INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Article

Development And Validation Of UV Spectroscopy For Determination Of Linagliptin In Bulk And Marketed Dosage Form

Reshma Dhakate*[1], Sachin Zende[2], Sakshi Renge[3], Jaydeep Pawar[4], Vikas Pawar[5], Nitin Salve[6]

[1]*Department of Pharmaceutical Chemistry, Sinhgad Institute of Pharmaceutical Sciences, Lonavala*
[2-6] *Student, Sinhgad Institute of Pharmaceutical Sciences, Lonavala, Pune.*

ARTICLE INFO

Received: 16 Feb 2024
Accepted: 20 Feb 2024
Published: 21 Feb 2024
Keywords:
Linagliptin, Development, Validation, Absorbance
DOI:
10.5281/zenodo.10688773

ABSTRACT

A simple, robust, precise UV spectroscopic method for quantitative determination of Linagliptin in bulk and marketed dosage form was developed . In this research work, method involved optimization of experimental conditions such as selection of wavelength, selection of solvent and linearity range. Calibration curve of standard solutions was prepared and various validation parameters were assessed. Linagliptin shows maximum absorbance at λmax 297nm. Linear relationship observed in the range 2-12 µg/ml showing correlation coefficient (r2) 0.9998. The accuracy of methods was assessed by recovery studies and found to be within range 98-102 %. The developed method was validated with respect to precision, linearity, LOD, LOQ, Repeatability. The obtained results were validated as per ICH guidelines. This developed method can be employed for determination of Linagliptin from marketed formulation with no any interference from excipients.

INTRODUCTION

Linagliptin or 8-[(3R)-3-aminopiperidin-1-yl]-7-but-2-ynyl-3-methyl-1-[(4-methyl-Quinazolin-2-yl) methyl] purine-2,6-dione (fig 1.) is an antidiabetic drug acting through inhibiting dipeptidyl peptidase-4, an enzyme that degrades the incretin hormones glucagon-like peptide-1 and glucose-dependent insulinotropic hormone. Linagliptin is soluble in methanol sparingly soluble in ethanol; very slightly soluble In isopropanol and the solubility in water is<1 mg/ml. When the produced insulin is not adequately use by the body or if pancreas is unable to produce insulin, a chronic disease occurs called diabetes. It refers to various metabolic disorders and if left untreated, characterized by hyperglycemia. Diabetes may causes serious complications like vision loss, nerve damage, kidney failure, stroke and heart attack. With the increase in diabetes

***Corresponding Author:** Reshma Dhakate
Address: *Department of Pharmaceutical Chemistry, Sinhgad Institute of Pharmaceutical Sciences, Lonavala*
Email : rpdhakate.sips@sinhgad.edu

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

cases in the world, the usage of antidiabetic drugs is also increasing. Therefore, the use of Linagliptin, as an antidiabetic agent, is increasing. As it is well known, dosage is a very important criterion for active drug ingredients. While the desired treatment cannot be provided below a certain dose, serious toxic effects can be observed and even deaths can occur in cases of overdose. This shows the necessity and importance of drug analysis and thus developing analysis methods. Up to now, mostly chromatographic technique have been developed for the quantification of Linagliptin. However, only a few spectroscopic methods were developed for Linagliptin analysis . Since UV spectroscopy has such advantages as low cost and easy application, developing a new spectroscopic analysis method is very useful. The aim of the present research is to develop a simple, rapid and reproducible UV spectroscopic method for estimation of Linagliptin in marketed dosage form. The objective of present analytical technique validation was to show that it is reasonable for estimation purpose and will be useful for the analytical studies of Linagliptin.

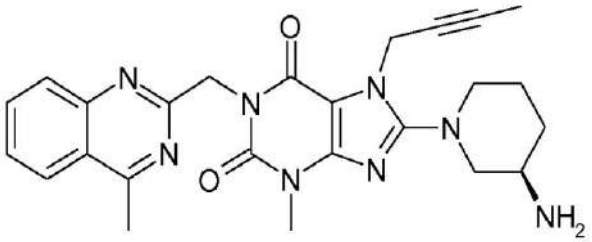

Fig 1. Structure of Linagliptin

MATERIAL AND METHODS

Materials and Reagents:

Linagliptin was received as a gift sample from Alkem Laboratories Limited, Mumbai, India which was used as a standard reference. Tablets of Ondero were purchased from local pharmacy, each tablet was labeled to contain 5 mg of Linagliptin. Analytical grade methanol was used for this experiment.

Instruments

A single beam UV Visible Spectrophotometer (Lab India Spectrophotometer) with two quartz cells or cuvettes was used for the detection of absorbance. Weighing Balance (Shimadzu AY220) used for experimental purpose. Ultrasonicator (Power Sonic 405, China) used for sonicating drug and sample solution.

Determination of maximum wavelength (λmax)

Appropriate dilutions of Linagliptin were prepared. An UV scanning (200-400nm) was carried out to choose maximum wavelength (λmax) for determination of linagliptin, because every drug should have adequate absorbance in the same solvent for simultaneous determination It was detected that the drug showed λmax at 297 nm. It was selected for detection of absorbance. Its spectra is shown in Fig 2.

Selection of Solvent:

Solubility test was performed in distilled water and methanol. UV spectra of drug in this solution were recorded. The absorbance value of Linagliptin was higher at 297nm with methanol as a solvent. Hence, Methanol was selected as a solvent for further investigation as it is more reliable.

Preparation of Standard Stock Solution:

About 10 mg of the Linagliptin was weighed and transferred in a dry and clean 10 ml volumetric flask. Then dissolved it with 6 ml of methanol and shake well. After that volume of solution were make up to 10 ml. Take 1 ml of this solution into another clean and dry 10 ml volumetric flask and diluted with methanol up to the mark to obtain a solution having concentration 100 ug/ml.

Preparation of Sample Stock Solution:

Twenty tablets were discarded from the strips and each tablet were weighed accurately. The average weight was determined and was found to be 180 mg. They are crushed into the powder form. Then weigh accurately 360 mg of tablet powder sample (equivalent to 10 mg of API) into a clean and dry 10 ml of volumetric flask. Diluted with 10 ml of methanol and the flask was kept in ultrasonic bath for shaking. Filter the solution through whatman filter paper. After filtration an aliquot of 0.4 ml of the solution was transferred into a clean 10 ml volumetric flask. The volume was made up to the mark with methanol. Absorbance of this solution were recorded at 297 nm.

Preparation of Calibration Curve:

Aliquots of 10 µg/ml from the standard stock solution of drug were taken using micropipette as 0.2ml, 0.4ml

0.6ml 0.8ml 1ml and 1.2 ml into a six series of 10 ml volumetric flasks. Then the volume was adjusted up to the mark to get a solutions 2, 4,6,8,10,12 µg/ml respectively. After mixing with methanol immediately transferred into cuvette and absorbance were recorded at 297 nm.

Method Validation

The developed method was validated for accuracy, precision, Linearity, Limit of detection, Limit of Quantification and Repeatability according to the ICH Q2 (R1) guidelines of validation of analytical procedures.

Accuracy

Accuracy refers to the degree of closeness of measured or calculated quantity to its actual value or true value. The recovery study was carried out as 80%, 100% and 120% of the test concentration as mentioned under ICH Q2 (R1) Guidelines. It was carried out for three times at each level. Accuracy was measured and expressed as percent recovery.

Precision

It refers to the degree to which repeated measurements under unchanged conditions shows the same results. It is consistency or reproducibility of results. Precision is crucial in ensuring the reliability and consistency of experimental data, numerical calculations and technological specifications. Precision was determined by intra-day and inter-day study.

Linearity

Linearity is a fundamental concept in analytical chemistry that refers to the ability of an analytical method to provide results directly proportional to the concentration of a substance within a given range. It is a crucial characteristic for ensuring the accuracy and reliability of quantitative measurements. A linearity correlation coefficient above 0.999 is acceptable for most methods, especially for major components in assay methods.

Limit of Detection

Limit of detection refers to the lowest concentration or amount of a substance that can be reliably detected, identified and quantified by a particular analytical method. The LOD is typically established by analyzing a series of samples with known low concentration of the target substance.

Limit of Quantification

It is a critical parameter in analytical chemistry that defines a lowest concentration or amount of substance that can be reliably measured and quantified with acceptable accuracy and precision. It allows researchers to make uniform decisions based on accurate and reproducible quantitative data

Repeatability

Repeatability refers to the ability to obtain consistent results when measuring the absorbance of a sample multiple times under the same conditions.

RESULTS AND DISCUSSION

The absorption spectra were measured in the wavelength region of 200-400 nm in UV method, the detected absorption maxima curve was shown in figure 2. The proposed method follows Beer's law in the concentration range of 2-12 µg/mL with good correlation coefficient of R2 =0.9993. Calibration data is presented in table 1. Beer's law range was confirmed by the linearity of the calibration curve of Linagliptin was shown in figure 3. The essential characteristics and the data concerning to the proposed method is represented in table 2. Precision of the method was reported in terms of relative standard deviation and it should be validated by evaluating minimum of 3 determinations for intraday and interday over which shows % RSD less than 2 indicates that the method was precise and the obtained results are presented in table 3 and table 4 respectively. Recovery studies were carried out for the developed method by addition of known amount of standard drug solution of Linagliptin to pre-analysed tablet sample solution at three different concentration levels. The resulting solutions were analysed by the proposed methods. The recovery (table 5) was in the range of 99 to 101 percentages. The limit of detection and limit of quantitation for estimation of Linagliptin were 0.7778 µg/mL, 2.3571 µg/mL respectively. The repeatability of the method was evaluated by determining absorbance for 9 times of 4 µg/ml solution at 297 nm. The percent relative standard deviation (% RSD) was calculated, the results are tabulated in table 6. The developed method was applied to the analysis of tablet formulations which was found to be within the proposed limits and the mean % assay value was found to be 99.09 %. The assay results are given in table 7. The developed method has good

linearity, accuracy and precision results indicates that the high quality of the method.

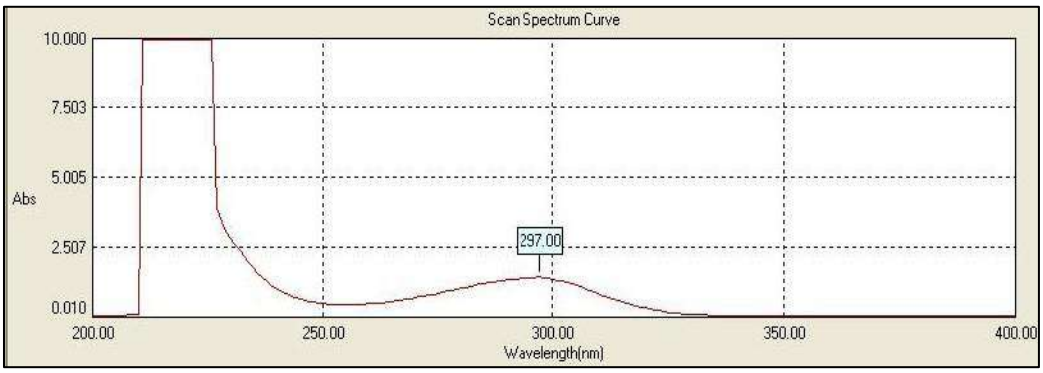

Fig 2. λmax Curve (297 nm)

Table 1. Concentration and absorbance of Linagliptin solution

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.085
3	4	0.156
4	6	0.223
5	8	0.306
6	10	0.377
7	12	0.448

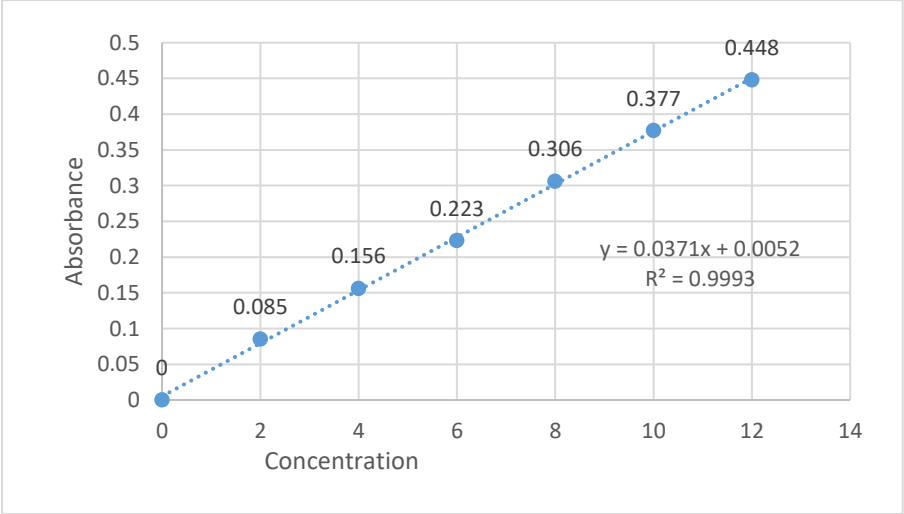

Fig 3. Calibration curve of Linagliptin

Table 2 Calibration curve of Linagliptin

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.085
3	4	0.156
4	5	0.223
5	8	0.306
6	10	0.377
7	12	0.448

Table 3. Summary of Validated Parameters

Parameters	Methods
Wavelength	297 nm
Linearity	2-12 µg/ml
Correlation Coefficient (r2)	0.9993
Regression Coefficient (y=mx+c)	0.0371x+0.0052
Slope (m)	0.0371
Intercept (c)	0.0052
LOD	0.7778 µg/mL
LOQ	2.3571µg/mL

Table 4. Intraday Precision

Sr. No.	Concentration (µg/ml)	Absorbance			Average	SD	%RSD
1	2	0.085	0.084	0.084	0.08433	0.000577	0.6846
2	6	0.223	0.220	0.219	0.220	0.002082	0.9434
3	10	0.388	0.387	0.383	0.386	0.002646	0.6854

Table 5. Interday Precision

Sr. No.	Concentration (µg/ml)	Absorbance			Average	SD	%RSD
1	2	0.085	0.083	0.082	0.08333	0.001528	1.833
2	6	0.223	0.218	0.216	0.219	0.003606	1.646
3	10	0.388	0.380	0.377	0.38166	0.005686	1.489

Table 6. Accuracy

Level	% Recovery			Average	SD	% RSD
80%	99.65	99.56	99.68	99.63	0.0624	0.0627
100%	100.65	100.45	100.62	100.57	0.1135	0.1112
120%	100.58	100.73	100.69	100.66	0.0776	0.0772

Table 7. Repeatability

Sr. No.	Concentration (µg/ml)	Absorbance	Average	SD	% RSD
1	4	0.156	0.15622	0.001716	1.098
2		0.156			
3		0.155			
4		0.160			
5		0.158			
6		0.155			
7		0.155			
8		0.156			
9		0.155			

Table 8. Potency Determination

Sr. no.	Assay	Concentration (µg/ml)	Label claim (mg)	% Assay	Amount found (mg)	Mean	SD
1	Assay-1	4	5	98.87	4.943	4.954	0.0756
2	Assay-2			97.71	4.885		
3	Assay-3			100.7	5.035		

CONCLUSION

The proposed UV spectroscopic method presented in this paper has advantages of simplicity, sensitivity, accuracy and cost effective for quantitative determination of Linagliptin in bulk and marketed formulation. This developed and validated method can be used for quality control of Linagliptin.

REFERENCES

1. Jain PS, Chaudhari AJ, Patel SA, Patel ZN, Patel DT. Development and validation of the UV-spectrophotometric method for determination of terbinafine hydrochloride in bulk and in formulation. Pharm Methods. 2011;2(3):198-202
2. Sharma Shivani, Goyal Swapnil, Chauhan, Kalindi. A review on analytical method development and validation. International Journal of Applied Pharmaceutics. 2018;10(6):8-15
3. Sujan Banik, MD Masud Kaisar, Mohammad Salim Hossain. Development and Validation of a Simple and Rapid UV Spectrophotometer Method for Assay of Linagliptin in Bulk and Marketed Dosage Form. Indian Journal of Novel Drug Delivery. 2013;5(4):221-224
4. Rane SS, Chaudhari RY, Patil VR, Barde LG, Development and validation of UV spectrophotometric method for simultaneous estimation of Empagliflozin and Linagliptin in bulk drugs and pharmaceutical dosage form, DIMPSIJ. 2021; 01(01):44-54
5. Avinash C, Gandhimathi R. Development and Validation of Analytical Method for Linagliptin Drugs in Pharmaceutical Dosage form by RP-HPLC. International Journal of Pharmaceutical Quality Assurance. 2023;14(1):203-207
6. Mishra AK, Kumar A, Mishra A, Mishra HV. Development of ultraviolet spectroscopic method for the estimation of metronidazole benzoate from pharmaceutical formulation. J Nat Sci Biol Med. 2014;5(2):261-264.
7. ICH Tripartite Guideline Q2 (R1), Validation of analytical procedures: text and methodology. International Conference on Harmonization (ICH), Geneva, Nov 2005.
8. Amruta Dalal, Varsha Tegeli, Rajashri Waghmode. Development and Validation of a Simple and Rapid UV Spectrophotometric Method for Linagliptin in bulk and marketed dosage form. Der Pharma Chemica. 2021;4(2):23-26
9. Govind Verma and Manisha Mishra. Development and optimization of UV-Vis spectroscopy-a Review. World J. Pharm. Res. 2018;7(11):1170-1180.
10. Manish Mishra, Govinda Verma. Analytical method development and validation for determination of Linagliptin in bulk and dosage form by UV spectroscopy. Journal of Emerging Technologies and Innovative Research. 2018;7(11):908-912.

HOW TO CITE: Reshma Dhakate, Sachin Zende, Sakshi Renge, Jaydeep Pawar, Vikas Pawar, Nitin Salve, Development And Validation Of UV Spectroscopy For Determination Of Linagliptin In Bulk And Marketed Dosage Form, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 2, 584-589. https://doi.org/10.5281/zenodo.10688773