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SPECTROPHOTOMETRIC DETERMINATION OF CLOPIDOGREL BISULFATE IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

A simple, sensitive and accurate spectrophotometric method was developed in ultraviolet region for the estimation of Clopidogrel bisulfate in pure drug, pharmaceutical formulation. Linear response obtained was in the concentration range of 25-50 µg/ml with correlation coefficient of 0.999 in 0.1 N HCl. Excellent recovery proved that the method was sufficiently accurate. There is no interference from any common pharmaceutical additives and diluents. Results of the analysis were validated by recovery studies according to ICH Q2B guidelines.

Keywords: Clopidogrel bisulfate, UV- Spectrophotometry, recovery, accuracy.

INTRODUCTION:

Clopidogrel bisulfate, chemically (+)-(S)- -(2-chlorophenyl)- 6,7-dihydrothieno [3,2-c] pyridine-5(4H)-acetic acid methyl ester sulphate is a potent oral antiplatelet agent often used in the treatment of coronary artery disease, peripheral vascular disease and cerebro vascular disease. The mechanism of action of clopidogrel is irreversible blockade of the adenosine diphosphate (ADP) receptor P2Y12 and is important in platelet aggregation, the cross-linking of platelets by fibrin. The blockade of this receptor inhibits platelet aggregation by blocking activation of the glycoprotein IIb/IIIa pathway. [1] It is not in any pharmacopoeia. Literature survey reveals the

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estimation of Clopidogrel bisulfate in pharmaceutical formulations by various chemometric[2], HPLC[3-6], HPTLC[7-8], TLC[9], and an LC- ESI-MS-MS[10] method was developed. There is no spectrophotometric method for Clopidogrel bisulfate, hence to develop simple, sensitive and accurate method.

MATERIAL AND METHOD

Clopidogrel bisulfate sample was supplied by Cadila Pharmaceutical Ltd. Ahmedabad, India as a gift sample and used as such 0.1 N HCl used and purchased from S. D. Fine Chemicals ltd., India. Spectral and absorbance measurements were made on a UV-Visible spectrophotometer (Shimadzu UV–1800) model with 10 mm matched pair of quartz cell and spectral band width of ±2nm.

Determination of λ max:-

Accurately weighed 10 mg of Clopidogrel bisulfate is transferred into a 100 ml volumetric flask and dissolved in 30 ml of 0.1 N HCl . It was then sonicated for 10 min, and made up to the mark with 0.1 N HCl to give a stock solution having 100 µg/ml concentrations. This solution was subjected to scanning between 200-400 nm and absorption maxima at 220 nm was determined. The effect of dilution maxima was studied by diluting the above solution to 20 µg/ml and scanned from 200-400 nm.

Standard solutions:-

Accurately weighed 100 mg of Clopidogrel bisulfate is transferred into a 100 ml volumetric flask and dissolved in 30 ml of 0.1 N HCl . It was then sonicated for 10 min, and made up to the mark with 0.1 N HCl to give a stock solution having 1000 µg/ml concentrations.

Working standard solution:

10 ml of stock solution was further diluted to 100ml with 0.1 N HCl to obtain a working standard solution containing 100 µg/ml.

Linearity and Calibration:-

The aliquots working standard solution was diluted serially with 0.1 N HCl to obtained the range 25-50 µg/ml. a calibration curve for Clopidogrel bisulfate was obtained by measuring the absorbance at the λ_{max} of 220 nm. It obeyed beer's laws in these concentration ranges[11]. Statistical parameters like slope, intercept, coefficient of correlation, standard deviation were determined.

Analysis of marketed tablet formulation: Determine the content of Clopidogrel bisulfate in conventional tablets (label claim: 75 mg Clopidogrel per tablet), twenty tablets were weighed.

Their mean weight was determined, they were finely powdered, and powder equivalent to 100 mg of Clopidogrel bisulfate was weighed and transferred into a 10 ml volumetric flask containing 10 ml 0.1 N HCl, sonicated for 10 min and the resulting sample solution was then filtered through Whattman filter paper (No. 41). The filtrate was further diluted to obtain the final concentration of 1000 µg/ml. Appropriate dilutions of Clopidogrel bisulfate were scanned over the range of 200-400 nm and the absorbance at wavelength 220 nm was measured. From calibration curve, the final drug concentration in tablet was calculated.

Method Validation

Method validation was performed in terms of specificity and selectivity, precision and accuracy, linearity [12].

Recovery studies:

Recovery studies were performed to judge accuracy of the method. 1ml of standard solution (100 µg/ml) was taken in three 10 ml volumetric flask and to it 80%, 100%, 120% of working standard solution (100 µg/ml) added respectively and made the volume upto the mark. The respective absorbance at 220nm was recorded against the blank. The amount of added concentration was determined from the obtained absorbance values and percent recovery was determined for each formulation.

RESULTS AND DISCUSSION

The UV scan of standard solution between 200-400 nm showed the absorption maxima at 220 nm, shown in Figure 1 and 2. The Beer's law was verified from the calibration curve by plotting a graph of concentration Vs absorbance. The plot shown in Figure 2. Regression analysis showed very good correlation. The calibration plot revealed zero intercept which is clear by the regression analysis equation Y= m X+C (where Y is absorbance, m is the slope and X is the concentration) the results obtained are depicted in Table. 1, 2, 3, 4. No significant variations were observed on interday and intraday analysis.

Table 1: Linearity regression data for Clopidogrel bisulfate

Parameters	Value for Clopidogrel bisulfate
Beer's law limit (µg/ml)	25-50 µg /ml
Correlation coefficient	0.999
Regression equation (Y*)	0.014x + 0.004
Slope	0.014
Intercept (A)	0.004

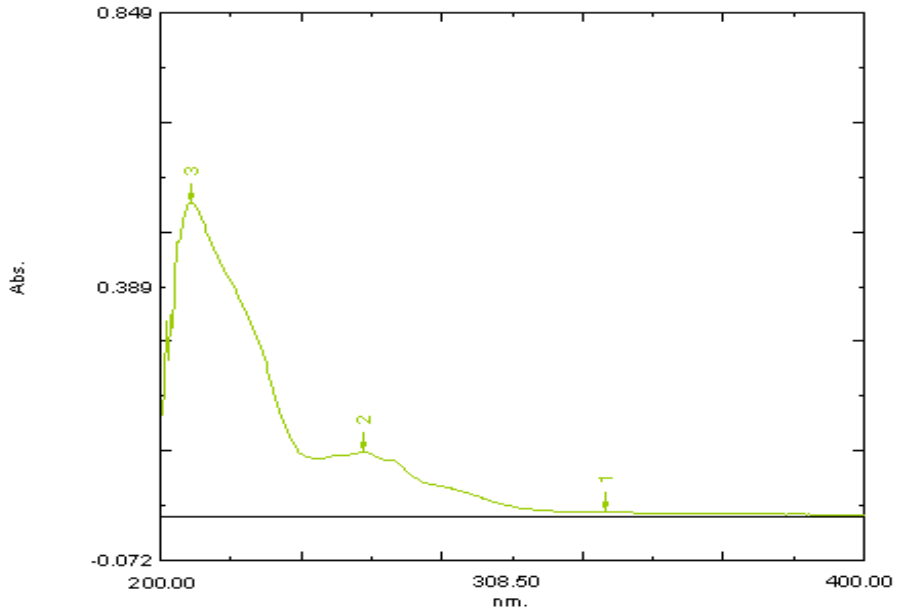

Figure. 1: Spectrum of Clopidogrel bisulfate at wavelength 200 to 400 nm

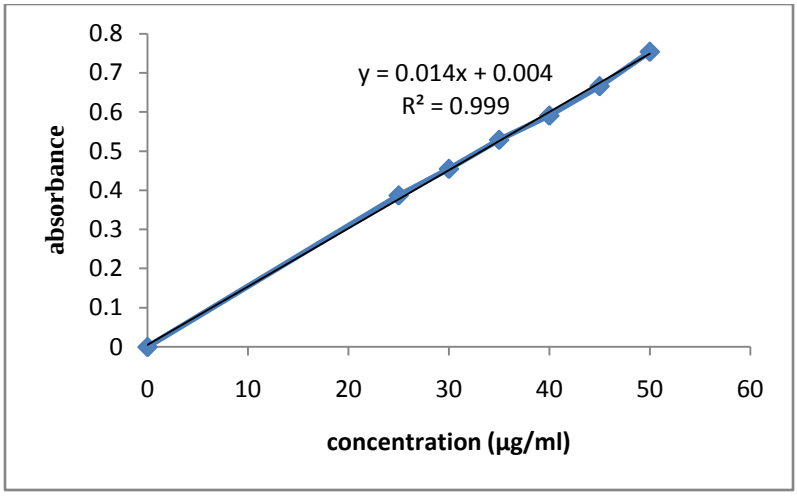

Figure. 2: Calibration curve of Clopidogrel bisulfate showing linearity relationship

Table 2: Results of analysis of laboratory samples

Label claim (mg/tab)	% Concentration estimated* (Mean ± % R.S.D.)
75 mg	74.76

* Average of nine determinations; R.S.D., Relative Standard Deviation

Table 3: Recovery data for Clopidogrel bisulfate

Level added (%)	Recovery (%)*	SD
80	98.45	0.9221
100	99.14	0.3129
120	99.84	0.2459

Table 4: Limit of detection and limit of quantitation for Clopidogrel bisulfate

L.O.D (µg/ml)	L.O.Q(µg/ml)
0.4890	1.4820

The spectrum of Clopidogrel bisulfate in 0.1 N HCl showed the absorption maxima at 220nm. No effect of dilution was observed on the maxima, which confirmed the maxima at 220nm. The statistical analysis of data obtained for the calibration curve of Clopidogrel bisulfate in the high level of precision for the proposed method. The coefficient of correlation was highly significant. The linearity range was observed between 25-50 µg/ml. the plot clearly showed a straight line passing through origin. The estimated method was validated by % RSD, accuracy, precision of the methods.

CONCLUSION

From the above result and discussion the method describe in this paper for the determination of Clopidogrel bisulfate from tablet formulation is simple, accurate, sensitive and economical. The proposed method utilizes inexpensive solvent. The proposed method could be applied for routine analysis in quality control laboratories.

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REFERENCES

1. RxList.com The Internet Drug Index for prescription drugs, medications and pill identifier, Available from: http://www.rxlist.com/plavix-drug.htm.
2. Rajput SJ, George RK, Ruikar DB. Chemometric Simultaneous Estimation of C lopidogrel Bisulfate and Aspirin from Combined Dosage Form. Indian J Pharm Sci 2008; 70: 450- 454.
3. Anandakumar K, Ayyappan T, Raghu RV, Vetrichelvan T, Sankar ASK, Nagavalli D. RP-HPLC analysis of aspirin and clopidogrel bisulphate in combination. Indian J Pharm Sci 2007; 69: 597-599.
4. Patel RB, Shankar MB, Patel MR, Bhatt KK. Simultaneous Estimation of Acetylsalicylic Acid and Clopidogrel Bisulfate in Pure Powder and Tablet Formulations by HPLC and HPTLC. JAOAC International 2008; 91: 750-755.
5. Vocilkova L, Opatrilova R, Sramek V. Determination of Clopidogrel by Chromatography. Cur Pharm Anal 2009; 5: 424-431.

6. Pankaj K, Kachhadia AS, Doshi HS. Validated Column HPLC Method for Determination of Aspirin and Clopidogrel in Combined Tablets in the Presence of Degradation Products Formed Under ICH Recommended Stress Conditions. JAOAC Int 2009; 92: 152-157.
7. Himani A, Neeraj K, Paradkar AR, Mahadik KR. Stability indicating HPTLC determination of clopidogrel bisulphate as bulk drug and in pharmaceutical dosage form. J Pharm & Biomed Anal 2003; 61: 581- 589.
8. Shinha PK, Mr inalini CD, Bothra KG. A validated stability indicating HPTLC method for determination of Asprin and Clopidogrel Bisulfate in combined dosage form. Eur J Chem 2009; 4: 152-160.
9. Anti D, Filipi S, Agbaba D. A simple and sensitive TLC method for determination of clopidogrel and its impurity SR 26334 in pharmaceutical product. Acta chromatogr 2007; 18: 199 206.
10. Patel NK, Subbaiah G, Shah H, Kundlik, Shrivastav M, Pranav S. Rapid LC-ESI-MS-MS Method for the Simultaneous Determination of Clopidogrel and its Carboxylic Acid Metabolite in Human Plasma. J Chromatogr Sci 2008; 46: 867-875.
11. Beckett AH, Stanlake JB. Practical Pharmaceutical Chemistry, CBS, Delhi. 4thEdn, 1998.
12. Validation of Analytical Procedures, Methodology Step-3 Consensus Guidelines, and ICH Harmonized Tripartite Guidelines, ICH Q2B, 1996.