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Extractive Spectrophotometric Estimation of Saxagliptin In Pure and In Pharmaceutical Dosage Form

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ABSTRACT

Two simple and sensitive ion-pairing spectrophotometric methods have been developed for the assay of saxagliptin in pure form and in tablet dosage form. The developed methods involve formation of yellow colored chloroform extractable ion-pair complexes of the drug with Bromocresol Green (BCG) and Bromothymol Blue (BTB) in acidic medium. The extracted complexes showed absorbance maxima at 420, 415 nm for BCG, BTB, respectively. Beer's law is obeyed in the concentration ranges 10-50 µg ml^{-1} in both methods with molar absorptivity of 3.164 x 10^3, 4.305 x 10^3, L $mole^{-1}$ cm^{-1} for BCG and BTB, respectively. These methods have been successfully applied for the assay of drug in tablets. Results of analysis were validated statistically and through recovery studies.

Keywords: Saxagliptin, extractive spectrophotometry, tablet analysis.

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INTRODUCTION

Saxagliptin is chemically (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxy-1-adamantyl) acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile, previously identified as BMS-477118, is a new oral hypoglycemic (anti-diabetic drug) of the new dipeptidyl peptidase-4 (DPP-4) inhibitor class of drugs[1]. Saxagliptin is recently approved for the treatment of type 2 diabetes mellitus[2]. Literature survey reveals that the drug can be estimated only by LC-MS/MS[3], UV method[4] and no visible spectrophotometric methods have been reported. The present study describes simple, sensitive, accurate and precise spectrophotometric methods for estimation of saxagliptin in bulk and tablet formulation.

MATERIALS AND METHODS

Instrumentation

The spectrophotometric measurements were carried out using an Elico UV/Visible double beam spectrophotometer SL- 164 with 1 cm matched quartz cells. Digital Balance: BL-220H, Shimadzu was used. A calibrated digital pH meter was used for pH measurements.

Reagents

All chemicals were of analytical reagent grade of E.Merck. Distilled water was used to prepare all solutions. Freshly prepared solutions were always employed. Potassium hydrogen phthalate buffer solution of pH 4 was also prepared. 0.12% (w/v) BCG and BTB were prepared. Tablets containing 5 mg active material were kindly supplied from local pharmacy stores.

Standard solution

Standard solution of saxagliptin was prepared by dissolving 100 mg in 100 ml of methanol and diluting 10 ml of this solution to 100 ml with methanol (100 µg ml^{-1}).

Procedure for pure drug

From the 100 µg ml^{-1} solution, 10, 20, 30, 40 and 50 µg of drug was transferred to a series of separating funnels and 2 ml of pH-4 buffer was added to each and then 1ml of 0.12 % w/v BCG was added and shaken well and 10 ml of chloroform was added to each and shaken well and kept for few minutes. The chloroform layer was separated and passed through anhydrous sodium sulphate and the absorbance of the solution at 420 nm was measured against reagent blank. The same procedure was followed for BTB dye also and absorbance measured at 415 nm. The standard calibration plots for drug-BCG and drug-BTB complexes were prepared to calculate the amount of the analyte drug in unknown samples.

Procedure for the determination of saxagliptin in tablets

Tablets containing saxagliptin were successfully analyzed by the proposed methods. Twenty tablets of saxagliptin were accurately weighed and powdered. Tablet powder equivalent to 10 mg of saxagliptin was dissolved in 25 ml of methanol and sonicated for 15 minutes, filtered and washed with methanol, the filtrate and washings were combined and the final volume was made to 50 ml with methanol. The suitable aliquot of solution was analyzed as given under the assay procedure for pure form of drug.

RESULTS AND DISCUSSION

In this study, saxagliptin forms extractable ion pair complex with BCB and BTB dyes, which is soluble in chloroform and measured quantitatively at 420 nm and 415 nm respectively. The optimum conditions were establish by varying one parameter at a time and keeping the other parameters fixed and observing the effect produced on the absorbance of chromogen. Potassium hydrogen phthalate buffer was found to be suitable for these methods. Carbon tetrachloride, dichloromethane and ether like solvents are used to extract the ion pair complex, but chloroform was preferred to other solvents for these methods for its selective and quantitative extraction. Optimum conditions were fixed by varying one parameter at a time while keeping other constant and observing its effect on the absorbance at 420 nm for BCG and 415 nm for BTB. The pH was studied by extracting the colored complex species at different absorbance was observed at the pH 4.0 and using 2 ml of buffer. 1 ml of 0.12% (w/v) BCG and BTB was found to be optimal for complete complexation. Absorption spectra of the yellow drug-BCG and drug-BTB ion-pair complexes with their λmax at 420 nm, 415 nm shown in the figure 1 and 2 respectively.

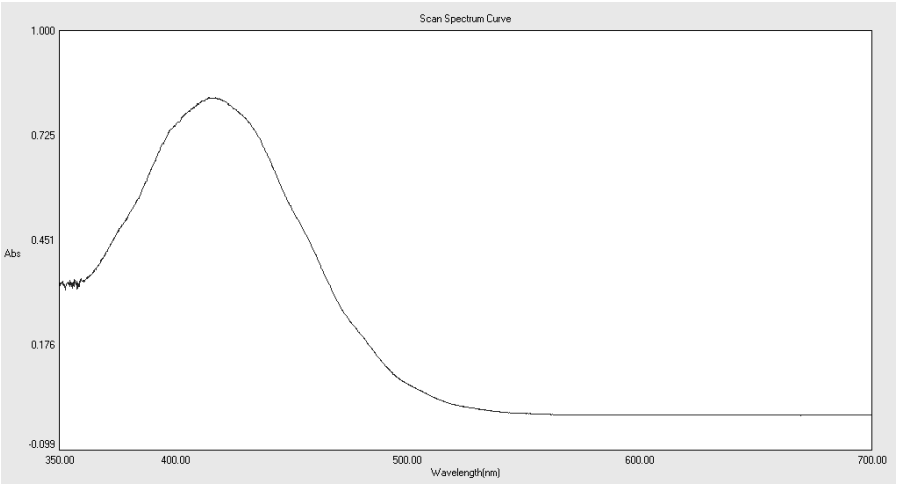

Figure 1. Absorption spectra of Saxagliptin -BCG complex extracted into 10 ml chloroform.

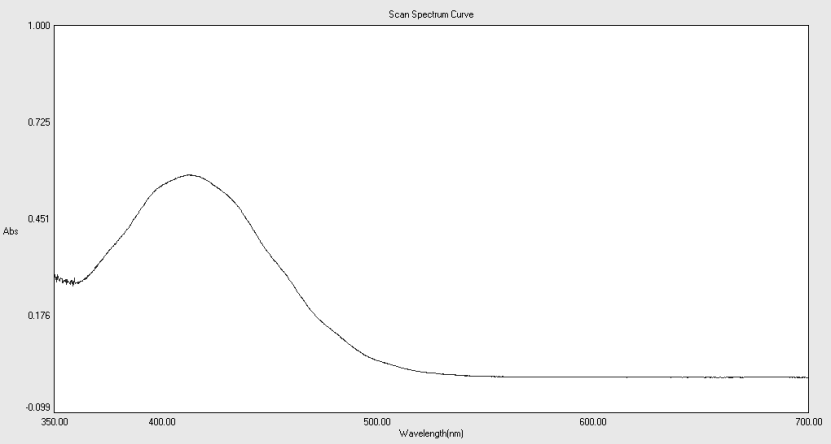

Figure 2. Absorption spectra of Saxagliptin -BTB complex extracted into 10 ml chloroform.

Beer's law range, molar absorptivity, Sandell's sensitivity, regression equation and correlation coefficient determined for the methods are given in Table 1. Recovery studies were performed to judge the accuracy of the methods. Recovery studies were carried out by adding a known quantity of pure drug to pre-analyzed formulations and the proposed methods were followed. From the amount of drug found, percentage recovery was calculated. The results of assay of tablets and accuracy studies are given in Table 2. Repeatability was determined by measuring absorbance for six replicates from independent stock solution. Inter-day and intra-day variation was taken to determine intermediate precision of the proposed methods (Table 2).

Table 1. Optical characteristics of proposed methods

Parameters	**BCG**	**BTB**
λ_{max} (nm)	420	415
Beer's law limit (µg ml^{-1})	10-50	10-50
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)	1.02 x 10^{-5}	1.38 x 10^{-5}
Molar absorptivity (l mol^{-1} cm^{-1})	3.218 x 10^{3}	4.342x 10^{3}
Limit of detection, µg ml^{-1}	0.4596	0.3546
Limit of quantification, µg ml^{-1}	1.3788	1.0637
Regression equation (Y = a + bc)		
Slope (b)	0.0101	0.0139
Intercept (a)	0.0016	-0.004
Correlation coefficient (r^2)	0.999	0.999

Table 2. Assay results, recovery and precision studies

Method	**Labeled amount (mg/ tablet)**	**(%) label claim* ± S.D**	**%Recovery***	**Precision**	
				Inter-day	**Intra-day**
BCG	5	99.83±1.4304	99.95 -100.01%	0.0031	0.0029
BTB	5	99.87±0.9527	99.95- 100.05%	0.0027	0.0025

* Average of six determinations. **SD of six determinations.

CONCLUSION

The proposed methods were simple, rapid, accurate, precise and inexpensive solvents were used. The methods can be used for routine analysis of saxagliptin in pure and tablets.

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