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EXTRACTIVE SPECTROPHOTOMETRIC DETERMINATION OF CLOPIDOGREL BISULFATE BY ACID DYE DRUG REACTION WITH BROMOCRESOL BLUE IN BULK AND TABLET DOSAGE FORM

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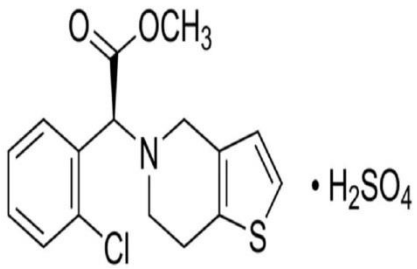
Abstract:
A simple, rapid, sensitive and reproducible extractive spectrophotometric method was developed for the determination of clopidogrel bisulfate (CPD). The method is based on the formation of ion pair complex between the basic nitrogen of the drug with bromocresol blue in acidic buffer. The formed complex was extracted with chloroform and measured at 412nm. Lambert Beer's law was obeyed by clopidogrel bisulfate (CPD) in the concentration range 5.0–25 µg/ml (r^2=0.9993). The parameters specified in ICH guidelines like linearity, accuracy, precision and specificity were also calculated. The % RSD was less than 2% which has shown high degree of precision for the proposed method. It has been applied successfully for the analysis of CPD in pure and in its tablet dosage form.
Keywords: Clopidogrel bisulfate, Bromocresol blue, Extractive spectrophotometric and ICH.

Introduction:

Clopidogrel is a prodrug which is activated in liver by cytochrome P450. It acts as platelet aggregation inhibitor and antithrombotic drug mainly used to prevent the clotting of blood and lowers the risk of coronary heart disease and cerebro vascular disease. It is chemically known as Chemically Clopidogrel is methyl (2S)-2-(2-chlorophenyl)-2-(6,7-dihydro-4H-thieno[3,2-c]pyridine-5-yl)acetate. (IP 2018) The extractive spectrophotometric methods are important for their sensitivity and selectivity in the estimation of drugs, the extractive spectrophotometric acid dye reaction method was employed in the present work for the estimation of CPD. The present research work and sensitive extraction visible spectrophotometric method for the determination of above cited drug. It concerns with the reaction of CPD with bromocresol blue followed by the acid dye reaction by using clopidogrel in 0.1 M HCl followed by the extraction of ion paired complex in chloroform. The method is fast and stable for successful determination of CPD in tablet dosage form. (Rele 2015)&(Sharma 2007).

Fig. 1 Structure of Clopidogrel Bisulfate



Materials and Methods:

Apparatus:

The proposed work was carried out on a Shimadzu UV Visible Spectrophotometer (Model 1800 series). The absorption spectra of reference and test solution was carried out in a quartz cell of 1 cm over a range 0f 200-800nm.

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Chemicals and Reagents:

Clopidogrel bisulfate was purchased by Tatvi chemicals, Bhopal. All chemicals including solvents and reagents were of analytical grade. All the solutions prepared for work should be protected from moisture and light. Tablet, Devigril 75(75 mg) was purchased from the local market.

Bromocresol blue solution: 1% solution of dye is prepared by dissolving 1 g of dye in distilled water and volume was made upto 100 mL with the same solvent.

0.1 M HCl solution: 8.5 mL of concentrated HCl is dissolved in distilled water and the volume was made upto 1liter to prepare the solution.

Preparation of Stock Solution:

Accurately weighed 100 mg of pure clopidogrel bisulfate(CPD) was transferred to a 100 ml of volumetric flask and dissolved in distilled water and finally the volume was made up to the mark with the same. The standard stock solution was prepared and labelled as 1000µg/mL.(Beckett 2002)

Preparation of Aliquots:

The standard stock solution is further diluted with distilled water to obtain 5, 10, 15, 20 and 25µg/mL. Detection wavelength of CPD was 412 nm. Then 3 mL of standard drug solution and add 1 ml of bromocresol blue dye solution and 3 mL of chloroform. Then the pale yellow layer of solution was pipette out and the absorbance was recorded by using 0.1 M HCl as a blank. The calibration curve was plotted with Absorbance Vs Concentration and the regression was calculated by the equation.

Analysis of Tablet:

20 tablets were weighed accurately to determine the average weight of tablets. Then tablets were crushed in a mortar and the powder equivalent to 75 mg of drug was transferred to 100ml standard flask. The powder was dissolved in 50 ml of 0.1 M HCl and made up to volume with of 0.1 M HCL. The sample was mixed thoroughly via sonication and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and 1 mL of dye solution was added and then 3 ml of chloroform to pipette out the pale yellow colored layer and analyzed for drug content by UV spectrophotometer at a λmax of 412 nm using of 0.1 M HCl as blank.

As per the International Conference on Harmonization (ICH) guidelines Validation of an analytical method has to be done Q2 (R1) (ICH, 2005). Following parameters of validation were evaluated: Linearity, accuracy (recovery study), precision, robustness, range LOD and LOQ.

Linearity for the preparation of calibration curve:

The linearity was evaluated on by taking the absorbance of aliquots of standard concentrations. Absorbances were recorded against 0.1 M HCl as blank. Calibration curve was plotted between concentrations versus absorbance. Spectra of CPD and calibration curve was shown in fig.2 and 3 respectively.

Fig.2 UV Spectra of Clopidogrel Bisulfate

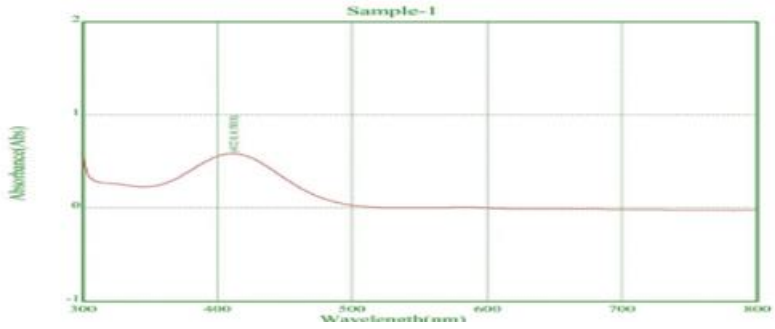

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Table 1 Linearity of Clopidogrel Bisulfate
(Average of 5 detrminations)

Standard Concentration µg/ml	**Mean**
0	0
5	0.142
10	0.282
15	0.446
20	0.5818
25	0.717
Correlation Coefficient	**0.9993**
Slope	**0.0289**
Intercept	**0.0012**

Fig.3 Calibration Curve of Clopidogrel Bisulfate

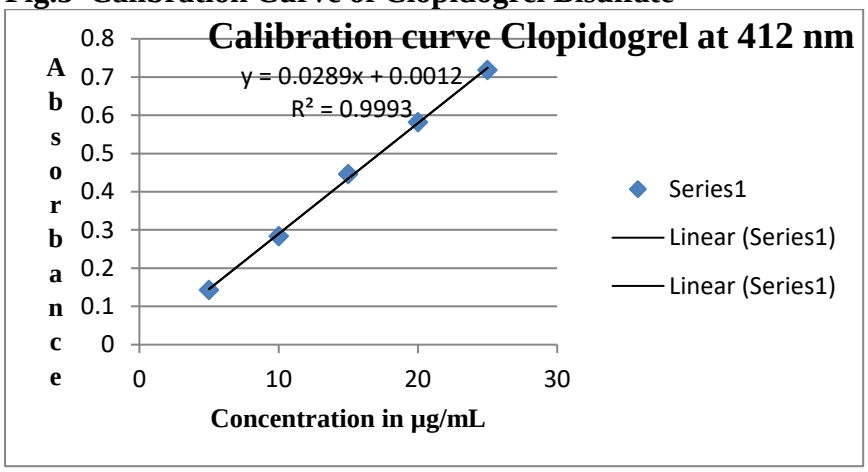

Table 2: Results of recovery studies on marketed formulations
(Average of 5 determinations)

Recovery level %	**% Recovery (Mean±SD)***
80	98.24±0.112
100	98.87±0.094
120	99.09±0.145

Table 3: Results of Precision Studies
(Average of 5 determinations)

Parameter	**(Mean±SD)***	**% RSD**
Repeatability	98.64±0.06	0.0608
Day to Day	99.23±0.15	0.151
Analyst to Analyst	98.21±0.13	0.132
Reproducibility	98.96±0.21	0.212

Result and Discussion:

The proposed spectrophotometric method is indirect and based on the determination of the clopidogrel bisulfate in marketed tablet using bromocresol green as chromogenic compound. Calibration curve has correlation coefficient (r^2) 0.9993 indicating good linearity over a concentration range of 5-25 µg/mL. The linear characteristics were reported in Table 1.The accuracy of the method was determined by investigating the recovery of drugs at concentration levels covering the specified range (five replicates of each concentration) Table 2. The %RSD was less than 1, showing high degree of precision of the above proposed method Table 3. The results of the method lie within the prescribed limit, showing that method is free from interference from all the excipients present in dosage form.

Conclusion:

Spectrophotometric analytical study is an important field in pharmacy since it offers distinct possibility in the assay of a particular component in dosage formulations. In the present study, the maximum color development of CPD with bromocresol green due to ion-pair complex formation was instantaneous, heating was not required. This method does not take more operator time and expertise such as HPLC and HPTLC. In terms of simplicity, rapidity, sensitivity, expense, and free from interference by common additives and excipients, especially with those based on chromatography or other reported spectrophotometric methods. The method is unaffected by slight variations in experimental conditions such as time and temperature. The proposed methods gave results with good accuracy to permit determination of low concentrations. The wide applicability of the described procedure for routine quality control is well established by the assay of CPD in pure form, as well as in tablets dosage forms.

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