

SPECTROPHOTOMETRIC DETERMINATION OF PRASUGREL IN BULK, DOSAGE AND BIOLOGICAL FLUIDS

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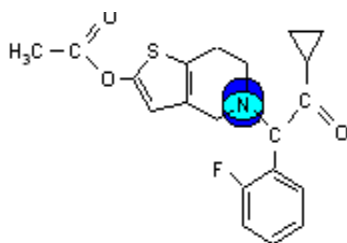
ABSTRACT

A new visible spectrophotometric method has been developed and validated for the estimation of Prasugrel hydrochloride in bulk, pharmaceutical dosage form and in biological fluids. The method makes use of ion pair complex formation between drug and bromophenol blue (BPB). The complex of Prasugrel showed λ_{max} at 416 nm. A good linearity with correlation coefficient within the limit was observed for the drugs at the concentration range of 50-100 $\mu\text{g/ml}$ for Prasugrel. The reagents used were optimized. The developed methods were assessed for precision, accuracy, sensitivity. Thus a simple, easy to perform, economical, precise and accurate visible spectrophotometric method has been developed for the estimation of Prasugrel in bulk, biological and solid oral dosage form.

Keywords: Ion – association complex, Platelet inhibitor, ADP

INTRODUCTION

Prasugrel^{1,2} is a platelet inhibitor belonging to the thieno pyridine class developed by Daiichi Sankyo Co. and produced by Ube and currently marketed in the United States in cooperation with Eli Lilly and Company for acute coronary syndromes planned for percutaneous coronary intervention (PCI). Prasugrel was approved for use in Europe in February 2009, and is currently available in the UK. On July 10, 2009, the US Food and Drug Administration approved the use of Prasugrel for the reduction of thrombotic cardiovascular events^{3,4} (including stent thrombosis) in patients with acute coronary syndrome who are to be managed with PCI.



Chemical Structure of Prasugrel

It acts as ADP receptor antagonists, which makes it different, is its safety profile and pharmacokinetic properties. Although clopidogrel is a widely prescribed agent, it has limitations such as: a modest anti-platelet effect, a delayed onset of action and considerable inter-patient variability in drug response. All these disadvantages motivated the development of more effective and predictable agents, such as the novel Prasugrel. Chemically it is 5-[2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4H, 5H, 6H, 7H-thieno [3,2-c]pyridin-2-yl acetate. It has a molecular mass of 373.441 and is sparingly soluble in water but completely soluble in methanol. It is available with brand names Effient and Prasita. Literature survey revealed very few methods for the estimation of Prasugrel hydrochloride such as LC-MS⁵, HPTLC⁶, UV-Visible spectrophotometric methods⁷⁻¹². The objective of this work is to develop new spectrophotometric method for its estimation in bulk and tablet dosage form and in biological fluid with good accuracy, simplicity, precision and economy.

MATERIALS AND METHODS

Apparatus

After due calibration of the instrument, spectral and absorbance measurements are made using Genesys 10 UV Spectrophotometer procured from Thermo Scientific company marketed by Merck. All the chemicals used were of analytical grade. All the solutions were

freshly prepared with milli Q water. Reagents were prepared afresh every day.

Preparation of Working Standard solution

100 mg of pure Prasugrel was transferred into a 100 ml volumetric flask. It was dissolved in 10 ml of methanol and then diluted with double distilled water up to the mark. 5 ml of the standard solution is transferred and diluted up to the mark in another 100 ml volumetric flask, and is used for preparing a standard curve.

Preparation of buffer solution and reagents

Sodium acetate- acetic acid buffer solution was prepared by mixing 84.7 ml of 0.1 M acetic acid and 15.3 ml of 0.1 M sodium acetate. Its pH was found to be 3.8. Dye solution was prepared by dissolving 100 mg of Bromo phenol blue in 5 ml of methanol and the solution was diluted to 100 ml in a standard flask.

Recommended Procedure for the determination of Prasugrel

Aliquots of standard Prasugrel (1 ml=100 μg) solution ranging from 1.5-2.0 ml were transferred into a series of 250 ml separating funnels. To that 1 ml of BPB (0.1%) and 2 ml of buffer was added and the total volume of the aqueous phase was made up to 10 ml with distilled water. About 10 ml of chloroform was added to each funnel and the contents were shaken for 2 minutes. The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 416 nm against the corresponding reagent blank. A calibration curve was prepared by plotting absorbance against concentration and the unknown was read from the calibration curve, or deduced using a regression equation, obtained from Beers' law data.

Procedure for pharmaceutical preparations

10 tablets (claiming for 10 mg of Prasugrel per tablet) were finely powdered and transferred into a small conical flask. It was then dissolved in 20 ml of methanol and 50 ml of distilled water. It was filtered through Whatmann filter paper No.42 into 100 ml volumetric flask. The filtrate was diluted to mark with distilled water. The stock solution was diluted to provide theoretical concentrations as mentioned above. The content of Prasugrel is determined with the above developed method.

Procedure for biological fluids

Aliquots of Prasugrel were transferred into separating funnel containing 5 ml of urine after deproteination using Trifluoroacetic acid. To this buffer and dye were added and extracted into chloroform and the amount was found from the regression equation.

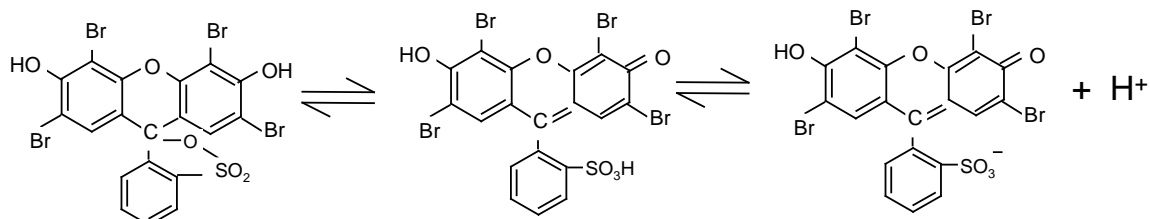
Recovery studies

Recovery studies were carried out for developed method by standard addition technique at three different concentration levels for each dosage form and biological samples. The resulting solutions were analyzed by proposed method.

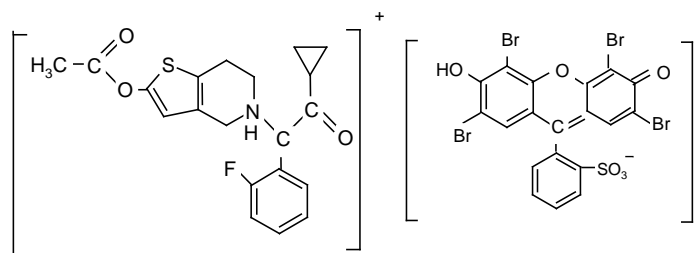
RESULTS AND DISCUSSION

The colorimetric method is based on formation of ion pair complex between the hetero atom of drug and dye (scheme 1). The complex is formed only in an acidic medium, provided by the addition of

acetate buffer solution. The complex is yellow in colour for which the maximum absorbance was observed at 416 nm give good linear relationship between absorbance and concentration. Any change in the volume or strength of the above reagents showed deviation from the linearity. Similarly the strength and volume of buffer and reagent were also optimized. It was observed that 2 ml buffer and 1ml reagent were optimal to ensure complete complexation and good colour intensity. Finally the concentration of the analyte was also studied. The correlation coefficient was found to be 0.999. The recovery was done by standard addition technique and results were found to be accurate (Table 1).



Scheme 1



Ion Pair Complex

Table 1: Spectral characteristics of Prasugrel hydrochloride

Parameters	Method
λ max (nm)	416
Beer's Law limits ($\mu\text{g/ml}$)	50-100mcg
Molar Absorptivity ($\text{L mol}^{-1}\text{cm}^{-1}$)	2.0721×10^4
Regression equation	$y = 0.0772x - 0.0145$
Standard Deviation	0.0787
Correlation Coefficient(r)	0.999
RSD (%) ^b	0.462
Recovery (%) ^c	99-100

Mean value of six determinations^b and Mean value of three determinations^c

CONCLUSION

New visible spectrophotometric method has been developed for the estimation of Prasugrel Hydrochloride. The method was found to be simple, selective, sensitive, accurate and reproducible. Thus the above proposed method could be applied for the quality control of Prasugrel Hydrochloride in pharmaceutical formulation in industry.

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