Research Article

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DEVELOPMENT OF SIMPLE UV-SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF VILDAGLIPTIN DRUG IN BULK AND ITS FORMULATION

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Abstract

The purpose of the investigation is to develop a simple, rapid, accurate, and precise UV-Spectrophotometric method for the estimation of Vildagliptin in bulk and formulations. The validation of the developed method was carried out according to ICH guidelines concerning linearity, precision, accuracy, the limit of detection, and the limit of quantification, formulation linearity. Calibration curves were obtained in the concentration range of 5 to 30µg/ml for Vildagliptin and with good correlation coefficients (R^2=0.9995). The precisions of the new method for the drug were less than the maximum allowable limit (%RSD <2.0) specified by the ICH. Therefore, the method was found to be accurate, reproducible, and sensitive for analysis of Vildagliptin in bulk and formulations.

Keywords: UV spectroscopy, Method development, Validation and Formulation.

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Introduction

Vildagliptin is a new oral anti-diabetic drug belonging to the class of Dipeptidyl peptidase-4 inhibitors. It is used to treat hyperglycemia in individuals with Type 2 diabetes mellitus. Chemically it is known as (s)-1-1[N-(3-Hydroxy-1adamantyl) glycyl] pyrrolidine-2-carbonitrile [1]. Its molecular formula is $C_{17}H_{25}N_3O_2$ and its molecular weight is 303.399 g/mol. It is marketed under the brand names Galvus and Eucreas. Vildagliptin decreases blood glucose levels by covalently binding to catalytic site of Dipeptidyl peptidase-4, eliciting prolonged enzyme inhibition which causes raise in intact GLP-1 levels and stimulates insulin secretion [2]. Adverse effects of Vildagliptin are head ache, excessive sweating, constipation, cough and heat burn.

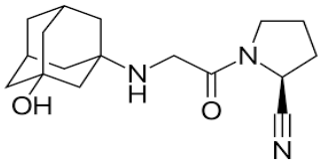

Figure 1: Structure of Vildagliptin 3

Experimental materials and methods

Materials

Active pharmaceutical ingredient Vildagliptin is obtained as a gift sample from century pharma. The pharmaceutical dosage form (Genace) were purchased from local pharmacy. The solvent used in this work is HPLC graded water.

Instruments

- ELICO Double beam SL ultraviolet –visible spectrophotometer consisting of two matched quartz cells with one cm light path.
- Electronic balance (Key Roy)
- Sonicator

Identification of the drug

The gift sample was identified as Vildagliptin by performing melting point test and the values were found to be 151, 152, 151 the average value is 151.33. The observed values are close to the reference values, so we identified that the sample drug is Vildagliptin.

Determination of solubility

Solubility: Capacity of solvent to dissolve a solute.

The sample is freely soluble in water and 0.1N HCl, Soluble in ethanol and methanol, sparingly soluble in 0.1N NaOH, Very Slightly soluble in Isopropanol.

Selection of solvent

After determining the solubility parameter we selected HPLC graded water as solvent.

Selection of detection wavelength

To determine the λ max 100g of Vildagliptin drug is weighed and transferred into a 100ml volumetric flask 3/4th filled with solvent and sonicate for 5 mins then add solvent up to mark and considered as standard stock solution. From this solution pipette out 1ml into a 10ml volumetric flask to give 100µg/ml solution and scanned in UV wavelength range of 200-400nm utilizing HPLC graded water as a blank.

Determination of stability

For determining the stability of the drug in the selected solvent, 10µg/ml Vildagliptin standard solution was prepared and measured absorbance at λ max for 2 hours at a time interval of 15mins by using HPLC graded water as blank. It showed good stability with the solvent.

Method validation

The method was validated according to ICH guidelines. The different validation parameters which were performed are following: Linearity, limit of detection, limit of quantification, formulation linearity, accuracy, precision.

Linearity

To determine linearity weigh accurately 100mg Vildagliptin and dissolve in 100ml of solvent to obtain 100µg/ml solution. Pipette out 0.5, 1, 1.5, 2, 2.5, 3 ml of above solution into a series of 10ml volumetric flask and make up the volume with solvent giving solutions of 5, 10, 15, 20, 25, 30.µg/ml concentration.

Linearity curve was prepared by taking absorbance readings of these solutions at λ max and plotted a graph by taking the concentration on x-axis and their respective absorbance on y-axis.

Limit of Detection (LOD) and Limit of Quantification (LOQ):

LOD and LOQ are calculated by taking slope values of six linearity curves.

Formulation linearity

20 tablets of Vildagliptin were weighed accurately and powdered by using mortar and pestle. The powder equivalent to 50mg of drug is taken into 100ml volumetric flask and add 3/4th volume of HPLC graded water. The solution is sonicate for 45min and solution was made up to 100ml by using HPLC grade water and filtered.

From the filtrate pipette out 1, 2, 3, 4, 5, 6ml into a series of 10ml volumetric flask and makeup the volume with solvent giving solutions of 5, 10, 15, 20, 25, 30µg/ml concentrations. The absorbance values of these solutions were measured at λ max and R2 value is as given in formulation linearity curve.

Accuracy

To check the accuracy of the developed method and to study the interference of formulation excipients, analytical recovery studies were conducted by taking 15 µg/ml concentration of standard Vildagliptin solution in each of three 10ml volumetric flasks and then adding 5,10,15 µg/ml solution of formulation to them respectively. These solutions were prepared in triplicate and measured absorbance at λ max 211nm.The absorbance values are used to calculate amount of drug recovered and then percentage recovery is calculated.

Precision

To check the precision of the proposed method the recovery studies performed three times in same day (intra-day) and recovery studies between three days (inter-day) were analysed. The relative standard deviation of intra-day and inter-day values were calculated and given in table.

The precision is expressed in form of percent relative standard deviation.

Results and Discussions

Identification of the drug

The gift sample was identified as Vildagliptin by performing melting point test and the values were found to be 151, 152, 151 the average value. The observed values are close to the reference values, so we identified that sample drug is Vildagliptin.

Determination of solubility

Capacity of solvent to be dissolved a solute is called as solubility. Vildagliptin is found to be freely soluble in water and 0.1N HCl, Soluble in ethanol and methanol, sparingly soluble in 0.1N NaOH, Very Slightly soluble in Isopropanol.

Determination of λ max:

Vildagliptin is freely soluble in water so by considering all parameters HPLC graded water was selected as solvent. In selected solvent drug shows 211 nm as λ max as given in fig 2.

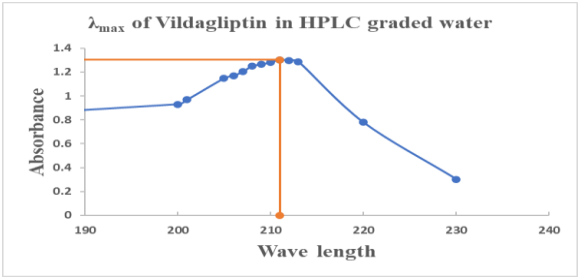

Fig 2 λ max of Vildagliptin in HPLC graded water

Determination of stability

The absorbance of 10 µg/ml standard solution of Vildagliptin was measured every 15 mins for 2 hours. The values are consistent throughout the experiment and can be seen in table 1.

Table 1 Stability study of Vildagliptin

S. No	Time	Absorbance
1	0	0.1810
2	15min	0.1812
3	30min	0.1809
4	45min	0.1811
5	1hr	0.1810
6	1hr 15min	0.1813
7	1hr 30min	0.1812
8	1hr 45min	0.1810
9	2hrs	0.1809

Linearity

The curve obtained was linear with co-relation coefficient 0.9995 which was represented in fig 3

Table 2 Linearity of Vildagliptin

S. No	Concentration(µg/ml)	Absorbance
1	5	0.1642
2	10	0.3422
3	15	0.5124
4	20	0.7025
5	25	0.8623
6	30	1.021
slope	**0.0344**	

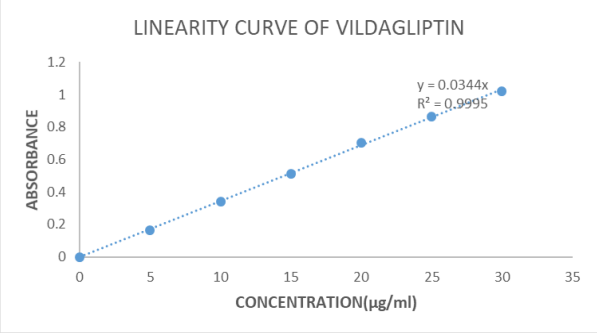

Figure 3 Linearity curve of Vildagliptin

LOD and LOQ

The limit of detection and limit of quantification were determined by taking 6 linearity and average slope. These were represented in figure 4, 5, 6, 7, 8, 9. The values of LOD and LOQ for the proposed method were found to be 0.032 µg/ml and 0.0975 µg/ml respectively and are represented in table 3

Table 3 LOD and LOQ

S. No	Slope	LOD(µg/ml)	LOQ(µg/ml)	SD
1	0.0344	0.0322	0.0975	0.0003
2	0.0348			
3	0.0353			
4	0.0344			
5	0.0347			
6	0.0349			

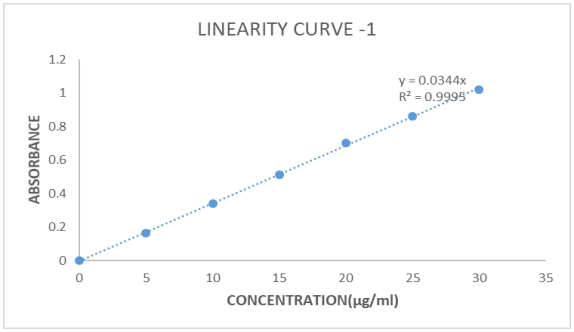

Figure 4 Linearity curve of Vildagliptin-1

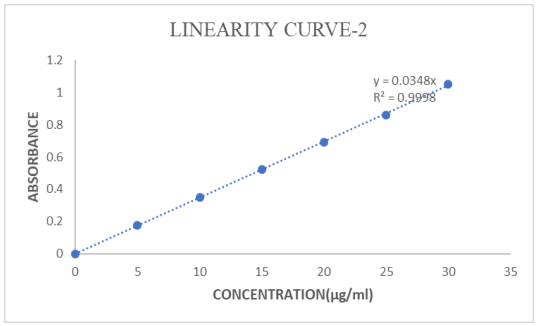

Figure 5 Linearity curve of Vildagliptin-2

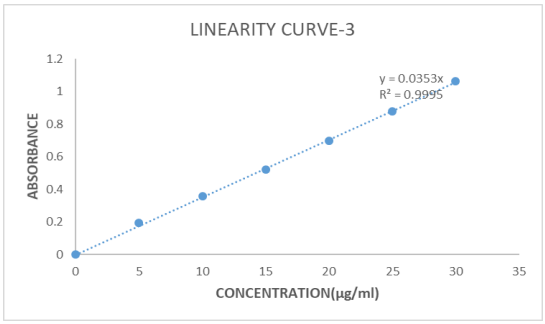

Figure 6 Linearity curve of Vildagliptin-3

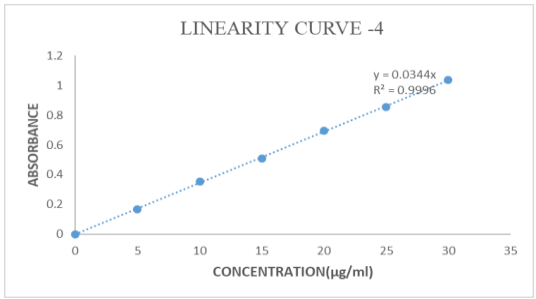

Figure 7 Linearity curve of Vildagliptin-4

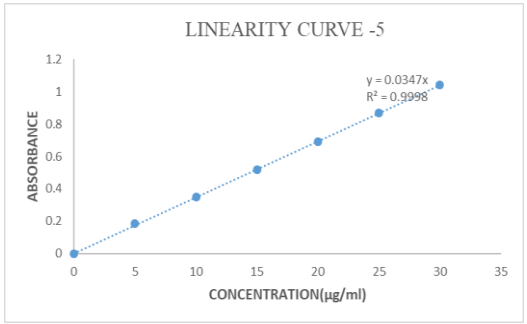

Figure 8 Linearity curve of Vildagliptin-5

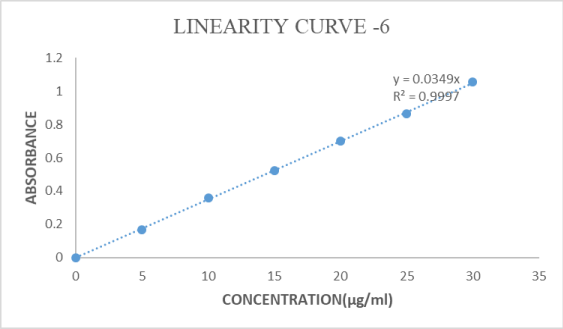

Figure 9 Linearity curve of Vildagliptin-6

Formulation linearity

From the absorbance values a linearity curve was plotted in the desired concentration range. The linearity curve obtained was with co-relation coefficient 0.9999 which is represented in fig 10

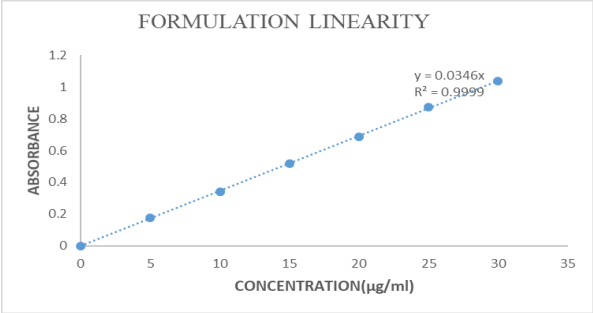

Figure 10 Linearity curve of Vildagliptin

Accuracy

The standard deviation value and percentage recovery values was calculated and found to be 0.28 and 99.84 respectively as given in table 4

Table 4 Recovery study of Vildagliptin

S. No	Amount of drug present µ (g/ml)	Amount added (µg/ml)	Absorbance	Amount recovered	% recovery	SD	RSD
1	15	5	0.6920	5.0	100	0.2887	0.002
2	15	5	0.6905	4.96	99.2		
3	15	5	0.6912	4.98	99.6		
4	15	10	0.8658	10.01	100.1		
5	15	10	0.8647	9.98	99.8		
6	15	10	0.8651	9.99	99.9		
7	15	15	1.0387	14.99	99.93		
8	15	15	1.0395	15.02	100.1		
9	15	15	1.0390	15.00	100		

Precision: It was found that the %RSD values of intraday and inter-day precision were 0.27 and 0.206 respectively i.e. < 2.0 and clearly show that the method is fairly precise.

Table 5 Vildagliptin intra-day recovery-1

S.NO	Amount of drug present (µg/ml)	Amount added(µg/ml)	Absorbance	Amount recovery (µg/ml)	%recovery	SD	RSD
1	15	5	0.6919	5.0	100	0.45	0.0045
2	15	5	0.6915	4.99	99.8		
3	15	5	0.6910	4.97	99.4		
4	15	10	0.8650	9.99	99.9		
5	15	10	0.8619	9.90	99		

6	15	10	0.8648	9.98	99.8		
7	15	15	1.0380	14.97	99.8		
8	15	15	1.0398	15.02	100.1		
9	15	15	1.0396	15.02	100.1		

Table 6 Vildagliptin intra-day recovery-2

S.NO	Amount of drug present (µg/ml)	Amount added (µg/ml)	Absorbance	Amount recovered µ g/ml)	%recovery	SD	RSD
1	15	5	0.6911	4.97	99.4		
2	15	5	0.6905	4.96	99.2		
3	15	5	0.6921	5.00	100		
4	15	10	0.8642	9.96	99.6		
5	15	10	0.8652	9.99	99.9		
6	15	10	0.8649	9.98	99.8		
7	15	15	1.0382	14.98	99.8	0.19	0.0019
8	15	15	1.0392	15.01	100		
9	15	15	1.0377	14.96	99.7		

Table 7 Vildagliptin Intra-day recovery-3

S.NO	Amount of drug present (µg/ml)	Amount added (µg/ml)	Absorbance	Amount recovery (µg/ml)	%recovery	SD	RSD
1	15	5	0.6922	5.01	100.2		
2	15	5	0.6909	4.97	99.6		
3	15	5	0.6913	4.98	99.6		
4	15	10	0.8686	10.00	100		
5	15	10	0.8640	9.97	99.7	0.191	0.0019
6	15	10	0.8648	9.98	99.8		
7	15	15	1.0381	14.97	99.8		
8	15	15	1.0393	15.01	100		
9	15	15	1.0383	14.98	99.8		

Table 8 Vildagliptin inter-day recovery-1

S.NO	Amount of drug present (µg/ml)	Amount added (µg/ml)	Absorbance	Amount recovery (µg/ml)	%recovery	SD	RSD
1	15	5	0.6907	4.96	99.2		
2	15	5	0.6924	5.01	100.2		
3	15	5	0.6925	5.02	100.4		
4	15	10	0.8641	99.6	99.6		
5	15	10	0.8655	10.0	100.0	0.152	0.001
6	15	10	0.8645	9.97	99.7		
7	15	15	1.0379	14.97	99.8		
8	15	15	1.0385	14.99	99.9		
9	15	15	1.0397	15.02	100.1		

Table 9 Vildagliptin inter-day recovery-2

S.NO	Amount of drug present (µg/ml)	Amount added (µg/ml)	Absorbance	Amount recovery (µg/ml)	%recovery	SD	RSD
1	15	5	0.6916	4.99	99.8		
2	15	5	0.6908	4.97	99.4		
3	15	5	0.6923	5.01	100.2		
4	15	10	0.8623	10.00	100.0		

5	15	10	0.8642	9.96	99.6	0.292	0.002
6	15	10	0.8639	9.95	99.5		
7	15	15	1.0391	15	100		
8	15	15	1.0386	14.99	99.9		
9	15	15	1.0400	15.03	100.2		

Table 10 Vildagliptin inter-day recovery-3

S.NO	Amount of drug present (µg/ml)	Amount added (µg/ml)	Absorbance	Amount recovery µ (g/ml)	%recovery	SD	RSD
1	15	5	0.6917	4.99	99.8		
2	15	5	0.6930	5.03	100.6	0.329	0.0032
3	15	5	0.6914	4.98	99.6		
4	15	10	0.8638	9.95	99.5		
5	15	10	0.8654	10.00	100		
6	15	10	0.8657	10.01	100.1		
7	15	15	1.0389	15.00	100		
8	15	15	1.0394	15.01	100.1		
9	15	15	1.0384	14.98	99.8		

Table 11 Validation summary report

S.NO	Parameter	Results
1	Detection of wavelength	211nm
2	Linearity concentration range	5-30µg/ml
3	Linearity	R2=0.9998
4	Regression equation (y= mx+c)	Y= 0.00344x-0.0014
5	LOD	0.032 µg/ml
6	LOQ	0.0975µg/ml
7	Formulation linearity	R2= 0.9999
8	Accuracy(%recovery)	99.84
9	Precision 1. Intraday precision 2. Inter-day precision	%RSD 0.277 0.206

Summary and Conclusion

Summary

A UV spectrophotometric method has been developed and validated for determination of Vildagliptin in pure form and its pharmaceutical dosage forms. The process was done by using HPLC grade water as a solvent with the detection wavelength set at 211nm. Vildagliptin was checked for its stability in the chosen solvent and found to be stable. The method was linear with correlation coefficient 0.9995 in the concentration range of 100ug/ml. The limit of detection and limit of quantification were 0.032µg/ml and 0.0975µg/ml respectively. The intraday and inter-day precisions were satisfactory; the relative standard deviations did not exceed 2%. The accuracy of the method is high as can be seen from the mean recovery values of Vildagliptin which were in the range of 200-1000ug/ml the method met the ICH regulatory requirements. The results of validation are summarized in table 11.

Conclusion

A simple, economical, rapid, precise and accurate UV spectrophotometric method was developed for the estimation of Vildagliptin in bulk and its formulations.

The method was developed by using HPLC GRADE water as solvent. The developed method was validated for parameters like accuracy, precisions, linearity, and limit of detection and limit of quantification as per ICH guidelines. All the parameters were found to be within the acceptance limits. The results indicated that the proposed method for the estimation of Vildagliptin is very accurate and cost effective and can be employed sample analysis of Vildagliptin in bulk and its formulation.

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Conflict of Interest

No Conflict of interest

Inform Consent and Ethical Statement

Not Required.

Author Contribution

1. Rama Krishna.M : Experimental design, and supervision, 2.Suresh Kumar.J.N : Overall drafting, verification, 3.Durga Sahithi.S and Gousha Bi.Sk: Experimental execution, 4 Meghana Haritha. M and Krishnaveni.T: Data collection, 5.Gopi.Y: Financial management

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