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Extractive Spectrophotometric Estimation Of Prasugrel In Pharmaceutical Formulation

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ABSTRACT

One simple, economical, precise, reliable and reproducible Visible Spectrophotometric method has been developed for the estimation of Prasugrel. The developed method is based on formation of chloroform extractable complex of Prasugrel with Bromocresol green which shows absorbance maximum at 418nm.The absorbance-concentration plot is linear over the range of 100-1000µg/ml. The different experimental parameters affecting the development and stability were studied carefully and optimized. Results of analysis for the method was validated statistically and by recovery studies.

Key words: Prasugrel, Bromocresol green, Ultraviolet-Visible double beam spectrophotometer.

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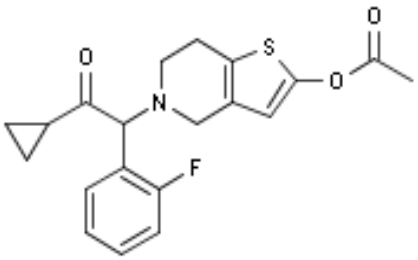
INTRODUCTION

Prasugrel [1,2] is a member of the Thienopyridine class of ADP receptor inhibitors, with a chemical name [5-[2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-yl acetate]. It is an antithrombotic drug. It is a prodrug, oxidation by intestinal and hepatic cytochrome P-450 enzymes convert Prasugrel into its active metabolite. Prasugrel has a rapid and almost complete absorption after oral ingestion of a loading dose. Its active form binds irreversibly to the adenosine diphosphate (ADP) $P2Y_{12}$ receptor on platelets for their life span, thereby inhibiting their activation and decreasing subsequent 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 [3,4,5,6].

Literature survey revealed that some analytical methods like LC-MS [7,8] have been reported for the estimation of Prasugrel and also HPTLC method was reported for its analysis [9] and one spectrophotometric method was reported [10]. Therefore the need for fast, low cost and selective method is obvious especially for routine Quality Control analysis of Pharmaceutical formulation. The present study describes simple, sensitive, accurate, rapid and economical spectrophotometric method for the estimation of Prasugrel in its formulation.



[5-[2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-yl acetate]

EXPERIMENTAL

INSTRUMENT

Elico double beam Ultraviolet-Visible double beam spectrophotometer SL-244 with 1cm matched quartz cells was used for all spectral measurements.

REAGENTS

All the chemicals used were of analytical reagent grade.

- **Phosphate buffer (pH 3.6):** It is prepared by dissolving 0.9 gm of anhydrous disodium hydrogen phosphate and 1.298 gm of citric acid monohydrate in sufficient water to produce 1000 ml.
- **Bromocresol green (0.2% w/v):** It is prepared by dissolving 0.2 gm in 100 ml of methanol.

- **Chloroform AR grade**

PROCEDURE

Standard stock solution

It is prepared by dissolving 25 mg of Prasugrel in 10 ml of methanol and the volume was made up to 25 ml with methanol to get a concentration of 1000 mcg/ml.

Assay procedure

Aliquots of standard drug solution of PRASUGREL containing 0.1-1.0 ml (100-1000 mcg/ml) were taken and transferred into series of graduated test tubes. To each test tube 1 ml of Bromocresol green, 4 ml of Phosphate buffer pH 3.6 and 10 ml of Chloroform were added. The solutions were shaken for 5 min and kept aside for the formation of colored complex for 30 min. The absorbance of the yellow colored chromogen was measured at 418 nm against reagent blank and a calibration curve was plotted. Similarly, the absorbance of the sample solution was measured and the amount of Prasugrel was determined by referring to the calibration curve.

Preparation of sample solution

Tablets containing Prasugrel were successfully analyzed by the proposed methods. Ten tablets of Prasugrel (PRASUTAB-5mg, ALEMBIC, Sunil Pharma) were accurately weighed and powdered. Tablet powder equivalent to 100 mg of Prasugrel was dissolved in 50 ml of methanol, sonicated for 15 min and filtered. The filtrate is combined and the final volume was made to 100 ml with methanol for the above method. The solution was suitably diluted and analyzed as given under the assay procedure for bulk samples. The analysis procedure was repeated three times with Tablet formulations and the results of analysis are shown in Table 2. None of the excipients usually employed in formulation of tablets interfered in the analysis of Prasugrel by the proposed method.

Recovery Studies

To ensure the accuracy and reproducibility of the results obtained, adding known amounts of pure drug to the previously analyzed formulated samples and these samples were reanalyzed by the proposed method and also performed recovery experiments. The percentage recoveries thus obtained were given in Table 2.

RESULTS AND DISCUSSIONS

In the present work a method has been developed for the estimation of Prasugrel from Tablet formulation. The developed method is based on formation of chloroform extractable

colored complexes with Bromocresol green. The conditions required for the formation of colored complexes were optimized. Statistical analysis was carried out and the results of which were satisfactory. Relative Standard Deviation values were low that indicates the reproducibility of the proposed method. Recovery studies were close to 100 % that indicates the accuracy and precision of the proposed method. The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table 1. The regression analysis using the method of least squares was made for slope (m), intercept (b) and correlation obtained from different concentrations and the results are summarized in Table 1.

In conclusion, the proposed method is simple, economical, sensitive, precise, reliable and reproducible for the routine estimation of Prasugrel in bulk as well as in tablet formulation.

Table 1- Optical characteristics and precision data

Parameters	Proposed method
λmax (nm)	418
Beer's law limit (mcg/ml)	100-1000
Molar absorptivity (I/mol.cm)	0.7431×10^3
Sandell's sensitivity (micrograms/cm^2/0.001 absorbance unit)	0.66
Regression equation* (Y) Slope (m)	 0.001
Intercept (c)	0.10
Correlation coefficient (r)	0.9989
Precision (% relative standard deviation)	1.33
Standard error of estimate	0.0524

*Y= mx+c, where X is the concentration in micrograms/ml and Y is absorbance unit

Table 2 - Assay of Prasugrel in tablet formulation

Tablet Formulation	Labelled amount (mg)	Amount obtained(mg)* by the proposed method	**% Recovery by the proposed method
1	5	4.54	97.6 %
2	5	4.85	98.06 %
3	5	4.90	98.1 %

*Average of three determinations
**After spiking the sample

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