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A New Second-Derivative Spectrophotometric Method for the Determination of Vildagliptin in Pharmaceutical Dosage Form

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ABSTRACT

An accurate derivative spectrophotometric method was developed and validated for the determination of dipeptidyl peptidase inhibitor vildagliptin in the pharmaceutical dosage form. The second derivative of the UV spectra has enabled the estimation of vildagliptin absorbance at 217 nm without any interferences. Linearity, precision, accuracy, detection (LOD), and quantification (LOQ) limits were established for method validation. Calibration curve was linear in the range of 10-60 μg/mL with a regression coefficient of 0.998. The method was validated as per the International Conference on Harmonization (ICH Q2 (R1)). The limit of detection and the limit of quantification were found to be 2.06 μg/mL and 6.25 μg/mL, respectively. Intra and inter-day precision data illustrated that the method has acceptable reproducibility as the percentage relative standard deviation (RSD) was less than 2 %, which indicates the precision of the method. The recovery was 98.39 % by the standard addition method. The percentage assay of vildagliptin was 98.06 % which showed good applicability. The following results indicate that the procedure is accurate, precise, and reproducible while being simple and less time-consuming. The method was demonstrated to be adequate for routine analysis in quality control.

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INTRODUCTION

Vildagliptin (VDG) is an effective anti-hyperglycemic agent of the dipeptidyl peptidase-4 (DPP-4) inhibitor class (Figure 1) (Lauster *et al.*, 2007). DPP-IV inhibitors represent a new therapeutic approach to the treatment of type 2 diabetes (He *et al.*, 2009). It is further developing glycemic control without the gain the weight and restrains the prevention of glucagon-like peptides by secretion of insulin. Due to the increased therapeutic effect, vildagliptin is considered as a first-line treatment in Japan for a patient suffering with type 2 diabetes (Seino *et al.*, 2016). It is safe and effective in single and combination with other medications. Derivative spectrophotometry is an alternative method to sort out the selective spectra and terminate background interferences. It is based on using the higher derivative of absorbance with the wavelength of parent zero-order spectra. A detailed review of the literature was studied for vildagliptin in single and combination forms such as spectrophotometric (Vaishali *et al.*, 2021; Samer *et al.*, 2019), HPLC (Abu *et al.*, 2018; Jayaprakash and Natesan, 2017), LC/MS/MS (Sakthimanigandan *et al.*, 2015) GC-MS (Uçaktürk, 2015) Capillary electrophoresis (Mahesh *et al.*, 2017) and HPTLC (Patil

et al., 2020). Derivative spectroscopy is an economical method with minimal reagents and development period when compared with other analytical techniques. As an alternative to the existing method, the present work aimed to quantify the second derivative UV spectrophotometric method for the quantitative determination of vildagliptin in the tablet.

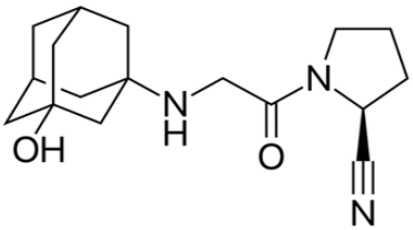

Figure 1: Chemical structure of Vildagliptin

MATERIALS AND METHODS

Instrument

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) with a software UV Probe with 10 mm quartz cells was used. The spectrum was measured in the range of 200-400 nm, with medium scan speed, a sampling interval of 1.0 nm, bandwidth ($\Delta\lambda$) 1.0 nm, and spectral slit width 1 nm.

Chemicals and Reagents

Vildagliptin were provided from Dr. Reddy Lab, Hyderabad. All chemicals and reagents used were of analytical grade. Tablet GALVUS (Vildagliptin 50mg per tablet) marketed by Novartis Health Pvt, Ltd., Mumbai, procured from medicare.

Standard Stock Solution

Weigh accurately 10 mg of vildagliptin was dispensed into the 10 mL volumetric flask and dissolved properly with methanol to accomplish a stock concentration of 1nmg/mL. Additional solutions were ready by weakened with phosphate buffer pH 7.5 to achieve 100 μg/mL.

Preparation of Diluent

2.446 g of sodium hydroxide and 1.575 g of potassium dihydrogen phosphate were taken and dispensed into 1000 ml capacity and made upto the mark with distilled water. The pH was acclimated to 7.5 with orthophosphoric acid or sodium hydroxide according to necessity.

Calibration curve solutions.

From the working standard solutions containing 100 μg/mL of vildagliptin, further calibration curve solution was prepared to get the concentration range 10-60 μg/mL. The concentration range selected according to beer's law and absorbance of these solutions was measured against a blank reagent buffer. At 217 nm, the absorbance of each solution was measured.

Preparation of sample solution

Twenty tablets of vildagliptin were accurately weighed and pulverized, and powder equivalent to 50 mg were diluted with methanol. The solution was filtered using Whatman filter paper. From the filtrate, an appropriate volume was taken and diluted with phosphate buffer to the desired concentration of 30 μg/mL. The response was estimated from respective linearity equations.

Method validation

It is an essential element ensuring the quality and safety of the analytical product. The developed methods were validated according to ICH guidelines (Q2, 2005).

Linearity

The calibration curve of the present method was estimation from a concentration in the range of 10-60 μg/ml. All absorbances were measured at 217 nm. A graph was plotted by taking concentration versus absorbance, and a correlation coefficient (r^2) was calculated.

Accuracy

A parameter was performed to estimate recovery by the standard addition method at three different levels. The percentage recovery as optical characteristics were calculated.

Precision

Precision measurements were carried out from freshly prepared 30 μg/mL vildagliptin sample solutions from a working standard solution, and % RSD was calculated. Intra-day and inter-day precision of present work was done by replicating the response within a day and three consecutive days.

RESULTS AND DISCUSSION

The normal spectrum of vildagliptin in phosphate buffer 7.5 showed an isobestic point at a wavelength above 217 nm. But, due to the lack of selectivity, a derivative method was applied. The second-order derivative spectrophotometric method (D2) was unique to resolve the selectivity problem (Figure 2).

Linearity

Six points calibration curves were graphed in a concentration range of 10-60 μg/mL for vildagliptin.

Table 1: Linearity study

Concentration μg/mL	Absorbance a Mean $\pm$ SD	% RSD
10	0.0012 $\pm$ 0.0002	0.91
20	0.0020 $\pm$ 0.0001	1.26
30	0.0029 $\pm$ 0.0006	0.45
40	0.0036 $\pm$ 0.0001	1.09
50	0.0044 $\pm$ 0.0002	1.87
60	0.0054 $\pm$ 0.0005	1.65

[a] Average of three determinations

Table 2: Recovery result

Component level	Amount of drug added (μg/mL)		Amount recovered ($	% Recovery	% RSD
	Pure	Formulation			
50 %	5	10	15.12	100.83	1.74
	5	10	14.62	97.50	
	5	10	15.00	100.00	
100 %	20	10	29.25	97.50	0.653
	20	10	29.00	96.69	
	20	10	29.37	97.91	
150 %	35	10	43.87	97.50	1.39
	35	10	45.00	100.00	
	35	10	44.00	97.72	

Table 3: Repeatability studies

Component	Concentration (μg/mL)		Intraday precisiona	Interday precisiona
Vildagliptin	30	0.0026		0.0026
	30	0.0027		0.0027
	30	0.0026		0.0026
	30	0.0026		0.0026
	30	0.0026		0.0025
	30	0.0027		0.0026
	% RSD	1.96		1.75

[a] Average of three estimates

Table 4: Results of the assay (n =3)

Drug	Label Claim	Amount of estimated (mg/tab)	Assay
Vildagliptin (Galvus -50)	50 mg	49.03 $\pm$ 0.436	98.06 $\pm$1.29

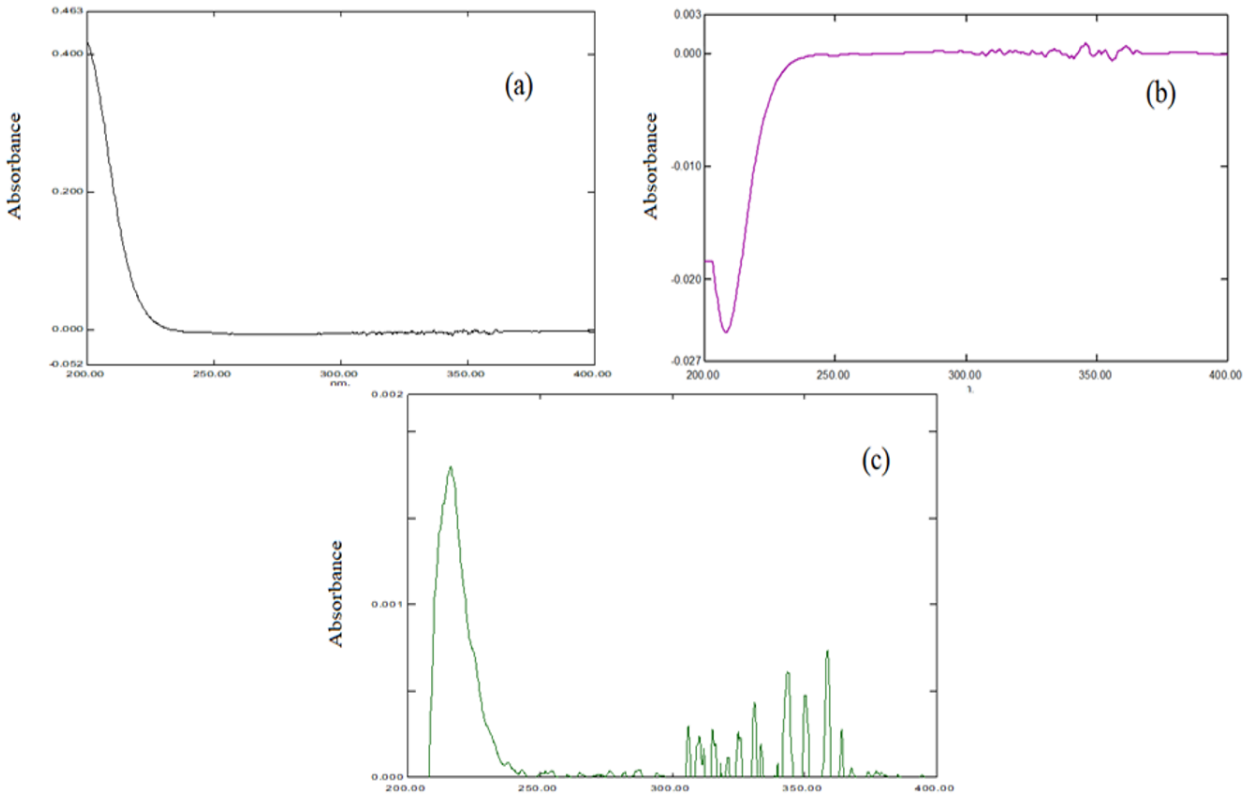

Figure 2: UV spectrum of vildagliptin reference standard a) Zero-order spectrum b) First order spectrum, and c) Second-order spectrum.

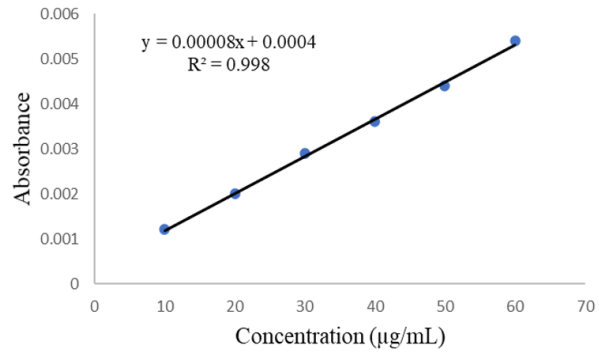

Figure 3: Calibration curve of vildagliptin

The linear regression equation was y = 0.00008x+0.0004 with a correlation coefficient of 0.998 (Table 1, Figure 3).

Accuracy

Derivative method for an accuracy determined by the standard addition method. Recovery studies were performed and calculated (Table 2). The % amount found was between 96.69 and 100.83 % with % RSD <2, indicating that derivative strategy is an exact method for the estimation of vildagliptin.

Precision

The following results showed that reproducibility of the test. Acceptable limits were found by the determination of relative standard deviation for the estimation of vildagliptin in the marketed formulation. Results of precision (intra and interday precision) were mentioned in Table 3.

Analysis of marketed formulation

The amount of the substance of vildagliptin in tablet dosage form the test results of the marketed formulations were tabulated (Table 4).

CONCLUSIONS

The Second derivative spectrophotometric strategy was determined for precision, linearity, and accuracy as per ICH rules Q2 (R1). Obtained results conclude present method is accurate, precise, simple, and cost-effective and can be utilized for further analysis of vildagliptin in drug measurement.

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Conflict of Interest

Authors do not have any conflict of interest in this research work.

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