

ESTIMATION OF PRASUGREL HYDROCHLORIDE IN BULK DOSAGE FORM BY UV

Dr. Juluri Krishna Dutta Tejaswi*

NRI College of Pharmacy, Krishna district, Vijayawada, Andhra Pradesh, India

Correspondence

Dr. Juluri Krishna Dutta Tejaswi*

Department of Pharmaceutical Analysis,
NRI College of Pharmacy, Agiripalli
Mandal, Krishna district Vijayawada,
Andhra Pradesh, India

✉ y2kteja@gmail.com

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ABSTRACT

Prasugrel is used to prevent blood clots in people with recent heart attack or with certain disorders of the heart. To optimize the diluent, various solvents were tested, the use of methanol resulted in no interference at λ_{\max} 218nm. The linearity was established by comparing various concentrations and absorbance's at absorption maximum. The linearity was found in the concentration range of 5 – 30 ppm. The limit of detection and limit of quantization values were found to be 1.209 ppm and 3.664 ppm. This indicates the sensitivity of the method. No interference peaks were found near the λ_{\max} during the estimation of the drug by the proposed UV method.

INTRODUCTION

Prasugrel, a thienopyridine derivative, is a platelet activation and aggregation inhibitor. FDA approved in 2009. Prasugrel⁽¹⁻²⁾ is an inhibitor of platelet activation and aggregation through the irreversible binding of its active metabolite to the P2Y12 class of ADP receptors on platelets. Healthy subjects, patients with stable atherosclerosis, and patients undergoing PCI show similar pharmacokinetics.

It is chemically 5-[2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydro thieno[3,2-c]pyridin-2-yl acetate Hydrochloride. Prasugrel Hydrochloride is a white to practically white solid. It also dissolves freely in methanol and is slightly soluble in 1- and 2-propanol and acetone. After through literature survey, the present method was developed as per ICH Guidelines⁽³⁻⁵⁾. In the present work, an attempt was made to provide a newer low cost UV spectrophotometric method for determination of Prasugrel Hydrochloride as shown in **Fig. 1**.

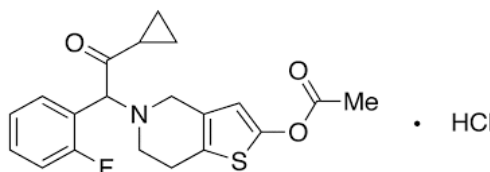


Fig. 1: Structure of Prasugrel Hydrochloride.

MATERIAL AND INSTRUMENT⁽⁶⁻⁸⁾

Prasugrel Hydrochloride was obtained from Sun Pharma, Baroda. Methanol used was Thermo Electron India Pvt Ltd; Lot No: 84776905-2. Ethanol used was Merck's Specialties Pvt Ltd; Batch no: SG0F600451.

Acetone used was Merck's Specialties Pvt ltd; Batch no: SF01600345. Single Pan Balance manufactured by SHIMADJU Corporation of model no AX200. UV-Spectrophotometer manufactured by ELICO SL159 India.

Preparation of drug in different solvents

Prasugrel Hydrochloride was known to be soluble in solvents like carbon tetrachloride, benzene, methanol, chloroform and acetone. In case of methanol the interactions between solvent peak and sample peak were lower compared to other solvents and hence methanol was selected as a solvent for estimating the various parameters of Prasugrel Hydrochloride.

Preparation of standard stock solution

Standard stock solution is prepared by dissolving 10 mg of Prasugrel Hydrochloride in methanol and the volume was made up to 100ml to obtain 100 ppm solution and dilutions were made.

Absorption maximum (λ_{Max})⁽⁹⁻¹¹⁾

The absorption pattern of resulting solution is measured against respective blank solution in UV range (200-400nm) and λ_{max} was found in each solvent. The λ_{max} was found at 218 nm in each of the solvent and it was compared with the UV cutoff and solvent peak as shown.

Assay of Prasugrel hydrochloride

20 tablets of Prasugrel Hydrochloride (EFIPLAT 10) were taken, and all the tablets were crushed to fine powder using a mortar and pestle. Powder equivalent to 10 mg of Prasugrel Hydrochloride was weighed and transferred in to a 100 ml volumetric flask. The contents were dissolved in methanol and sonicated for about 30 min and filtered through Whatmann.

METHOD VALIDATION⁽¹²⁻¹⁵⁾

Linearity

Aliquots of standard solutions of Prasugrel Hydrochloride ranging from 5 – 30ppm were transferred in to a series of 10 ml volumetric flasks. The volume of each flask was made up to the 10 ml mark with methanol and the absorbance were measured at 218 nm. A graph was drawn by plotting concentration on X axis and absorbance on Y axis and the graph has shown a good linearity with a correlation coefficient of 0.9967 as shown in **Fig. 2-3** and **Table 1**.

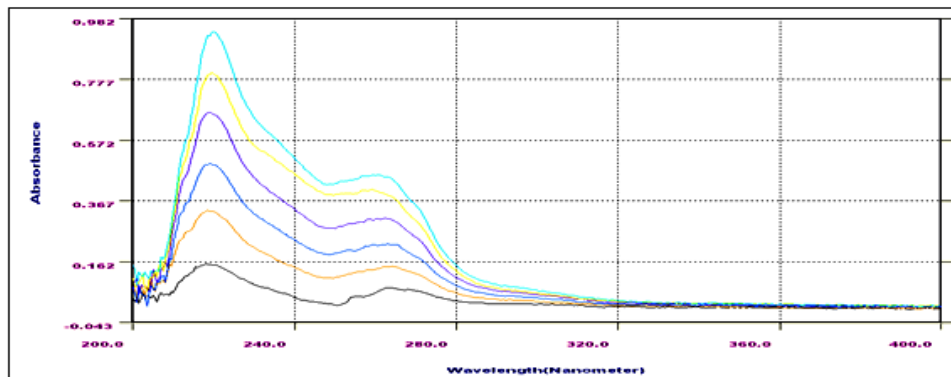


Fig. 2: Overlay Spectrum of Prasugrel Hydrochloride.

Table 1: Linearity Values of Prasugrel Hydrochloride.

S. No	Concentration (ppm)	Absorbance
1.	5	0.135
2.	10	0.256
3.	15	0.412
4.	20	0.561
5.	25	0.658
6.	30	0.798

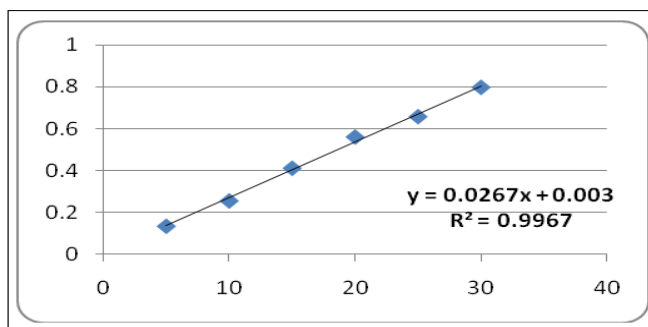


Fig. 3: Calibration Curve of Prasugrel Hydrochloride.

Precision - Repeatability

The absorbance was observed repeatedly six times under same experimental conditions as shown in **Table 2**. RSD for absorbance of six measurements was found to be not more than 1.0%.

Table 2: Precision Values of Prasugrel Hydrochloride.

S.No	Concentration (ppm)	Absorbance
1.	20	0.561
2.	20	0.562
3.	20	0.560
4.	20	0.560
5.	20	0.562
6.	20	0.563
Mean = 0.5613		
Standard deviation = 0.0012		
% Relative standard deviation = 0.213		

Precision - Intermediate Precision

a. **Analyst-Analyst:** Four samples of 20ppm concentration of Prasugrel Hydrochloride were prepared by four different analysts was observed under same experimental conditions as shown in **Table 3**.

Table 3: Precision Values – Analyst – Analyst of Prasugrel Hydrochloride.

S. No	Sample No	Concentration	Analyst 1	Analyst 2	Analyst 3	Analyst 4
1.	Sample 1	20	0.561	0.560	0.561	0.562
2.	Sample 2	20	0.562	0.560	0.562	0.561
3.	Sample 3	20	0.560	0.561	0.561	0.562
4.	Sample 4	20	0.563	0.563	0.562	0.561
Mean = 0.5613						
Standard deviation = 0.0009						
% Relative standard deviation = 0.16						

- b. **Spectrometer-Spectrometer:** Four samples of 20ppm concentration Prasugrel Hydrochloride were prepared and absorbance was observed using different equipments as shown in **Table 4**.

Table 4: Precision Values - Spectrometer-Spectrometer of Prasugrel Hydrochloride.

S. No	Equipment	Concentration	Absorbance-1	Absorbance-2	Absorbance-3
1.	Equipment-1	20	0.562	0.565	0.561
2.	Equipment-2	20	0.567	0.564	0.559
3.	Equipment-3	20	0.570	0.568	0.562
4.	Equipment-4	20	0.563	0.564	0.567
Mean = 0.5642					
Standard deviation = 0.0035					
% Relative standard deviation = 0. 62					

- c. **Day-Day:** Four samples of 20ppm concentration of Prasugrel Hydrochloride were prepared and absorbance was observed. Again three fresh samples of the same concentration were prepared on the following day and absorbance was measured as shown in **Table 5**.

Table 5: Precision Values - Day-Day of Prasugrel Hydrochloride.

S. No	Day	Concentration	Absorbance-1	Absorbance-2	Absorbance-3
1.	Day 1	20	0.561	0.563	0.564
2.	Day 2	20	0.555	0.552	0.558
3.	Day 3	20	0.561	0.563	0.564
4.	Day 4	20	0.555	0.552	0.558
Mean = 0.5588					
Standard deviation = 0.0047					
% Relative standard deviation = 0.84					

Precision

Reproducibility

Four samples of 20ppm concentration of Prasugrel Hydrochloride were prepared and absorbance was observed in different labs as shown in **Table 6**. RSD for measured absorbance was found to be not more than 1.0% in all the cases indicating that the method has good precision.

Table 6: Precision Values - Lab-Lab of Prasugrel Hydrochloride.

S. No	Lab	Concentration	Absorbance-1	Absorbance-2	Absorbance-3
1.	Lab -1	20	0.562	0.565	0.561
2.	Lab -2	20	0.567	0.564	0.559
3.	Lab -3	20	0.570	0.568	0.562
4.	Lab -4	20	0.555	0.552	0.558
Mean = 0.5642					
Standard deviation = 0.0035					
% Relative standard deviation = 0.62					

Accuracy

The accuracy of the method was determined by analyzing three solutions containing Prasugrel Hydrochloride in 75%, 100 % and 125% of the standard taken (20 ppm) as shown in **Table 7**. Mean recovery was found to be between 98% - 102% indicating that the test method has an acceptable level.

Table 7: Accuracy Values of Prasugrel Hydrochloride.

S.No	Concentration	Weight Taken	Absorbance	Weight Recovered	Percentage Recovery	Statistical Analysis		
						Mean	S.D	%R.S.D
1.	75%	22.59	0.419	22.50	99.58	99.97	1.361	1.36
2.	75%	22.60	0.421	22.61	100.05			
3.	75%	22.60	0.422	22.67	100.29			
4.	100%	30.12	0.568	30.47	101.17	100.2	0.799	0.79
5.	100%	30.13	0.561	30.13	100.00			
6.	100%	30.13	0.559	30.02	99.64			
7.	125%	37.65	0.700	37.58	99.82	99.96	0.14	0.14
8.	125%	37.65	0.702	37.69	100.10			
9.	125%	37.66	0.701	37.64	99.96			

Robustness

The absorbance of 20 ppm Prasugrel Hydrochloride solution was measured at different wavelengths. (218 +/- 5 nm) as shown in **Table 8**.

Table 8: Robustness Values of Prasugrel Hydrochloride.

S.No	Concentration (ppm)	Wavelength (nm)	Absorbance
1.	20	213	0.626
2.	20	214	0.627
3.	20	215	0.626
4.	20	216	0.627
5.	20	217	0.627
6.	20	218	0.628
7.	20	219	0.628
8.	20	220	0.627
9.	20	221	0.626
10.	20	222	0.625
11.	20	223	0.625
Mean = 0.626			
Standard deviation = 0.0010			
% Relative standard deviation = 0.159			

System Sensitivity and Stability

The linearity range of the standard can be found from linearity curve and accuracy data. The results were found to be linear in the concentration range of 5 – 30ppm.

a. Limit of Detection: Based on the standard deviation of the responses and the mean of the slopes, the detection limit was found.

$$\begin{aligned} \text{LOD} &= 3.3 \sigma / S \\ &= 3.3 \times 0.0096 / 0.0262 \\ &= 1.209 \text{ ppm} \end{aligned}$$

b. Limit of Quantification: The quantization limit can be quantitatively determined with suitable precision, accuracy and reliability by the proposed method.

$$\begin{aligned} \text{LOQ} &= 10 \sigma / S \\ &= 10 \times 0.0096 / 0.0262 \\ &= 3.664 \text{ ppm} \end{aligned}$$

c. Sandells Sensitivity: It was found using the mean of the slopes.

$$\text{Sandells sensitivity} = 0.001 / \text{Mean of slopes}$$

$$= 0.001 / 0.0262$$

$$= 0.0381 \mu\text{g} / \text{cm}^2 / 0.001 \text{ AU}$$

d. Determination of Molar Absorptivity ($A^{1\%}_{1\text{cm}}$):

$A = abc$, $a = A^{1\%}_{1\text{cm}}$, $b = \text{path length} = 1\text{cm}$, $c = \text{concentration in gm} / 100\text{ml} = 0.002$

$A = \text{absorbance} = 0.628$

$0.628 = a \times 1 \times 0.002$

$a = 314 \text{ Lit mol}^{-1} \text{ cm}^{-1}$

CONCLUSION

The proposed method was checked for the performance characteristics and has also been validated and the method can easily and conveniently be adopted for the estimation of Prasugrel Hydrochloride.

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