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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF SAXAGLIPTINE A NOVEL DIPEPTIDYL PEPTIDASE IV INHIBITORS IN PURE AND TABLET DOSAGE FORM BY UV-VIS SPECTROSCOPY

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ABSTRACT

A simple, rapid and accurate spectrophotometric method was developed for the determination of Saxagliptine in pure and tablet dosage form. Saxagliptine exhibiting absorption spectra of wavelength maxima 274 nm. This method has successfully used for the analysis of drug in marketed preparations in the range of 40-90 µg/ml with correlation coefficient of 0.987. The percentage recovery was found to be 99.42-100.26%. LOD and LOQ were found to be 7.14 and 21.63 µg/ml respectively. This method has been validated for linearity, accuracy and precision and found to be rapid, precise, accurate and economical and can be applied for routine estimation of Saxagliptine in solid dosage form. The validation of method was carried out utilizing ICH-guidelines.

INTRODUCTION

Saxagliptin (SXG) is chemically (1S, 3S, 5S)-2-[(2S)-2-Amino-2-(3 hydroxytricyclo [3.3.1.13, 7] dec-1-yl) acetyl]-2-azabicyclo [3.1.0] hexane-3-carbonitrile previously identified as BMS-477118.This is new oral hypoglycemic agent of the new dipeptidyl peptidase- 4 (DPP-4) inhibitor class of drugs. The empirical formula is $C_{18}H_{25}N_3O_2$, H_2O and the molecular weight is 333.43.The structural formula is:

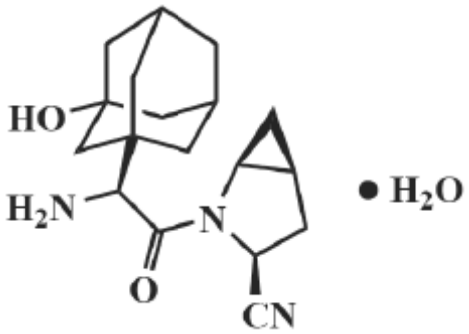

Fig 1 Structure of saxigliptine

SXG recently approved for the treatment of type-2 diabetes mellitus. It has been used in conjunction with exercise and diet to improve glycaemic control in patients with type 2 diabetes and is to be used with metformin, a sulphonyl urea or pioglitazone when blood sugar levels are not adequately controlled by one of these agents alone[1-8]. Literature survey reveals that the drug can be estimated only by LC-MS/MS[9], Spectrophotometric method[10] have been reported. The present study describes a simple, sensitive, accurate and precise spectrophotometric method for the estimation of SXG in bulk and tablet formulation.

EXPERIMENTAL

Apparatus

A Shimadzu model 1800 double beam UV-Visible spectrophotometer with spectral width of 1 nm, wavelength accuracy of ± 0.1 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software (version 2.34).

Reagents and Materials

All chemicals and reagents were used of AR grade. Authentic of SXG was obtained as gift samples from Matrix laboratories limited, Hyderabad and the tablet dosage form (Onglyza tablets) containing 5 mg SXG was procured from local market.

Selection of detection wavelength

Solution of drug in was scanned over the range of 200-400 nm. The absorbance maximum was found 274nm.

Preparation of standard stock solutions

SXG was weighed (100 mg) and dissolved in 100 ml of distilled water .The final concentration of solution containing 1000 µg/ml.

Preparation of working solutions

Aliquot from the stock solutions of SXG was appropriately diluted with distilled water to obtain working standard.

METHOD DAVELOPMENT AND VALIDATION

The developed method was validated for its linearity, accuracy, precision and specificity.

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of SXG. The results are shown in table 1.

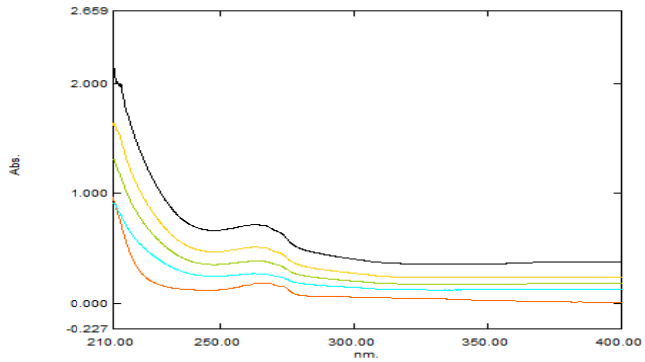

Fig 2 UV spectra of Saxagliptine

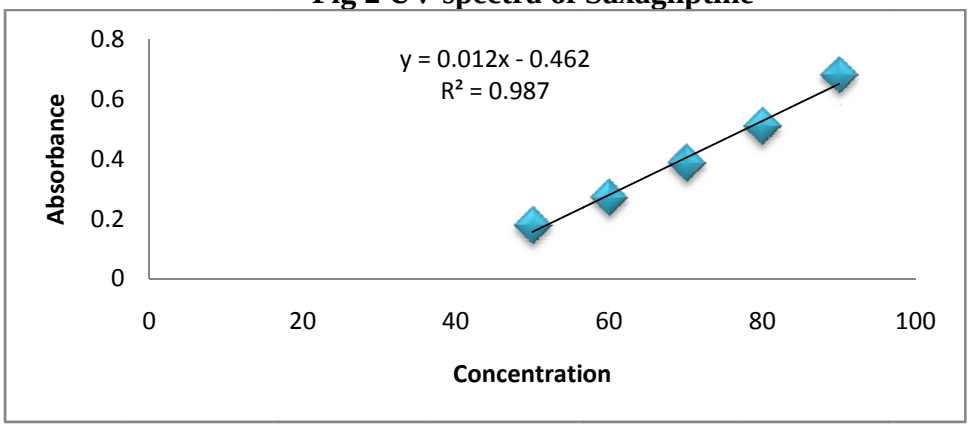

Fig 3 Calibration curve of saxagliptine

Table 1 Method validation Parameters

S.no	Parameter	Saxagliptine
1	Wavelength Maximum(nm)	274
2	Linearity range (µg/ml)	50– 90
3	Correlation coefficient	0.987
4	Slope (m)	0.012
5	Intercept (c)	0.462
6	LOD (µg/ml)	7.14
7	LOQ (µg/ml)	21.63
8	Sandell's sensitivity (mg/cm^2/0.001 absorbance unit)	0.195
9	Precision (% RSD) Repeatability Inter-day (n=5)	 0.330 0.280

LOD and LOQ

The LOD and LOQ were calculated from the equations, LOD =3.3 σ/S and LOQ = 10 σ/S, where σ is the standard deviation of the lowest standard concentration and S is the slope of the standard curve. The results are shown in table 1.

Precision

The precision of the proposed method was determined by analyzing different concentrations (50-90µg/ml) at different time intervals on same day (Intra-day precision) and on three different days (Inter-day precision). The results are shown in table 1.

Accuracy

To ascertain the accuracy of the proposed method, recovery studies were carried out by standard addition method. The results are shown in table 2.

Table 2 Accuracy

% Recovery study	Amount present	Amount added	Amount recovered	% Recovery
80	50	40	90.24	100.26
100	50	50	99.97	99.97
120	50	60	109.36	99.42
			Mean	99.58
			SD	0.616
			% RSD	0.618

*Mean of three determinations in each level

Specificity

Interference and non-interference of excipients and binders was confirmed by performing the specificity study. Specificity was performed by spiking placebo with standard drug.

Estimation of Saxagliptin from tablet.

Marketed preparation of SXG (ONGLYZA) selected for the purpose of analysis. Twenty tablets were accurately weighed and powdered quantity equivalent to 100 mg of SXG was transferred in 100 ml volumetric flask and sonicated for 30 min. Then the volume was made upto the mark with distilled water and the solution was filtered using Whatman filter paper no. 42 to obtain sample stock solution. 0.5 ml of filtrate was further diluted to 10ml with same solvent and absorbance of sample was measured against blank. The amount of SXG was calculated from the calibration curve. The results of assay are shown in table 3.

Table 3 ASSAY OF DOSAGE FORM (ONGLYZA)

Drug	Label Claim (mg/tablet)	Amount Estimated (mg/tablet)*	Percentage Label Claim (%)
Saxagliptine	5	4.95	99

***Mean of three reading

RESULTS AND DISCUSSION

As shown in fig. 2, Saxagliptin showed wavelength maxima at 274nm in distilled water. As shown in fig. 3 and table 1, the calibration curve was found to be linear in the range of 50-90 µg/ml with regression equation of y = 0.012X -0.462; (r^2 = 0.987) which clearly indicates linearity

of developed method. % Recoveries for Saxagliptin was found to be satisfied i.e. 99.42 to 100.26% as shown in table 2; clearly indicate that the developed method is accurate. Results of intra-day and inter-day precision is expressed in % RSD and found to be 0.330 and 0.280 respectively. As, % RSD is within the allowable limit of ≤ 2% it clearly indicate that the developed method is precise. Results of specificity study shows that the excipients present in the formulation do not interfere with the estimation of Saxagliptin. As, shown in table 3, assay result is in good agreements with the label claim. Hence, the proposed method can be successfully used for its analysis and quality control of marketed solid dosage preparation with good linearity, accuracy and precision.

CONCLUSION

From the above results it can be concluded that, the developed method is simple, rapid, accurate, precise, specific and economical. Hence, this method can be applied for quantitative analysis of Saxagliptin in bulk and pharmaceutical formulation like tablet dosage form.

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