CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1323740

Available online at: http://www.iajps.com *Research Article*

METHOD DEVELOPMENT AND VALIDATION OF TICAGRELOR AN ANTIPLATELET DRUG BY SPECTROPHOTOMETRY IN BULK DRUG AND PHARMACEUTICAL FORMULATION.

P. Pravalika Reddy[1], Dr.G.Tulja Rani[2], Dr. Narottam Pal[3], B. Navya[4], A. Prathyusha[5]

Department of Pharmaceutical Analysis.

[1,2,4,5] Malla Reddy Pharmacy College, Dhulapally, Maisammaguda, Secunderabad-500100.

[3] Bhaskar Pharmacy College, Moinabad, Hyderabad.

Abstract:

In present work a simple, precise, accurate and cost effective extractive spectrophotometric method has been developed with Bromophenol Blue for determination of Ticagrelor in bulk and pharmaceutical formulations. It is based on the formation of an Ion Association complex between the drug and bromophenol blue in a buffer solution at pH 1.2 (0.1N HCl). The optimum conditions for the analysis of drug were established and λ max was found to be 430nm. The developed method was validated as per guidelines of the International Conference on Harmonization (ICH)[1] including parameters like linearity, accuracy, and precision, limit of detection and limit of quantification. Linearity range was found to be 100-500µg/ml and the regression equation was Y= 0.001963x-0.0463 with correlation coefficient of 0.999. From the results it was observed that good correlation exist between drug concentration and absorbance. The percentage recovery of Ticagrelor was found to be 100.3. The precision was evaluated and relative standard deviation (RSD) was less than 2%. The method was applied successfully to marketed formulation. The results suggest that this method can be employed for routine analysis of Ticagrelor in bulk and pharmaceutical formulations.

Keywords: *Ticagrelor, Spectrophotometic method, Bromophenol Blue, Validation.*

*** Corresponding author:**

P. Pravalika Reddy,
Malla Reddy Pharmacy College,
Dhulapally, Maisammaguda,
Secunderabad-500100

Please cite this article in press P. Pravalika Reddy et al., ***Method Development And Validation Of Ticagrelor An Antiplatelet Drug By Spectrophotometry In Bulk Drug And Pharmaceutical Formulation.,*** *Indo Am. J. P. Sci, 2018; 05(07).*

INTRODUCTION:

Ticagrelor is an antiplatelet drug. It is chemically known as (1S,2S,3R,5S)-3-[7 -[(1R,2S) -2 -(3,4-Difluoro phenyl)] - 5 -(propylthio) - 3H - [1,2,3] triazolo [4,5 - d] pyrimidin -3-yl] -5 (2-hydroxyethoxy) cyclopentane- 1,2 – diol. It is a P2Y platelet inhibitor indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS).Literature survey reveals few analytical methods like UV Spectrophotometric method[2], HPLC Methods[3-4] and Visible methods are reported. The aim of the present work is to develop a simple accurate and precise Spectrophotometric method for the estimation of Ticagrelor in bulk and pharmaceutical formulation using bromophenol blue as dye and to validate the developed method as per ICH guidelines.

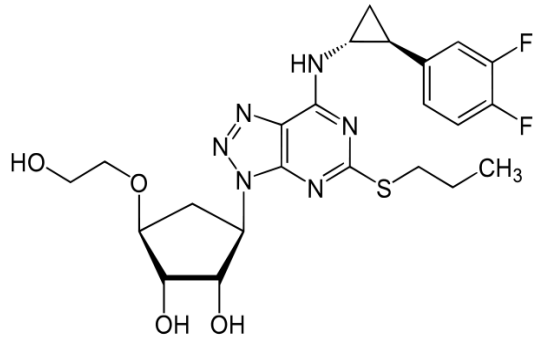

Fig 1 Chemical structure of Ticagrelor

MATERIALS AND METHODS:

UV Spectrophotometer from Shimadzu, Model no: UV-1800.

Ticagrelor was obtained from Dr. Reddy's Labs, Hyderabad and formulations from local pharmacy. Bromophenol Blue, chloroform and Methanol of Analytical Grade were purchased from Finar Reagents.

Experimental details:

Preparation of stock solution and dilutions:

Standard stock solution was prepared by dissolving 100mg of Ticagrelor in 100ml methanol to get a concentration of 1mg/ml. Different aliquots of drug solutions 1, 2, 3, 4,5ml were transferred to 10ml volumetric flask. Then add 3ml of 1%w/v bromophenol blue dye to each dilution finally make up the volume with buffer solution of pH 1.2(0.1N Hcl), then transfer the solution into 125ml separating funnel and add 10ml of chloroform. Contents were shaken for 1min, two layers are formed after proper shaking. In that lower layer was separated and collected into dry test tube. Then absorbance of the standard solution was scanned from 400-800nm to determine λ_{max}. The absorption maxima is found to be at 430nm as shown in Fig 2 and absorbance of all dilutions are measured at same wavelength.

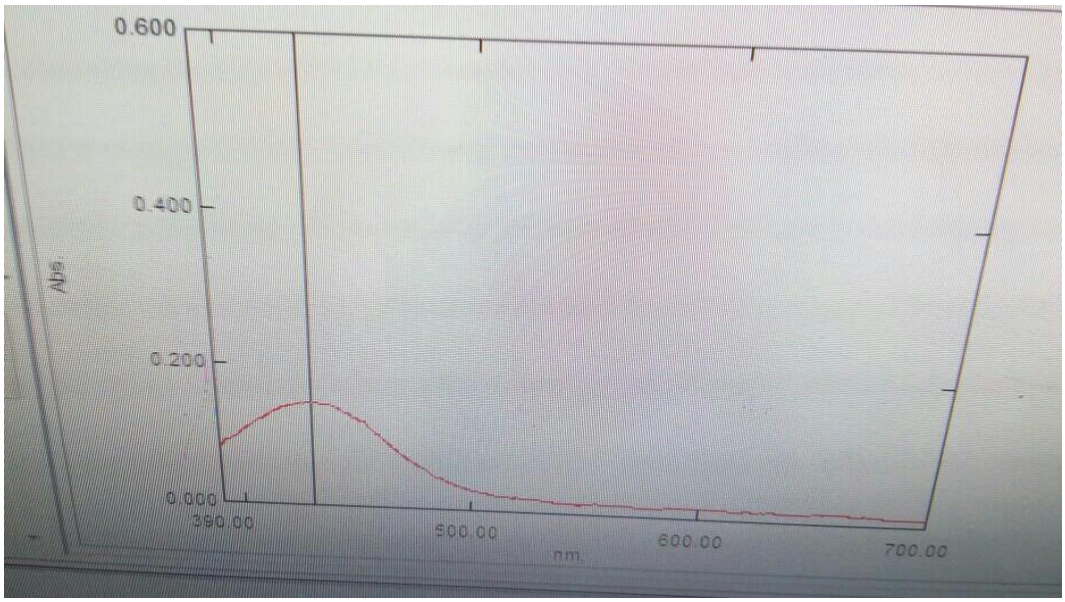

Fig 2: Absorption maxima

Fig 3: Showing series of dilutions

Application of proposed method for formulation

Procedure for assay of drugs in dosage forms:

Ten tablets of commercial samples of Ticagrelor are accurately weighed and powdered. A quantity of powder equivalent to 100mg of Ticagrelor was taken in a 100ml volumetric flask, sonicated for 30 min and the volume was made up to the mark with methanol and filtered using whatmann filter paper. An aliquot of drug solution of 2ml were transferred to 10ml volumetric flask, then add 3ml of 1%w/v bromophenol blue dye was added and volume was made upto the mark with buffer solution of pH 1.2(0.1N Hcl), and was transferred into 125ml separating funnel ,to this 10ml chloroform was added. Contents were shaken for 1min, two layers were allowed to separate and the chloroform layer was collected and absorbance of this solution was measured at 430nm.

RESULTS AND DISCUSSION:

Validation of the method:

The proposed method was validated as per ICH guidelines .The method was validated in terms of linearity, accuracy and precision**.**

Table 1: Linearity Data:

S.NO	CONCENTRATION (µg /ml)	ABSORBANCE
1	100	0.158
2	200	0.341
3	300	0.535
4	400	0.738
5	500	0.941

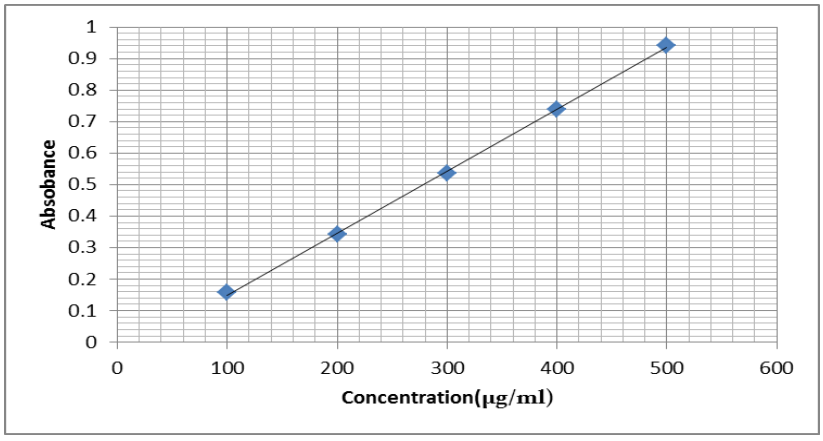

Fig 4:Calibration curve:

Accuracy:

Recovery studies were carried out by spiking the sample solution with standard solutions of Ticagrelor. At each level % recovery was determined three times. To ensure the reliability of the method recovery study was carried out by mixing standard quantity of standard drug with the pre analyzed sample formulation and the contents were re analyzed by proposed method.

Table 2: Recovery studies:

Sample	Concentration (µg/ml)		% Recovery of pure drug
	Pure drug	Formulation	
50%	100	200	100.3
100%	200	200	100.1
150%	300	200	99.9

The results of recovery studies showed that the % amount found is between 99.9% to 100.3%.

Precision

Precision is the method to check degree of repeatability of results. Precision of the method is carried out by intraday and interday studies. Six samples containing 200µg/ml solution of Ticagrelor was taken and analysed on the same day and on the consecutive days. The % R.S.D. value is found to be less than 2, so the method developed was precise. The results obtained are presented in the table 3.

Table 3: Intraday precision and Interday precision

S.NO	Intraday precision	Interday precision
1	0.343	0.341
2	0.342	0.342
3	0.343	0.339
4	0.341	0.341
5	0.342	0.340
Mean	**0.3422**	**0.3406**
SD	**0.00083**	**0.00114**
%RSD	**0.242**	**0.334**

Limit of detection (LOD) and limit of quantification (LOQ)

LOD and LOQ decide about the sensitivity of the method.LOD and LOQ were calculated by LOD=3δ/s and LOQ=10δ/s, respectively, where δ is the standard deviation and s is slope of calibration.

Robustness: The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage. Robustness is checked by varying the wavelength by ±1nm.

Table 4: Robustness

CONC(µg/ml)	WAVELENGTH (nm)	ABSORBANCE
100	429	0.151
100	430	0.158
100	431	0.155

Application of proposed method for pharmaceutical formulation:

Table 5: Analysis of formulation.

Dosage form	Label claim (mg)	Conc (µg/ml)	Amount found	% Recovery	Statistical analysis	
AXCER	90	200	199.84 199.82 199.86	99.92 99.91 99.93	Mean SD %RSD	99.92 0.01 0.0001

All the optical characteristics are presented in table 6.

Table 6: Optical characteristics

Parameter	Value
Absorption maximum (nm)	430 nm
Beer's law limit (µg/ml)	100-500µg/ml
Correlation coefficient (R^2)	0.999
Regression equation (Y= mX+c)	Y=0.001963x - 0.0463
Intercept(c)	0.0463
Slope(m)	0.001963
Sandell's sensitivity (µg/cm^2×0.001 absorbance unit)	0.632
LOD(µg/ml)	0.24
LOD(µg/ml)	0.82

CONCLUSION:

The developed Extractive spectrophotometric method was simple, sensitive cost effective with good accuracy and precision. The parameters were validated as per ICH guidelines. The findings of work suggest that the method may be applied for quality control estimation of Ticagrelor in bulk drug and pharmaceutical dosage forms. Hence this method can be used in the routine work of quality control aspects.

ACKNOWLEDGEMENTS;

The authors are thankful to the management of Malla Reddy Pharmacy College for their constant encouragement. We are also thankful to the Dr.Reddy Labs, Hyderabad for providing sample.

REFERENCES:

1.International conference on Hormonisation, Draft guideline on validation of analytical procedure :Definition and terminology ,Federal register,Volume 60,1995,11260.

2. Darshan pandya,Madhavi patel et.al.,UV-Visible spectrophotometric assay determination of oral antiplatelet drug ticagrelor in pharmaceutical formulation ;application to content uniformity.2016,8(1);316-321.

3.L.Kalyani, A. laxamanarao ,A validated stabilizing indicating HPLC method for determination of ticagrelor in bulk and its formulations, Iint J pharm 2013;3(3):634-642.

4. M.A.Ambasana, N.P.Kapuriya, An Improved assay method method for the estimation of ticagrelor hydrochloride by reverse phase liquid chromatography.IJPSR,2016;vol.7(5);2009-2014.

5.Praveen Kulkarni and gk.gajare: development and validation of RP-HPLC method for estimation of Ticagrelor in pharmaceutical dosage formulation.