in a further reduction in platelet function after one week. When patients receive a loading dose of prasugrel prior to switching from clopidogrel, the reduction in platelet function occurs within two hours.[1-4]

Literature survey revealed that some analytical methods like LC-MS and HPTLC have been reported for the estimation of Prasugrel but no spectrophotometric method was reported.[5-9] Hence the objective was to develop a simple, sensitive, accurate and precise method for determination of Prasugrel Hcl by uv-visible spectrophotometric method in the pure form and its tablet formulation as per ICH guidelines.[10]

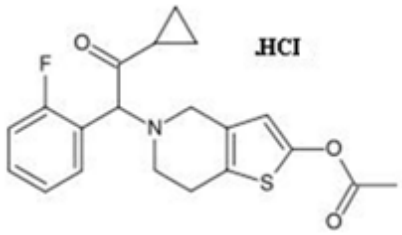

Figure 1. Chemical Structure of Prasugrel . HCl

MATERIALS AND METHODS

Chemicals and Reagents

Prasugrel Hcl gift sample was supplied by Hetero Drugs Limited (India).

Instrumentation

A double beam UV-VIS spectrophotometer (UV-1800,Labindia Double beam UV / Visible spectrophotometer) connected to computer loaded with spectra manager software UV Probe was employed with spectral band-width of 1nm wavelength accuracy of ± 0.3 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (Denver, Germany).

Preparation of stock solution:

The stock solution of PRL was prepared by dissolving accurately 25 mg of drug in distilled water

in a 25 ml volumetric flask to obtain a concentration of 1000 µg/ml. From this solution, 2.5 ml was taken and diluted with 0.1N Hcl in a 25 ml volumetric flask to prepare a working standard solution (100 µg/ml).

Zero-derivative spectrometry:

Series dilutions of standard solutions were prepared in 10 ml volumetric flasks with 0.1N Hcl to get the concentration ranging from 5-25 µg/ml. The above solutions were scanned over the range of 400 nm to 200 nm against reagent blank. The λ max was found to be 208 nm and 248.0 nm. But the present study was carried out at 248.0 nm as the results were in good agreement with Beer-Lambert's law. The calibration curve was constructed by plotting concentration against absorbance at 248.0 nm. The optical characteristics were shown in Table 1.

First-Derivative spectrometry

The above mentioned zero-order spectrums were derivatised to get first-order derivative spectra. The dA/dλ of the corresponding minima at 248 nm were measured and plotted against concentration. The optical characteristics were shown in Table 2.

METHOD VALIDATION:

Precision

The Inter-day precision was determined on three different days at three different levels (5, 10, 50 µg /mL) and the Intraday precision was determined at three different levels (5, 10, 50 µg /mL) by the same analyst. The % RSD values were found to be 1.422891 (Intraday) and 1.777358 (Interday) which are less than 2% indicating that the method is more precise.

Accuracy

Recovery studies were carried out by adding different amounts (50%, 100%, 150%) of bulk samples of Prasugrel within the linearity range to pre-analyzed formulation as per ICH guidelines and the %RSD values were found to be less than 2% indicating that the method is more accurate.

Assay-content Estimation

Calibration curve:

Aliquots of standard solution from 5 to 25mcg/ml were prepared and diluted as required. The wavelength is measured at 248 nm. The calibration curve that is linearity is computed by taking above data.

Sample solution:

Tablets containing Prasugrel (Epiflat, Sun Pharma Ltd) were successfully analyzed by the proposed method. Tablets of Prasugrel were accurately weighed and powdered. Tablet powder

equivalent to 154.75mg of Prasugrel was dissolved in a 250ml volumetric flask and filtered. The solution was suitably diluted and analyzed as given under the procedure for bulk samples. The results were represented in table. None of the excipients usually employed in the formulation of tablets interfered in the analysis of Prasugrel by the proposed method.

RESULTS AND DISCUSSION

Prasugrel Hcl obeys Beer-Lambert's law in the concentration range of 5-25 µg/ml in the developed method. The % RSD values in precision study were found to be 1.422891 (Intraday) and 1.777358 (Interday) which are less than 2% indicating that the method is more precise. The % RSD values in accuracy study were found to be less than 2% indicating that the method is more accurate. The present method is employed for the assay content of Prasugrel in pharmaceutical formulations, prasugrel tablet successfully and the recovery studies were close to 100% that indicate the accuracy and precision of proposed method and it indicates the non-interference of the formulation excipients.

Table. 1:Optical characteristics and validation data of Prasugrel HCl upon first-order derivatization:

Parameters	Results
Lambda Max [λ max]	248 nm
Regression Equation [Y]	Y = 0.017x+0.001
Slope [m]	0.017
Intercept [c]	0.001
Correlation Coefficient [R^2]	0.999
%RSD	1.777
LOD	0.591
LOQ	1.970

Table 2: Optical characteristics and validation data of prasugrel upon first-order derivatization:

Parameters	Results
Lambda Max [λ max]	248nm
Regression Equation [Y]	Y = 0.010x+0.002
Slope [m]	0.010
Intercept [c]	0.002
Correlation Coefficient [R^2]	0.999
%RSD	0.339
LOD	0.165
LOQ	0.55

Table 3:Assay of Prasugrel in pharmaceutical formulation:

Labeled Amount(mg)	Obtained Amount By Proposed Method (mg)	% Recovery By Proposed Method	Mean Recovery %
5.0 mg	5.08	101.7%	100.05%
10.0 mg	9.92	99.26%	
15.0 mg	14.87	99.14%	

Table 4: Assay of Prasugrel in pharmaceutical formulation upon first-order derivatization:

Labeled Amount(mg)	Obtained Amount By Proposed Method (mg)	% Recovery By Proposed Method	Mean Recovery %
5.0 mg	4.97	99.4%	99.8%
10.0 mg	10.08	100.8%	
15.0 mg	14.9	99.6%	

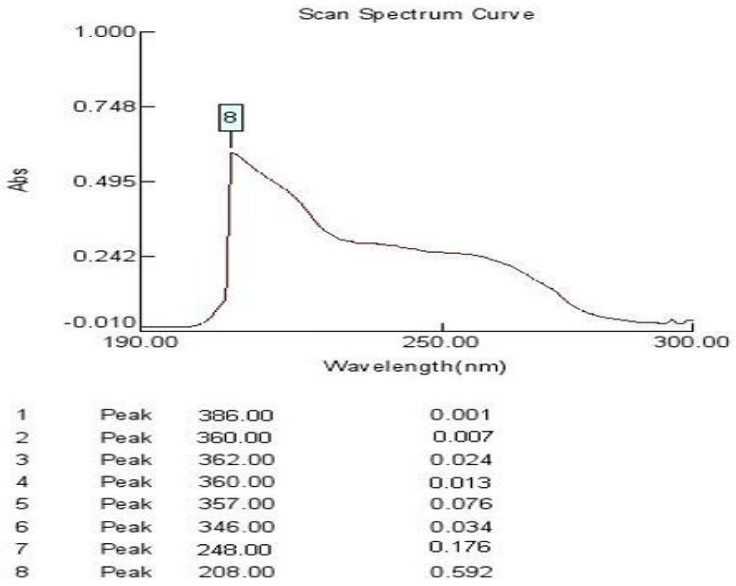

Figure 2. Absorption spectrum of Prasugrel in 0.1N Hcl

Wavelength (nm): 248.00, Absorbance: 0.176

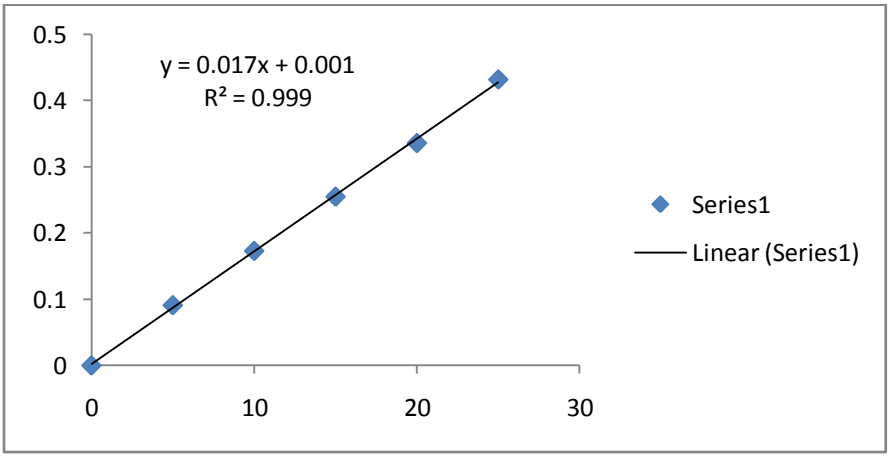

Figure 3:Linearity of Prasugrel HCl In Methanolupon Zero Order Derivatization:

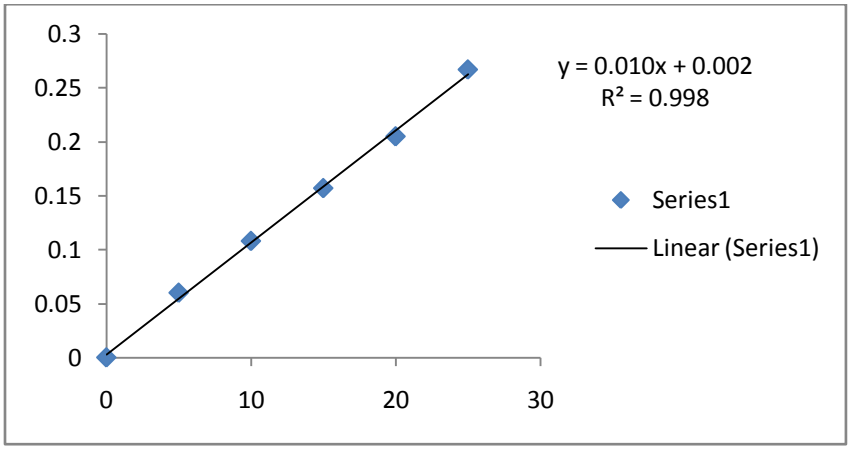

Figure 4: Linearity of Prasugrel HCl In Methanol Upon First Order Derivatization

CONCLUSION:

A simple UV Spectrophotometric method was developed for the determination of Prasugrel in pure and its dosage form using methanol. The absorbance of the drug complex formed with this reagent/solvent was maximum at the wavelength 248 nm against the corresponding reagent blank. The above method was simple, precise, and rapid for detection of Prasugrel in its pure and dosage form .The statistical parameters and recovery study data clearly indicate reproducibility and accuracy of the method. This method can thus be conveniently adopted for routine analysis of Prasugrel in pure as well as in its dosage forms.

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