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Development and Validation of a Simple and Rapid UV Spectrophotometeric Method for Linagliptin in Bulk and Marketed Dosage Form

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ABSTRACT

A simple, rapid, accurate and precise UV spectrophotometric Method for Linagliptin in Bulk and marketed tablet dosage form has been developed. The λmax of Linagliptin was found to be 295 nm. The method was linear in the range of 2-10 µg/ml presenting a good correlation coefficient (R2 = 0.9991). Method is validated as per ICH guideline and statistically significant as all the statistical parameters are within the acceptance range (%RSD < 2.0 and SD < 2. 0) for both Accuracy and precision.

Keywords: Linagliptin; UV - method; Development; Validation; Spectrometric method

INTRODUCTION

Linagliptin is a dipeptidyl peptidase4, also DPP-4 inhibitor developed by Boehringer Ingelheim for the treatment of type II diabetes. Linagliptin differs from other DPP-4 inhibitors in that it has a non-linear pharmacokinetic profile, is not primarily eliminated by the renal system, and obeys concentration dependent protein binding. Linagliptin was approved by the FDA on May 2, 2011[1].

Linagliptin is described chemically as 1H-purine-2, 6-dione, 8-[(3R)-3-amino-1-piperidinyl]-7-(2-butyl-1-yl)-3, 7-dihydro-3-methyl-1[(4-methyl-2-quinazolinyl) methyl]. The empirical formula is $C_{25}H_{28}N_8O_2$ and the molecular weight is 472.5. The structural formula is shown in figure 1. Linagliptin is a white to yellowish substance. It is very slightly soluble in water. Linagliptin is soluble in methanol, sparingly soluble in ethanol, very slightly in isopropanol and very slightly soluble in acetone [2].

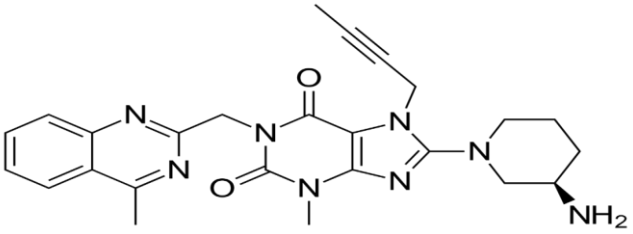

Figure 1: Chemical structure of Linagliptin

MATERIALS AND METHOD

Materials

Linagliptin was obtained as a gift sample from Micro Labs Ltd. Bangalore, INDIA. Tablets of Ondero were purchased from local market; each

tablets was labeled to contain 5 mg of Linagliptin. All chemicals and regents were of analytical.

Instruments

A single beam UV Visible Spectrophotometer (Systronic-119 Spectrophotometer) was used for the detection of absorbance, and Weighing Balance (SHIMADZU AY220) used for experimental purpose.

Chemical and Reagent

Disilled methanol, distilled water, whatman filter paper were used.

Method Development

Selection of solvent

Solubility of Linagliptin was performed in solvent methanol and UV spectra of drug in this solution were recorded. The absorbance value of drug was higher at λ_{max} with methanol as a solvent. Hence, methanol was selected as a solvent for further investigation as it is more economical.

Determination of Wavelength

An UV Spectrophotometric scanning (200-400) was carried out to select the wavelength (λ_{max}) for detection of Linagliptin, because of every drug should have adequate absorbance in the same solvent for the simultaneous determination.

Preparation of Standard stock solution

Weigh accurately about 10 mg of Linagliptin pure drug into a clean and dry 10 ml of volumetric flask. Dilute with 6 ml of distilled methanol (used as solvent) and shake well. Then the makeup volume to the mark with the same solvent. Further pipette out 1 ml of Linagliptin stock solution into a 10 ml of volumetric flask and dilute up to the mark with diluent (100µg/ml) [3].

Preparation of Sample Stock Solution

Twenty tablets were weighed accurately and their average weight was determined and crushed to powder. Then weigh accurately about 10 mg of powder sample into a clean and dry 10ml volumetric flask. Diluted with 10 ml of methanol. Then the volume was made up to 10 ml using methanol and mix well. Filter the solution through whatman filter paper. After filtration an aliquot of 0.4ml of this solution was transferred into a clean 10 ml volumetric flask and the volume was adjusted upto the mark with methanol. Absorbance of this solution at 295 nm was recorded [4].

Preparation of Calibration curve

Aliquots of 10 µg/ml from the standared stock of solution of Linagliptin were pipette into a six series of 10 ml of volumetric flasks. Then the mixture was serially with distilled methanol to get a Linagliptin solutions 2,4,6,8 and 10 µg/ml the content of each flask were mixed and immediately transferred to the spectrophotometric cell. The absorbance was recorded at its λ_{max} nm.

Validation of method as per ICH guidelines [5-7]

Linearity

The linearity of the purposed UV spectroscopic method was evaluated by analyzing different concentrations of standard solution of Linagliptin and by plotting absorbances of analyte against concentration of analyte. Beer's law was obeyed for method in the concentration range of 2-10 µg /ml. The linearity was evaluated by linear regression analysis, which was calculated by the least square regression method.

Precision

Precision studies were carried out to ascertain the reproducibility of the proposed Method. Intraday Precision study was carried out by preparing drug solution of three different concentrations (0.2, 0.6 and 1µg/ml of Linagliptin) and analyzing it at three different times in a day. Interday precision Study was carried out by preparing drug Solution of three different concentration (0.2, 0.4, and1µg/ml) and analyzing it at three different days.

Accuracy

The accuracy is the measure of how close of experimental value is to the true value. The recovery study was carried out as 50%, 100%, and 150% of the test concentration as ICH Guidelines. The recovery study was performed three times at each level. Accuracy was determined and expressed as percent recovery.

Limit of detection: (LOD)

Limit of detection is defined as the lowest concentration of analyte that gives a detectable response. LOD was determined by the analysis of sample with known concentration of analyte and by establishing and minimum level at each the analyte can be reliably detected.
LOD was calculated using the following equation.
$LOD = 3.3 \times S_o/b$,
Where, S_o and b are standard deviation of the response and the slope of calibration curve.

Limit of Quantification: (LOQ)

LOQ was determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte could be quantified with acceptable accuracy and precise.
LOQ was calculated using the following equations.
LOQ =10 × S_o/b,
Where, S_o and b are the standard deviation of the response and the slope of the calibration curve.

RESULT AND DISCUSSION

The main purpose of the current method is to develop a simple, sensitive and precise UV- Vis spectrophotometric method for the assessment of Linagliptin for the routine quantitative estimation of samples which will reduce dreary sample preparations, cost of resources manpower obligatory to perform analysis. The spectral analysis indicated that the λ_{max} of Linagliptin is 295 nm. Simple diluent distilled methanol was selected for the standard and sample solution of Linagliptin drug substance. Thus, the established UV-Vis spectroscopic method for the analysis of Linagliptin in its API from enables analysis of several samples at the same time to its simplicity in performing the analysis.

Table 1: Absorbance of Linagliptin solution of varying concentration at 295 nm

Sr. No	Conc. (µg/ml)	Absorbance
1	0	0
2	2	0.060
3	4	0.114
4	6	0.161
5	8	0.219
6	10	0.270

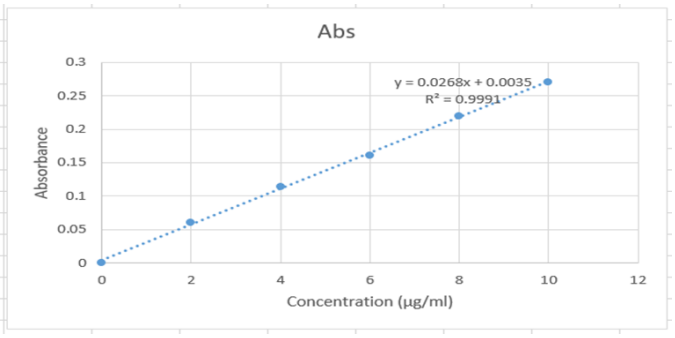

Figure 2: Calibration curve of Linagliptin

Table 2: Summary of Validated Parameters

Parameters	Methods
Wavelength detection	295 nm
Range	2-10 µg/ml
Correlation coefficient (r^2)	0.9991
Regression equation (y=mx+c)	Y=0.0268x+0.0035
Slope (m)	0.0268
Intercept (c)	0.0035
LOD	0.3271 µg/ml
LOQ	0.9909 µg/ml

Table 3: Precision (Intraday and Interday)

Conc. (µg/ml)	Intraday precision of Linagliptin			Interday precision of Linagliptin		
	Absorbance	Absorbance mean ± SD (N=3)	%RSD	Absorbance	Absorbance mean ± SD (N=3)	%RSD
2	0.061			0.051		
	0.063	0.06167 ± 0.00116	1.8725	0.050	0.05067 ±0.00058	1.1396
	0.061			0.051		
6	0.171			0.183		
	0.169	0.17067± 0.001528	0.8950	0.180	0.162 ± 0.003	1.8518
	0.172			0.182		
10	0.282			0.267		

	0.285	0.28234± 0.002517	0.8913	0.260	0.00360 ± 0.00360	1.3658
	0.280			0.265		

Table 4: Repeatability

Sr.No	Conc. (µg/ml)	Absorbance
1	10	0.271
2	10	0.278
3	10	0.279
4	10	0.272
5	10	0.276
6	10	0.271
Mean		0.2745
SD		0.003619
% RSD		1.31854

Table 5: Accuracy

Sr. No	Level Recovery	% Recovery ± SD	% RSD
1	50%	97.09 ± 0.01	0.0103
2	100%	97.90 ± 0.0057	0.005897
3	150%	98.17 ± 0.0057	0.005881

CONCLUSION

The developed UV spectrophotometric method was found to be simple, accurate, precise, easy, economic, reproducible and highly sensitive and can be used for routine determination of Linagliptin in bulk and tablet formulation.

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