ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research

Vol. 16, Issue, 09, pp.*29984-29986*, September, 2024
DOI: https://doi.org/10.24941/ijcr.47827.09.2024

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF SITAGLIPTIN IN BULK AND TABLET FORMULATION BY UV SPECTROPHOTOMETRY

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ARTICLE INFO

Article History:
Received 20th June, 2024
Received in revised form
19th July, 2024
Accepted 19th August, 2024
Published online 30th September, 2024

Key words:
Sitagliptin Phosphate, Accuracy, UV Spectrophotometer, Method Development.

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ABSTRACT

Sitagliptin phosphate is antidiabetic drug. A simple UV Spectrophotometric method was developed for the determination of Sitagliptin using distilled water and linearity was observed in the concentration range of 10 to 100µg /ml. The proposed method was statistically validated. From the results obtained for precision, it was found that % RSD is less than 2% indicating that the proposed method has good reproducibility. For Accuracy, it was found that Percentage Recovery values of pure drug from the analyzed formulation were in between 99 - 101% which indicates that the method is accurate and commonly used excipients and additives present in the formulation were not interfering in the proposed method. The quantification was achieved by the spectroscopy method at 267 nm for Sitagliptin phosphate.

Citation: Tadikonda Rama Rao and Dasam Bhagyalakshmi. 2024. "Analytical method development and validation of sitagliptin in bulk and tablet formulation by uv spectrophotometry". *International Journal of Current Research*, 16, (09), 29984-29986.

INTRODUCTION

The chemical name for Sitagliptin is (3R)3-[Amino-1-(trifluoromethyl) 3-] [1,2,4] [4,3-a]-6,8-dihydro-5H-triazolo[7-ylpyrazin]. The molecular weight of 4-(trifluorophenol, 2,4,5-) butan-1-one is 407.31, with an empirical formula of $C_{16}H_{15}F_6N_5O$ (Namratha Sunkara, 2017; Tian Yan Zhou and Wei Lu, 2011). It is utilized for treating diabetes. This is a medication taken by mouth to lower blood sugar levels. Sitagliptin blocks DPP-4 resulting in higher GLP-1 and GIP levels, lower glucagon levels, and enhanced insulin reaction to glucose (Parag Pathade, 2011). This enzyme divides the incretins GLP-1 and GIP, which are gut hormones released after eating (Bhavya, 2022) .This medication is not included in any pharmacopoeia. Managing diabetes effectively is crucial as the number of diabetes cases continues to rise globally. Sitagliptin has recently been suggested for treating diabetes mellitus to enhance glycemic control (Herman, 2006). Various analytical methods, such as UV Spectrophotometry, RP-HPLC, and LC-MS/MS, have been documented for determining sitagliptin phosphate in human, rat and dog plasma and urine (Jeyabalan, 2022). It is slightly less potent than metformin when used alone. Unlike sulfonylureas, it does not lead to weight gain and causes less hypoglycemia. Sitagliptin is recommended as a second-line treatment (in combination with other medications) if diet/exercise and metformin combination therapy is unsuccessful[7]. The composition of the chemical was shown in Fig. No. 1.

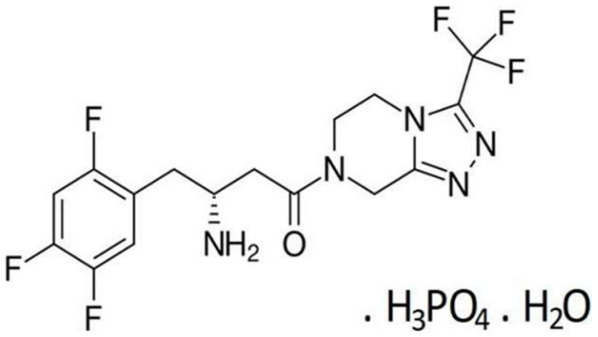

Fig. No. 1. Chemical structure of Sitagliptin

MATERIALS AND METHODS

Selection of solvent: A number of trails were made to find out the ideal solvent system for dissolving the drug. The solvents such as water, HCl, methanol and acetonitrile were tried based on solubility of the drug. Better absorption maximum was found to be 267 nm with distilled water. So water was selected as optimized solvent in this spectrophotometric method.

Instrument used: For recording UV-spectra of the study Model: T60 UV- visible spectrophotometer and quartz cells of 10 mm path length has been used.

Materials: Sitagliptin pure drug was obtained from Almelo Private Limited., Hyderabad. Marketed drug was purchased from local pharmacy.

Solubility: Sitagliptin is a white to off-powder and exhibits pH dependent aqueous solubility. It is soluble in water and N, N - dimethyl formamide, slightly soluble in methanol, soluble in ethanol, acetone and acetonitrile and insoluble in isopropanol and isopropyl acetate.

Preparation of stock solution: Standard stock solution was prepared by accurately weighing 100 mg of sitagliptin and transferred in to 100 ml of volumetric flask and then dissolved in water until it solubilizes and the volume was made up to the mark with water to obtain the concentration of 1 mg/ml or 1000 µg/mL (standard stock solution-1). From stock 1 solution pipette out 10 ml and transfer to 100 ml volumetric flask and made up to the mark with water, to obtain the concentration of 100 µg/ml (standard stock solution-2).

Selection of wavelength for analysis of sitagliptin: Accurately measured 10 ml of standard stock solution-1 was transferred into 100 ml volumetric flask and diluted to 100 ml with water to give the concentration of 100 µg/ml and it was used for initial spectral scan in the UV range of 200-400 nm to detect the maximum wavelength and further dilutions for linearity were prepared from the stock solution.

Preparation of serial dilutions: The serial dilutions were prepared from the standard stock-2 solution to get a respective concentration of 10 µg/mL, 20 µg/mL, 40 µg/mL, 60 µg/mL, 80 µg/mL & 100 µg/mL and absorbances of all the solutions were measured at 267 nm.

Validation of Developed Method: The method which has been developed was validated according to ICH guidelines. The validation parameters studied were Linearity, Accuracy, Precision, LOD, LOQ, Robustness and Assay of marketed dosage form.

METHOD VALIDATION (ICH, 1996; ICH, 1995):

LINEARITY: Linearity was determined by preparing six samples of different concentrations of Sitagliptin The concentration range from 10-100 µg/ml. These concentrations were taken from stock solution and made up final volume using solvent. A calibration curve is plotted by taking concentration on x-axis and absorbance on y axis. The absorbance values of these solutions were measured at 267 nm and the correlation coefficient, intercept, slope is calculated. The linearity data is shown in Table No.1.

Discussion: Calibration curve was plotted & correlation coefficient was found to be 0.9992. System Suitability Parameters are shown in Table No. 2.

PRECISION: Precision of proposed method was determined by repeatability i.e., intraday precision and intermediate precision i.e., inter day precision.

The proposed method was determined by analyzing the mid concentrations i.e., the standard solutions [40 µg/ml] at different intervals on same day in six replicate absorbance [intra day precision] and on two different days [inter day precision]. The %RSD was calculated and results expressed as %RSD. The intraday and inter day precision results are shown in Table No. 3.

Discussion: The %RSD for intraday and inter day precision was found to be ≤2%. It indicates that the method was precise.

LOD & LOQ: The LOD and LOQ values are calculated from average slope and standard deviation from the calibration curve as per ICH guidelines. The LOD & LOQ data are shown in Table No. 4.

$LOD = 3.3\times\sigma/S$
$LOQ = 10\times \sigma /S$

Where, σ = Standard deviation of calibration curve
S = Mean slope of the calibration curve

Discussion: The results of LOD & LOQ Values for Sitagliptin were found to be 1.2 µg/ml and 3.75 µg/ml respectively, it indicates that the method is sensitive.

ACCURACY: Accuracy is a measure of closeness of agreement between obtained value to that of true value. The accuracy was performed by diluting the stock solutions in three different concentrations levels i.e., 80%, 100%, 120%. The method was performed by spiking the 4.0 ml of standard solution with different volumes of working standard solutions and these are diluted to 10 ml with the solvent and carried out in triplicates. The data of accuracy is shown in Table No. 5.

Discussion: The average % recovery of Sitagliptin was found to be within limits i.e., 99-101%.

ROBUSTNESS: Robustness was evaluated by small changes in the method like changing wavelengths of solvents. As wavelength changes to 265 nm, 267 nm, 269 nm the data of robustness was given in Table No. 6.

Discussion: There was no much variation in absorbance with the change in wavelength.

ASSAY: The sitagliptin content in its marketed formulation (Sitara 50 mg) was estimated using pre-validated UV Spectrophotometric method. 10 tablets were accurately weighed, and average weight was calculated, they were crushed to fine powder. The powder equivalent to 100 mg sitagliptin was dissolved in water with the help of sonication and volume was made up to the mark of 100 ml volumetric flask using water, gives the concentration of 1000 µg/ml. The stock solution was filtered using Whatman filter paper and the solution was further diluted with water to give 100 µg/ml. Measure the absorbance of the solution at 267 nm and the % Assay was calculated. The results of Assay are shown in Table No. 7.

RESULTS

Table No. 1. Linearity data of Sitagliptin

Concentration(µg/ml)	Absorbance
10	0.062
20	0.106
40	0.203
60	0.308
80	0.403
100	0.492

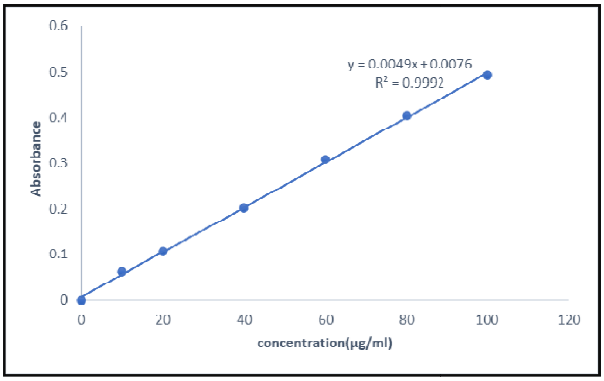

Fig. No. 2: Calibration curve of Sitagliptin at 267 nm

Table No. 2: Optical characteristics of Sitagliptin

Parameters	Sitagliptin
λ_{max}	267 nm
Slope	0.0049
Linearity	10 to 100 µg/ml
Correlation coefficient	0.9992
Intercept	0.0076

Table No. 3. Intra and Inter day Precision Data

Concentration (µg/ml)	Intraday absorbance Day-1	Inter day absorbance Day -2
40	0.203	0.205
40	0.201	0.203
40	0.201	0.201
40	0.205	0.201
40	0.203	0.203
40	0.203	0.205
MEAN	0.2026	0.2033
STD DEV	0.001506	0.0019
%RSD	0.7	0.93

Table No. 4. LOD and LOQ data

Parameters	Sitagliptin (µg/ml)
LOD	1.2
LOQ	3.75

Table No. 5. Accuracy data of Sitagliptin

Sample (% level)	Amount Taken (µg/ml)	Amount Added (µg/ml)	Amount Recovered (µg/ml)	% Recovery
80	30	24	54.28	100.48%
100	30	30	60.12	100.20%
120	30	36	65.74	99.61%

Table No. 6. Robustness data of Sitagliptin

S. No.	Wavelength	Absorbance
1	268	0.201
2	270	0.203
3	272	0.205

Table No. 7. Assay of Sitagliptin: (n = 6)

Label claim	Amount found	Assay (%)
50 mg	50.20 mg	100.4

CONCLUSION

From the above experimental results and parameters it was concluded that, this developed UV- Spectroscopy method for the estimation of sitagliptin was found to be simple, precise, accurate, robust, economic and rapid makes this method more acceptable and cost effective and it can be effectively applied for routine analysis in research institutions and quality control department.

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