WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 9, 1099-1112. Research Article ISSN 2277–7105

THE ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF VILDAGLIPTIN IN BULK AND TABLET FORMULATION BY USING RP-HPLC

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Article Received on 05 April 2026,
Article Revised on 25 April 2026,
Article Published on 01 May 2026,

https://doi.org/10.5281/zenodo.19880133

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How to cite this Article: [*1]Mr. S. Murugesan, [2]Dr. S. K. Senthil Kumar, [3]D. K. Sanjay, [4]K. Sanjay, [5]S. Sanjay, [6]S. Santhosh Kumar, [7]K. Saranya. (2026). The Analytical Method Development and Validation of Vildagliptin In Bulk and Tablet Formulation By Using Rp-Hplc. World Journal of Pharmaceutical Research, 15(9), 1098–1112.

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ABSTRACT

The present study focuses on the development and validation of a simple, precise, and reliable analytical method for the estimation of vildagliptin in bulk and tablet dosage form using reverse phase high performance liquid chromatography (RP-HPLC). The primary objective of this work was to establish an efficient chromatographic method suitable for routine quality control analysis. Chromatographic separation was achieved using a C18 column with a mobile phase consisting of methanol, formic acid buffer in the ratio of 90:10. The analysis was carried out at a detection wavelength of 267 nm. The optimized conditions provided a well-defined chromatogram with good peak shape and resolution for vildagliptin. The developed method was validated according to ICH guidelines, demonstrating acceptable levels of accuracy, precision, linearity, and specificity. The method showed consistent and reproducible results for the quantification of vildagliptin in both bulk and tablet formulations.

KEYWORDS: *VILDAGLIPTIN, HPLC, METHOD DEVOLOPMENT, VALIDATION.*

INTRODUCTION

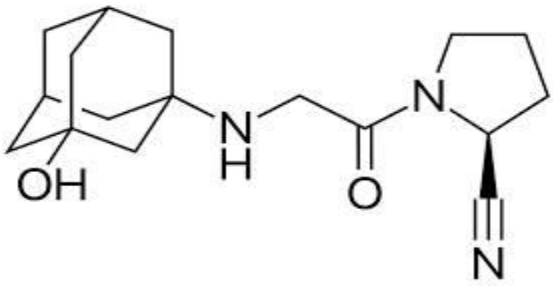
Vildagliptin acts primarily by inhibiting DPP-4, the enzyme responsible for the degradation of the incretin hormones GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide). The administration of vildagliptin results in a rapid and complete inhibition of DPP-4 activity resulting in increased tasting and postprandial endogenous levels of the incretin hormones GLP -1 and GIP. Vildagliptin decreases the release of glucagon from pancreatic alpha cells, which reduces glucose production in the liver.

High performance liquid chromatography is an efficient type of chromatography that uses a high-pressure gradient, rather than simply gravity, to propel a sample through a column. A sample is injected, then a pump containing high amount of pressure helps to move the sample along a packed column, where it is separated and quantitated as individual components. The separation is than analysed by a detector to results.

Most of the drugs in the multi components dosage forms can be analysed by HPLC method because of the several advantage like rapidity, specificity, accuracy, precision and ease of automation in this method. HPLC method eliminates tedious extraction and isolation procedure.

The principle of separation in normal phase and reverse phase mode is adsorption. When a mixture of components is introduced into a HPLC column, they travel according to their relative affinities towards the stationary phase. The component which has more affinity towards the adsorbent travels slower. The components which have less affinity towards the stationary phase travel faster. Since no two components have the same affinity towards the stationary phase, the components are separated. HPLC system suitability parameters include resolution, tailing factor, theoretical plates, retention time, signal-to-noise ratio, and precision, which collectively ensure accurate and reproducible chromatographic performance.

DRUG PROFILE



Chemical name : (2S)-1-[2-[(3-hydroxy-1- adamantyl) amino]acetyl] pyrrolidine-2-carbonitrile.

Molecular formula : $C_{17}H_{25}N_3O_2$

Molecular weight : 303.4g/mol

Appearance : white crystalline powder

Melting point : 148-155°C

Route of administration : orally (tablets).

Dosage form and strength

- Tablets :50 mg,100mg
- Combination tablets :50+100mg,50+850mg.

Storage : Stored at room temperature (20-25°C) in a cool and dry place

Approval date: September 26, 2007

Mechanism of action

Vildagliptin selectively inhibits the DPP-4 enzyme, which is responsible for breaking down incretin hormones. By inhibiting DPP-4, vildagliptin increases the levels of incretin hormones. The increased GLP-1 and GIP stimulate the pancreas to release insulin in a glucose-dependent manner (only when blood glucose levels are high).Vildagliptin decreases the release of glucagon from pancreatic alpha cells, which reduces glucose production in the liver.

Contraindication

Hypersensitivity to the vildagliptin, severe hepatic impairment, or chronic liver disease.

Adverse effects

Most common adverse reactions seen in adult and paediatric patients are,

- Nasopharyngitis,
- Dizziness,
- Headache,
- Nausea/Constipation.

MATERIALS AND METHODS

Chemicals and reagents

- Methanol (HPLC Grade)

- Milli-Q Water (HPLC Grade)
- Formic acid (Laboratory Grade)
- Acetonitrile (HPLC Grade)

Instrumentation

- Digital Balance
- SHIMADZU – HPLC-DLC20AD
- Sonica Ultra sonic cleaner – model 2200 MH
- SHIMADZU - IR Spectroscopy
- Digital PH Meter

PROCEDURE

Preparation of buffer solution:(1% v/v of formic acid)

Pipette out 1ml of formic acid that miscible in 800 ml of HPLC grade water in 1000 ml standard flask and then make up into 1000 ml by using HPLC grade water.

Preparation of mobile phase

0.1% v/v of formic acid in water (90%) and (10%) of methanol was taken into a 1000 ml volumetric flask and mixed properly. Then, this mobile phase is sonicated for 15 min and used as the mobile phase by isocratic elution method.

Preparation of standard stock solution

Weigh accurately about 50mg of vildagliptin and transferred into a 100 ml volumetric flask, then add 30 ml of solvent and make up the volume upto the mark with the same solvent. Then pipette out 1ml from the above solution and transferred into 10ml of volumetric flask, then add 5 ml of solvent shake vigorously and make up the volume upto mark with the same solvent. The concentration of the resultant solution was 50 µg/ml.

Preparation of sample solution

Weigh equivalent about 50mg of vildagliptin from tablet and transferred into a 100 ml volumetric flask, then add 30 ml of solvent and make up the volume up to the mark with the same solvent. Then pipette out 1ml from the above solution and transferred into 10ml of volumetric flask, then add 5 ml of solvent shake vigorously and make up the volume upto mark with the same solvent. The concentration of the resultant solution was 50 µg/ml.

METHOD DEVELOPMENT

The developed method was fully validated for the parameters as per ICH guidelines.

Linearity

Weigh accurately and transfer about 50mg of vildagliptin into 100ml of volumetric flask dissolve and make up with solvent. Take 0.5ml, 0.75ml,1ml,1.25ml,1.5ml of stock solution is transfer into 10ml of volumetric flask and make up with solvent upto the volume. To make the linearity concentration of 50%, 75%, 100%, 125%, 150%.

Accuracy

Weigh accurately tablet average weight of sample and transfer into 100ml of volumetric flask dissolve and makeup to the volume with the solvent. Take 0.8ml, 1ml, 1.2ml of stock solution was transferred into 10ml of volumetric flask and makeup with solvent upto the volume. To make the concentration of 80%, 100%, 120%.

Precision

Weigh accurately tablet average weight of sample and transfer into 100ml of volumetric flask dissolve and makeup to the volume with the solvent.1ml of stock solution was transferred into 10ml of volumetric flask and makeup with the solvent upto the volume. Six-time replicate of injection to produce the similar of the result no maximum deviation.

Robustness

Small deliberate changes in method like flow rate, wavelength, mobile phase and ratio were made but there was no recognized change in the result and were within range as per ICH guidelines. Robustness conditions like flow minus, flow rate, wavelength decreasing, wavelength increasing, mobile phase decreasing, mobile phase increasing, ratio increasing and ratio decreasing was maintained and sample were injected in duplicated manner system suitability parameters were not much effected and all the parameters were passed. % RSD was within the limit.

Ruggedness

Ruggedness is a measure of reproducibility of test results under normal, expected operational conditions from laboratory to laboratory and from analyst to analyst. The method was fully validated for the parameters as per ICH guidelines.

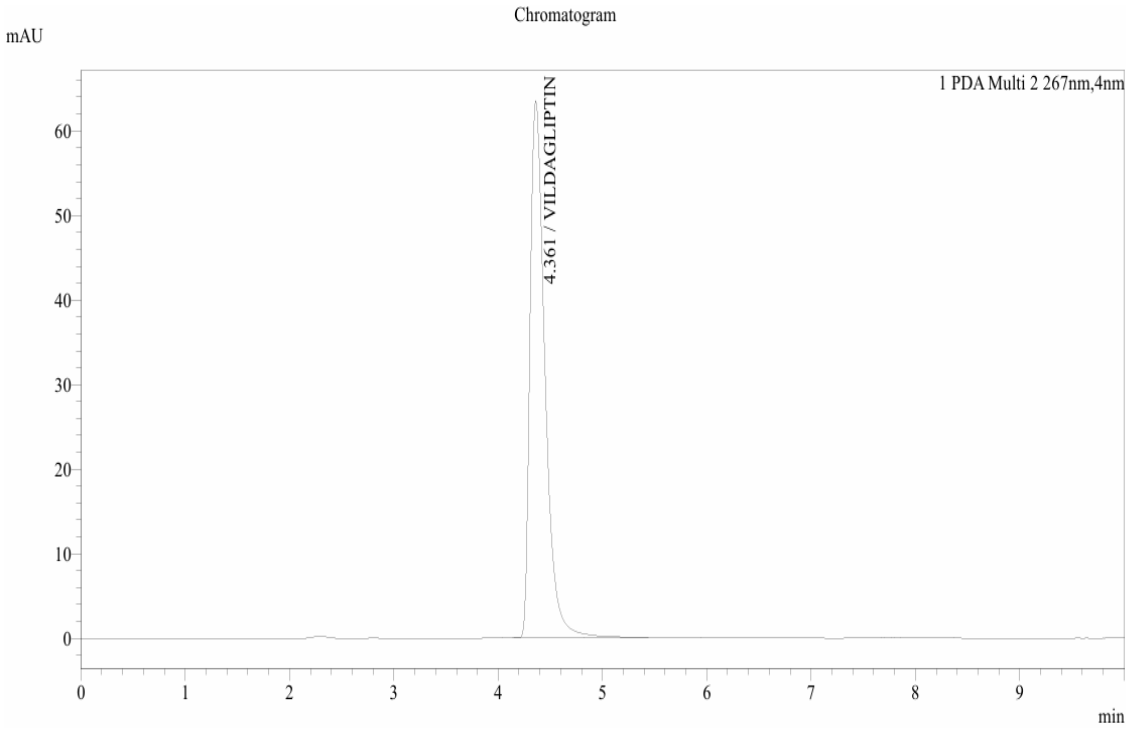
RESULTS AND DISCUSSION

A simple Reverse phase high performance liquid chromatographic method has been developed and subsequently validated for vildagliptin.

The separation was carried out by using a Buffer (1% v/v of formic acid) methanol : formic acid [90:10]. The detection was carried out at 267 nm. The column used is C18 Column (250 mm x 5,4.5micron). The flow rate was selected as 0.9mL/min.

Method development

Mode of operation : Isocratic
Stationary phase : C18 Column (250 mm x 5,4.5micron)
Mobile phase : methanol : 0.1 % v/v of formic acid (90:10)
Detection wavelength : 267 nm
Flow rate : 0.9ml/min
Temperature : 25℃
Retention time :4.4minutes
Run time :10minutes



Peak	Retention time	Area	Theoretical plate	Tailing factor
1	4.361	634073	4709	1.595
Total		634073		

Linearity

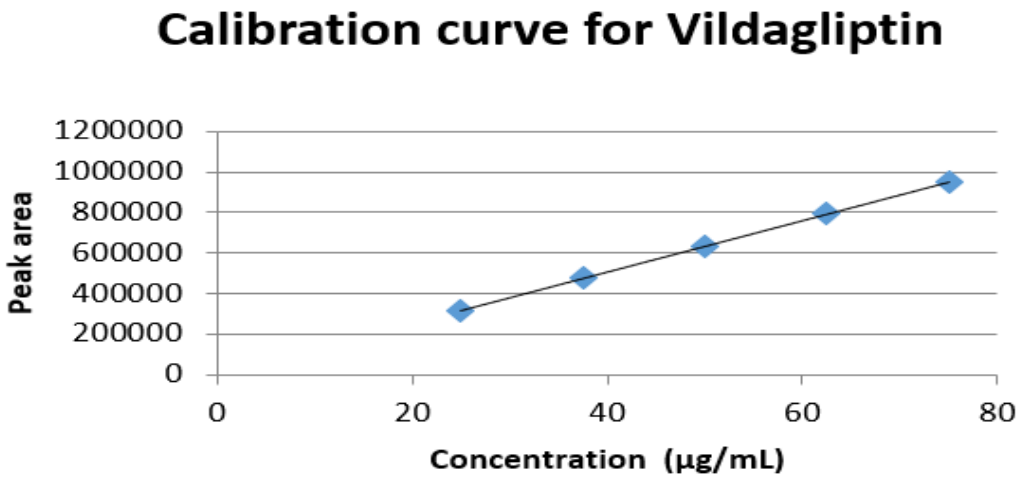
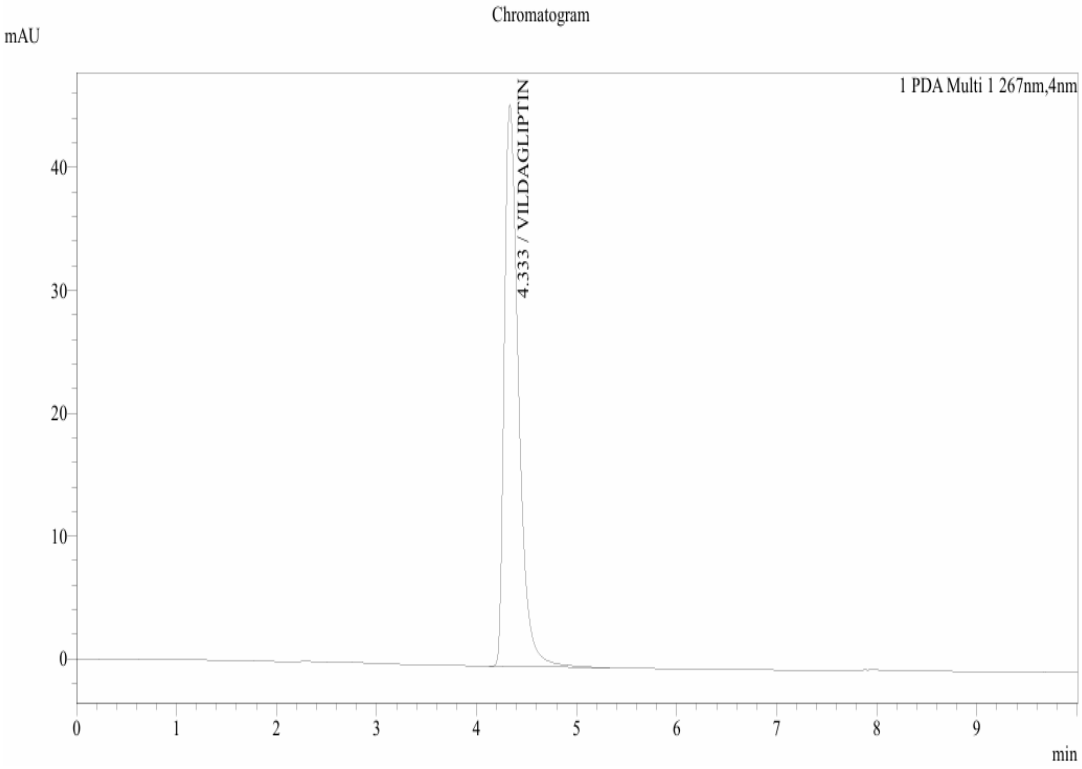


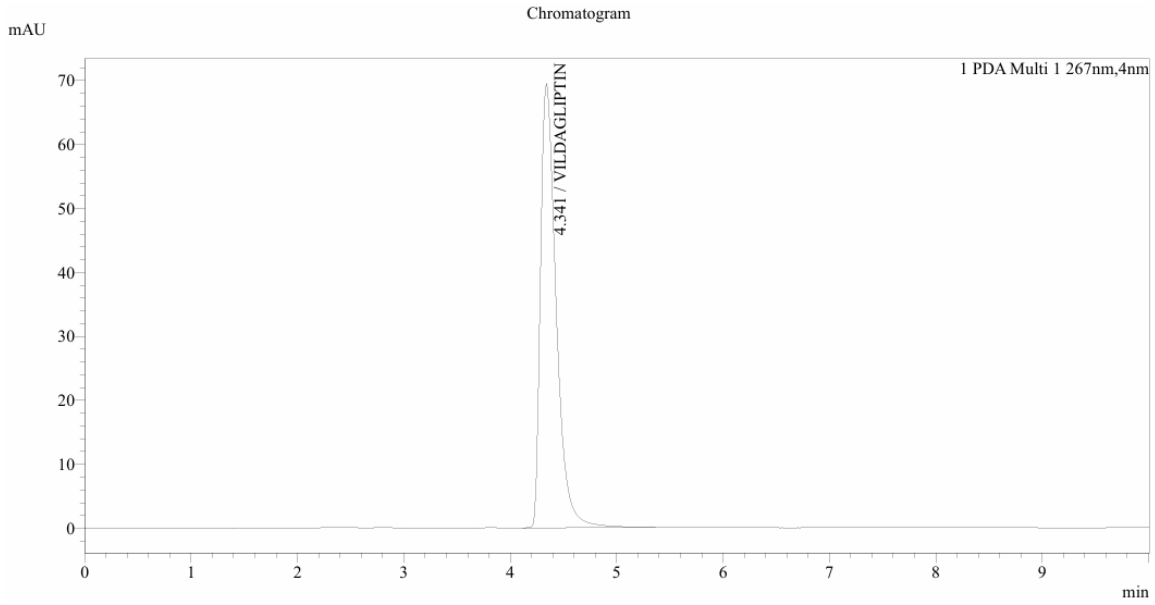
Table 1: linearity.

Concentration	Retention time	Area	Theoretical plate	Tailing factor
50%	4.322	317148	3591	1.688
75%	4.316	476518	3533	1.710
100%	4.324	634816	3622	1.670
125%	4.315	793965	3515	1.709
150%	4.303	952216	3382	1.742

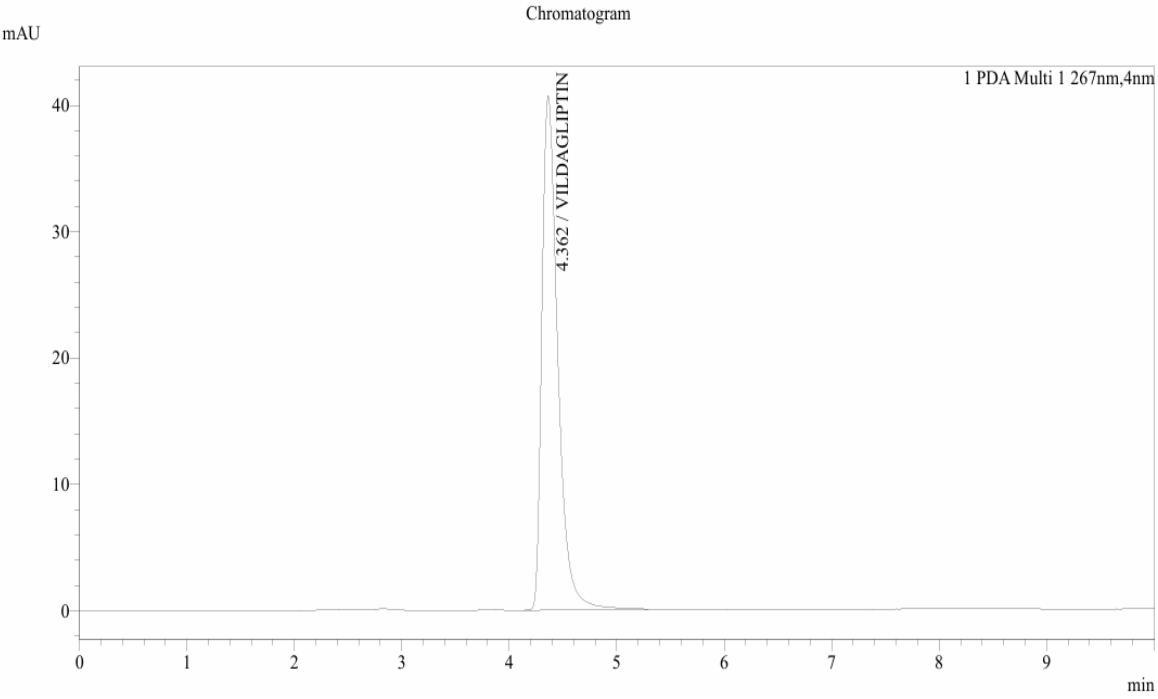
Accuracy



Accuracy – 80%



Accuracy -100%.

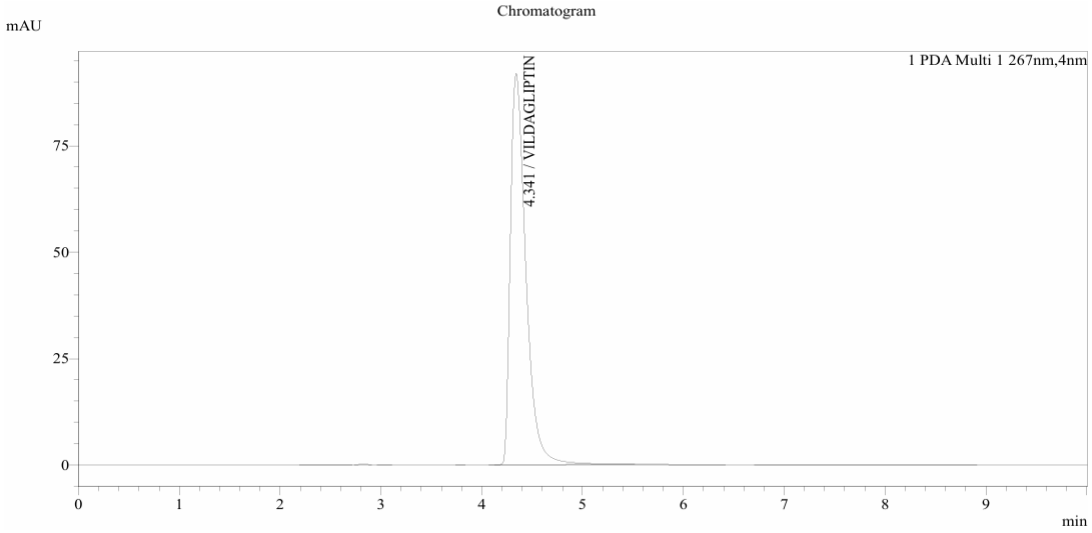


Accuracy -120%

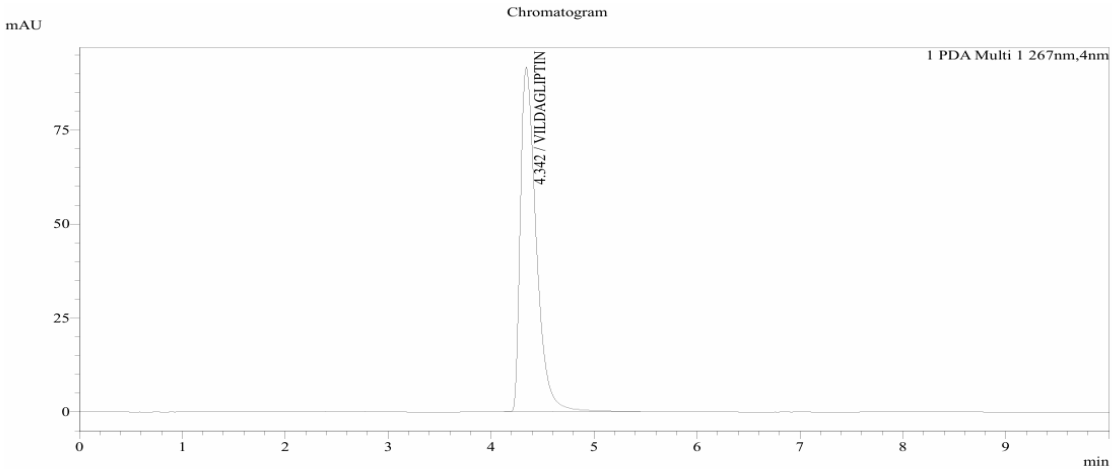
Table 2: Accuracy.

S.NO	% CONCENTRATION	AVERAGE AREA	PERCENTAGE RECOVERY	MEAN RECOVERY	SD	% RSD
1	80%	512477	100.1615%		255.126	0.0497
2	100%	640726.5	99.3804%	99.6248%	32.511	0.0050
3	120%	768502.5	99.3326%		263.021	0.0342

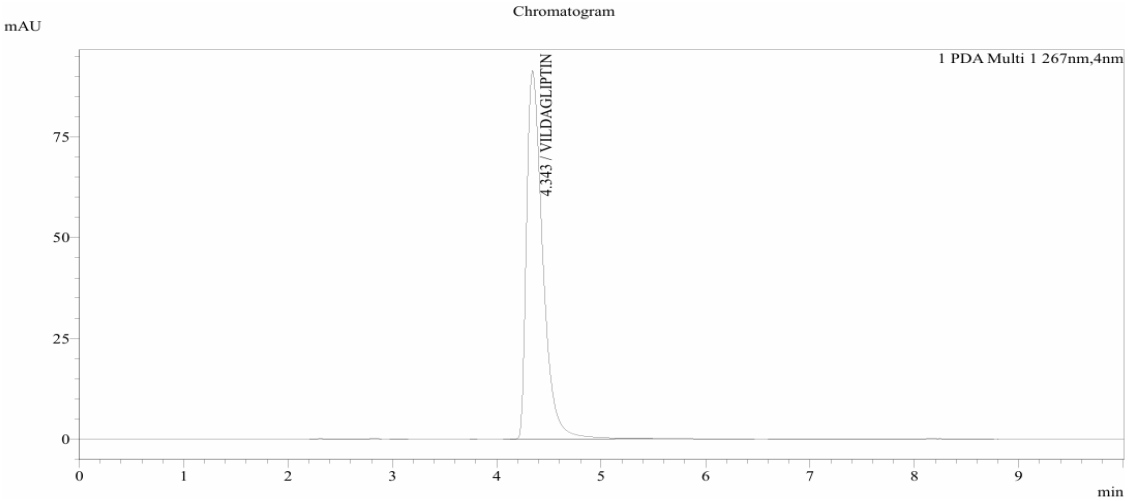
Precision



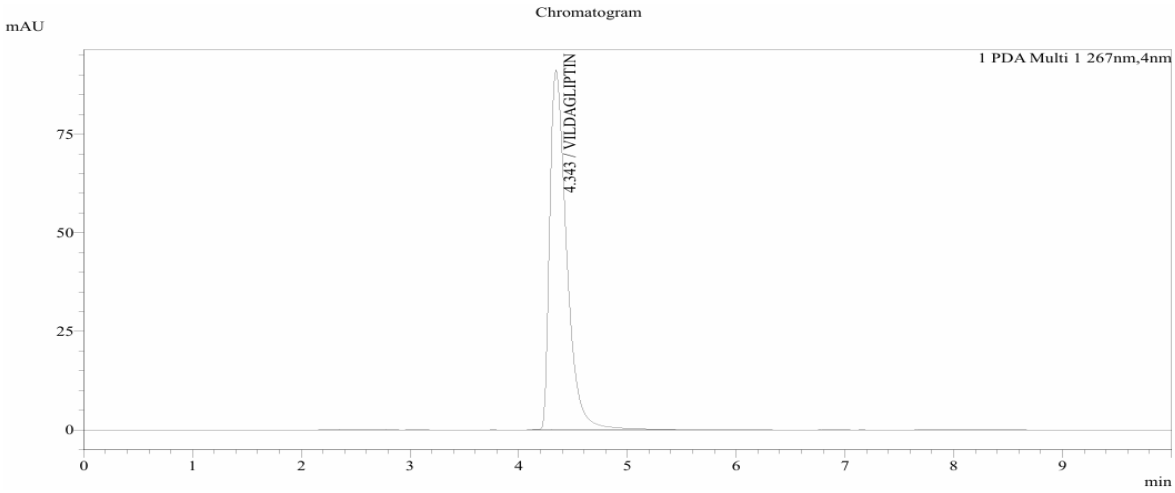
Precision injection – 1.



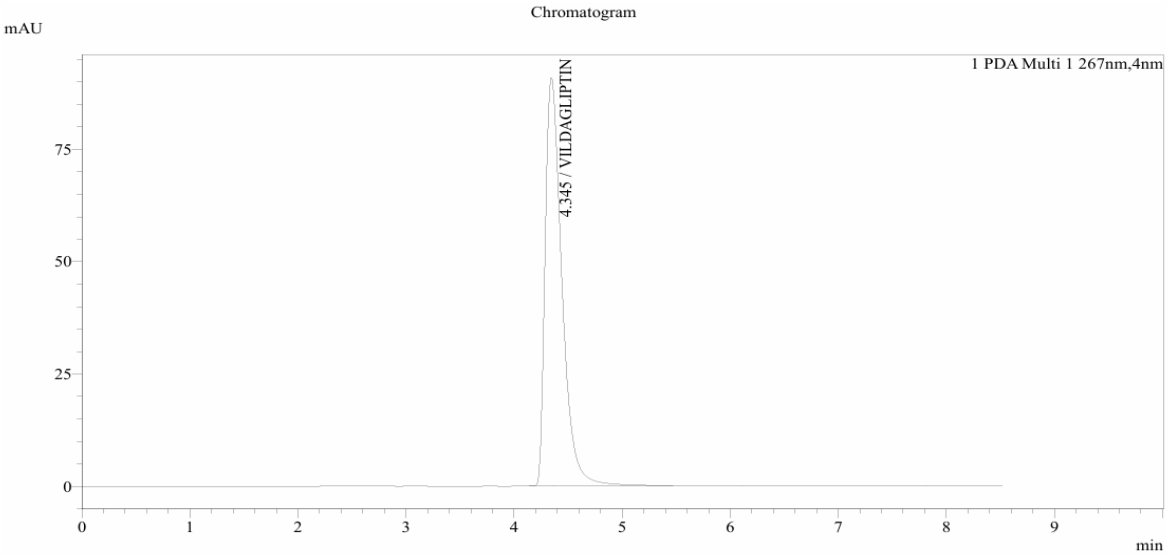
Precision injection – 2.



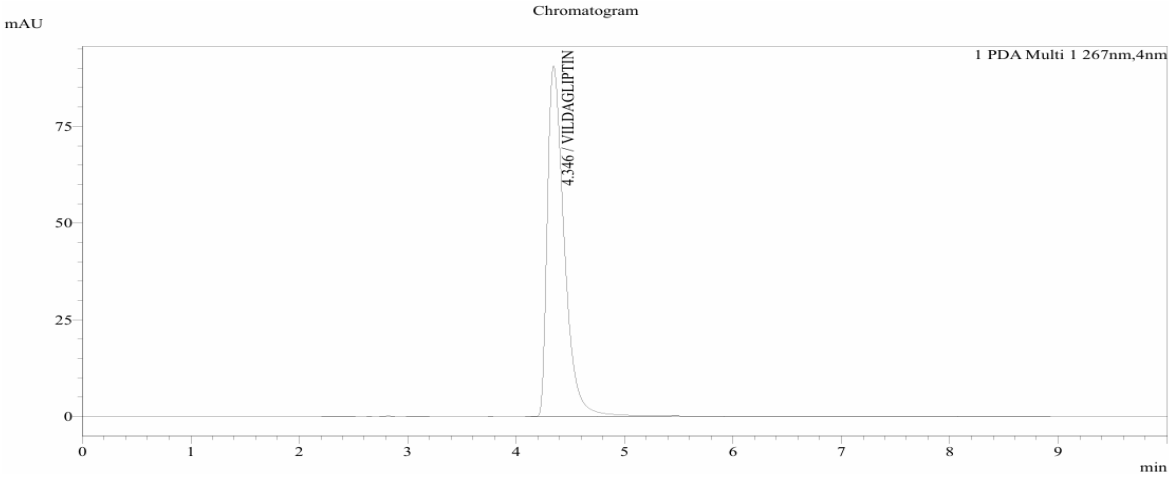
Precision injection – 3.



Precision injection – 4.



Precision injection – 5.

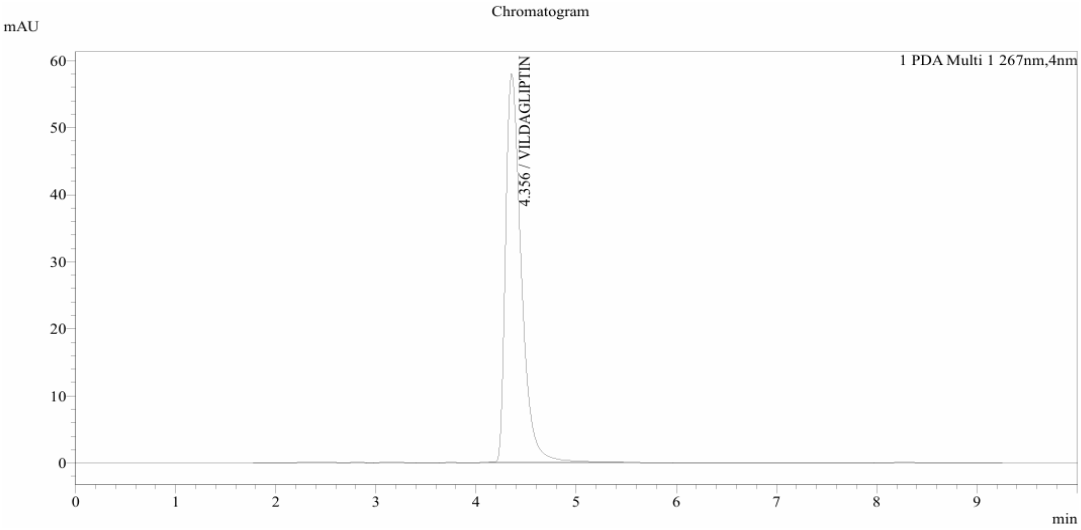


Precision injection – 6.

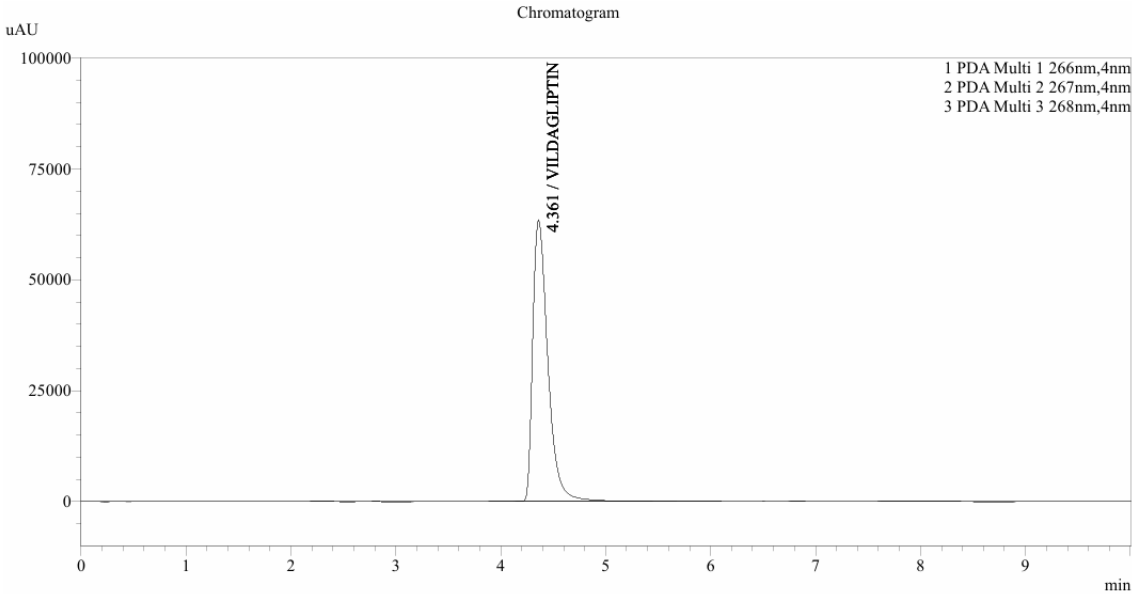
Table 3: precision.

Interday precision			Intraday precision		
Injection	Retention time	Area	Injection	Retention time	Area
1	4.341	680383	1	4.394	696088
2	4.342	679559	2	4.394	695533
3	4.343	679432	3	4.395	695490
4	4.343	679031	4	4.394	695414
5	4.345	679684	5	4.393	694665
6	4.346	680172	6	4.391	694410

Robustness



Robustness [change in mobile phase ratio]



Robustness [change in wavelength]

Table 4: Robustness.

	Retention time	Area	Theoretical plate	Tailing factor
Change in mobile phase	4.356	62812	3974	1.561
Change in wavelength	4.361	635310	4708	1.595

Ruggedness

Table 5: Ruggedness.

Analyst	Average percentage	Average standard area	SD	%RSD
Analyst-1	100.92792	634446.833	832.3038	0.13118
Analyst-2	100.76741	634692	459.8478	0.07245

CONCULSION

Analytical methods using RP-HPLC were successfully developed for estimation of Vildagliptin.

The developed methods were validated with various parameters like accuracy, precision, linearity, robustness, ruggedness, interday precision etc,. as per ICH guidelines. The results obtained were within the limits of Indian pharmacopoeia (IP).

The simple, rapid, accurate and an isocratic RP-HPLC method showed excelled sensitivity, reproducibility, accuracy, and repeatability. Hence it is suggested that the proposed an isocratic RP-HPLC method can be effectively applied for the routine quality control analysis of the drug Vildagliptin in bulk and in tablet formulation.

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