EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 8
427-432
Year: 2022

DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC METHOD FOR ESTIMATION OF VILDAGLIPTIN IN TABLET DOSAGE FORM

Gayatri A. Gaikwad* and Pranav P. Tambe

Department of Pharmaceutics, Poona College of Pharmacy, Bharati Vidyapeeth (Deemed to be) University, Erandwane, Pune (MH), INDIA 411038.

***Corresponding Author: Gayatri A. Gaikwad**
Department of Pharmaceutics, Poona College of Pharmacy, Bharati Vidyapeeth (Deemed to be) University, Erandwane, Pune (MH), INDIA 411038.

Article Received on 10/06/2022 **Article Revised on 30/06/2022** **Article Accepted on 20/07/2022**

ABSTRACT

Objective: To develop and validate simple, rapid, linear, accurate, precise and economical UV Spectroscopic method for estimation of Vildagliptin in tablet dosage form. **Methods:** The drug is freely soluble in 0.1% NaOH. The drug was identified in terms of solubility studies and on the basis of melting point done on melting point apparatus of Equiptronics. It showed absorption maxima were determined in 0.1% NaOH. The drug obeyed the Beer's law and showed good correlation of concentration with absorption which reflect in linearity. The UV spectroscopic method was developed for estimation of Vildagliptin in tablet dosage form and also validated as per ICH guidelines. **Results:** The drug is freely soluble in 0.1% NaOH, Soluble in ethanol and DMSO. So, the 0.1% NaOH is used as a diluent in method. The melting point of Vildagliptin was found to be 141-142˚C (uncorrected). It showed absorption maxima 227 nm in 0.1% NaOH. On the basis of absorption spectrum the working concentration was set on 50µg/ml (PPM). The linearity was observed between 10-90 µg/ml (PPM). The results of analysis were validated by recovery studies. The recovery was found to be 98.75, 101 and 98.33% for three levels respectively. The % RSD for precision was found to be 0.33% and for Ruggedness is 0.48%. **Conclusion:** A simple, rapid, linear, accurate, precise and economical UV Spectroscopic method has been developed for estimation of Vildagliptin in tablet dosage form. The method could be considered for the determination of Vildagliptin in quality control laboratories.

KEYWORDS: Vildagliptin, UV Spectrophotometer, Melting Point, Assay Method, Validation, Accuracy, Linearity, Ruggedness, Precision.

INTRODUCTION

Vildagliptin, a member of the class that enhances islet cell insulin secretion via an augmented incretin effect, is a high affinity dipeptidyl-peptidase-4 (DPP-4) inhibitor that improves glycaemic control.[1] The administration of vildagliptin results in rapid and near-complete inhibition of DPP-4 activity. Vildagliptin shows weak inhibition of, and rapid dissociation from DPP-8 and DPP-9, compared to DPP-4.[2,3] It has one adamantane backbone containing three condensed cyclohexane rings and a heterocyclic ring containing nitrogen. Viewing its basic nature, it ionizes in acidic medium figure1, it is a potent dipeptidyl peptidase IV (DIP-IV) inhibitor, increases glucagon-like peptide-1 and regulates blood glucose levels. It is well tolerated and improves glycaemic control in patients with type 2 diabetes when given as monotherapy or in combination with metformin, thiazolidinediones, sulfonylureas or insulin. Vildagliptin is rapidly absorbed when administered orally.[4,5] About 70% vildagliptin is metabolized by hydrolysis, and 85% is excreted through renal excretion, with 23% of the oral dose excreted unchanged drug in the urine.[6,7] Food ingestion does not alter the pharmacokinetics of the drug. It does not inhibit or induce the major P450 enzymes. It also does not show drug interactions with commonly used medication (such as metformin, glyburide, pioglitazone, warfarin, digoxin, simvastatin, ramipril valsartan, amlodipine). The pharmacokinetics of vildagliptin is not affected by Age, gender, BMI, and race.[8]

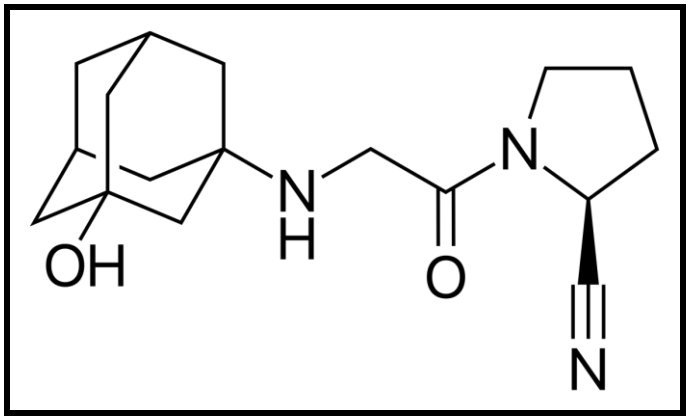

Fig. 1: Chemical Structure of Vildagliptin.

Literature survey revealed that A few methods were reported for the determination of vildagliptin, in plasma[9,10] in bulk and in tablet dosage form.[11-13] HPLC methods[14,15] were reported for its determination in bulk and pharmaceutical formulations as a single component and simultaneously with metformin[16,17] in dosage forms. Some of these methods lack adequate sensitivity, and some are expensive and time consuming. Therefore, it is important to develop new simple and sensitive methods for the UV spectrophotometric determination of Vildagliptin in tablet dosage form.

MATERIALS AND METHODS

- **Instruments**

Shimadzu double beam UV-visible spectrophotometer 1700 Ultra with matched pair.

Quartz cells corresponding to 1 cm path length and spectral bandwidth of 1 nm, Bath sonicator and citizen weighing balance.

Melting point apparatus of Equiptronics were used.

- **Materials**

Vildagliptin was obtained as a gift sample. Vildagliptin tablets were procured from local pharmacy. Analytical grade 0.1% NaOH is used throughout the experiment. Freshly prepared solutions were employed.

Method development

A. Determination of ƛ max (200 PPM)[16,17]

100 mg weighed amount of Vildagliptin was dissolved into 100 ml of volumetric flask with 0.1% NaOH. Pipette out 2 ml and added in 10 ml of volumetric flask dissolved and diluted up to the mark with 0.1% NaOH. This solution was subjected to scanning between 200-400 nm and absorption maximum was determined.

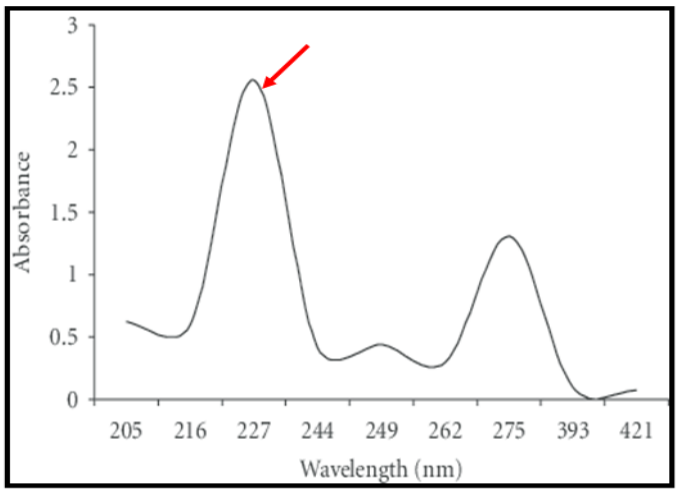

Fig. 2: Calibration Curve.

B. Preparation of Working concentration

Preparation of Standard stock solution

Standard stock was prepared by dissolving 50 mg of Vildagliptin in 100 ml of 0.1% NaOH to get concentration of 500 µg/ml (PPM).

Preparation of Standard solution

Pipette out 5 ml from standard stock solution and diluted up to 50 ml with 0.1% NaOH to get concentration of 50 µg/ml (PPM).

C. Procedure for UV reading

Blank Solution: (For Auto zero)
Fill the cuvette with 0.1% NaOH. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Standard Solution
Fill the cuvette with standard solution. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Sample Solution
Fill the cuvette with sample solution. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

D. Procedure for sample preparations[18,19,20]

For analysis of commercial formulations; twenty tablets are taken weighed it and powdered. The powder equivalent to 50 mg of Vildagliptin was accurately weighed and transferred into the 100 ml of volumetric flask, added 70 ml 0.1% NaOH, the solution was sonicated for 20 min. After sonication cool the flask and diluted upto 100 ml with 0.1% NaOH. Filtered the solution through nylon syringe filter 0.45 µ. Pipette out 5 ml of the filtered solution and diluted up to 50 ml with 0.1% NaOH. The absorbance was measured at 227 nm. The absorbance was recorded:

Table 1: Absorbance of Dosage Form.

Knoll Healthcare Pvt LTD (100 mg)		
Sr. no.	**Sample**	**Absorbance**
1	Blank	0.0000
2	Standard	0.6274
3	Sample	0.6241

Table 2: Dosage Form Specifications.

Type	Brand / Company	M.D.	E.D.	Batch No.	Avg wt (g)	Assay (%)
1	VILDANOL - 50 Knoll Healthcare Pvt LTD (100mg)	02/2022	04/2024	MT 20481	0.1201	99.47

E. Method of validation[18,20,21]

The proposed method was developed by using linearity, accuracy, precision and ruggedness as per ICH guidelines, 1996.

Linearity
The linearity of the proposed assay was studied in the concentration range 10 - 90 PPM at 227 nm. The calibration data showed a linear relationship between concentrations.

Table 3: Linearity Studies.

Sr. no.	Sample Concentration	Absorbance
1	10 PPM	0.1453
2	30 PPM	0.3858
3	50 PPM	0.6264
4	70 PPM	0.8970
5	90 PPM	1.1875
Correlation coefficient		0.9981 ~ 0.998

Accuracy
To ensure the accuracy of the method, recovery study was performed by preparing 3 sample solutions of 80, 100 and 120% of working concentration and adding a known amount of active drug to each sample solution and dissolved in 100ml of volumetric flask with 0.1% NaOH and measuring the absorbance at 227nm.

Table 4: Accuracy Studies.

SPECTROPHOTOMETRIC METHOD			
Accuracy (%)	**Qty weighed (mg)**	**Qty found (mg)**	**Recovery (98-102%)**
80	0.8	0.79	98.75
100	1	1.01	101.00
120	1.2	1.18	98.33

Precision

The precision of the method was demonstrated by inter-day and intra-day variation studies. Five sample solutions were made and the %RSD was calculated.

Table 5: Precision studies.

Sr. No.	Sample Solution	Absorbance
1	Sample Solution 1	0.6252
2	Sample Solution 2	0.6254
3	Sample Solution 3	0.6211
4	Sample Solution 4	0.6257
5	Sample Solution 5	0.6225
MEAN		0.6240
SD		0.0021
% RSD		0.3299 ~ 0.33

Ruggedness

Ruggedness is a measure of the reproducibility of a test result under normal, expected operating condition from instrument to instrument and from analyst to analyst.

Table 6: Results for Ruggedness Studies.

Sr. No.	Analyst	Results	Mean	% Assay	% RSD
1	Analyst 1	0.6219	0.6223	99.18	0.4757 ~ 0.48
		0.6226			
2	Analyst 2	0.6245	0.6265	99.85	
		0.6284			

RESULTS

1. Solubility of Vildagliptin

Solubility test was passed as per criteria.

Table 7: Results for solubility studies.

Sr. no.	Title	Result
1	0.1% NaOH	Freely Soluble
2	Ethanol	Soluble
3	DMSO	Practically insoluble

2. Melting point of Vildagliptin

The melting point of Vildagliptin was found to be 141-142˚C (uncorrected).

3. Results for linearity for assay method of Vildagliptin

The linearity of method was determined at concentration level ranging from 10 to 90 µg/ml (PPM). The correlation coefficient value was found to be **(R^2) 0.9981 ~ 0.998.**

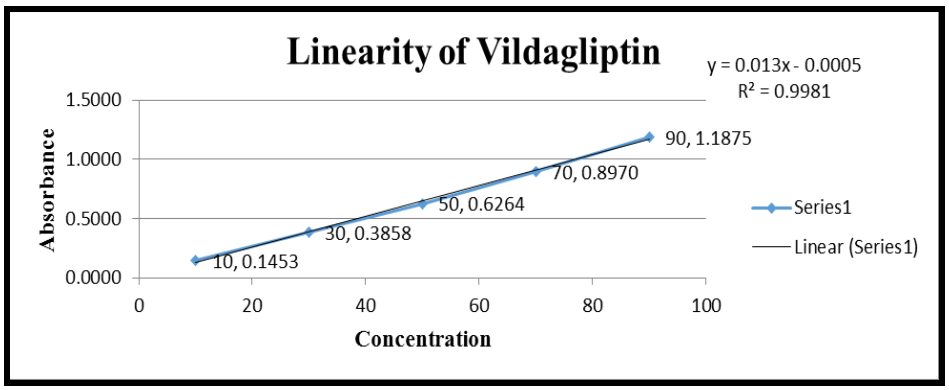

Fig. 3: Vildagliptin Standard Curve.

4. Results for accuracy for assay method of Vildagliptin

The accuracy of the method was determined by recovery experiments. The recovery studies were carried out and the percentage recovery were calculated and represented in Table - 4. The high percentage of recovery indicates that the proposed method is highly accurate. Accuracy results were found within acceptance criteria that are within 98-102%.

5. Results for precision for assay method of Vildagliptin

The % RSD for different sample of precision was found to be 0.3299 ~ 0.33 and it is within acceptance criteria represented in Table - 5.

6. Results for ruggedness for assay method of Vildagliptin

The %RSD for different sample of ruggedness was found to be 0.4757 ~ 0.48 and it is within acceptance criteria represented in Table - 6.

CONCLUSION

A method for the estimation of Vildagliptin in tablet form has been developed. From the spectrum of Vildagliptin, it was found that the maximum absorbance was 227 nm in 0.1% NaOH. A good linear relationship was observed in the concentration range of 10-90 µg/ml (PPM). The high percentage recovery indicates high accuracy of the method. This demonstrates that the developed spectroscopic method is simple, linear, accurate, rugged and precise for the estimation of Vildagliptin in solid dosage forms. Hence, the method could be considered for the determination of Vildagliptin in quality control laboratories.

ABBREVARTIONS

1. PPM - Parts per Million
2. nm - Nanometer
3. HPLC - High Performance Liquid Chromatography
4. UV - Ultra violet
5. MS – Mass Spectroscopy
6. LC - Liquid Chromatography
7. ICH - International Council for Harmonization
8. RSD - Relative Standard Deviation
9. SD - Standard Deviation
10. Qty - Quantity
11. °C - Degree Celsius
12. M.D. - Manufacturing Date
13. E.D. - Expiry Date
14. µg/ml - Microgram per milliliter
15. Avg - Average
16. Wt - Weight
17. g - gm
18. DPP - dipeptidyl-peptidase
19. ED - Erectile Dysfunction
20. HIV - Human Immunodeficiency Virus

REFERENCES

1. *https://en.wikipedia.org/wiki/Vildagliptin* accessed on 01-07-2022.
2. *https://go.drugbank.com/drugs/DB04876* accessed on 01-07-2022.
3. Kleppinger EL, Helms K. The role of vildagliptin in the management of type 2 diabetes mellitus. Ann Pharmacother, 2007; 41: 824–32.
4. Baggio LL, Drucker DJ. Biology of incretins: GLP-1 and GIP. Gastroenterology, 2007; 132: 2131–57.
5. McIntosh CH, Demuth HU, Pospisilik JA, Pederson R., Dipeptidyl peptidase IV inhibitors. How do they work as new antidiabetic agents? Regul Pept., 2005; 159–165.
6. Idris I, Donnelly R. Dipeptidyl peptidase-IV inhibitors: a major new class of oral antidiabetic drug. Diabetes Obes Metab., 2007; 9: 153–65.
7. Serge Halimi, Anja Schweizer, Biljana Minic, James Foley, and Sylvie Dejager; Combination treatment in the management of type 2 diabetes: focus on vildagliptin and metformin as a single tablet: Vasc Health Risk Manag, Jun 2008; 4(3): 481–492.
8. Sunkara G, Sabo R, Wang Y, et al. Dose proportionality and the effect of food on vildagliptin, a novel dipeptidyl peptidase IV inhibitor, in healthy volunteers. J Clin Pharmacol, 2007; 47: 1152-8.
9. Kumbhar, Ab, Galgatte, UC and Warkad SH, Santhakumari B, Development and Validation of A Sensitive Bioanalytical Method For The Determination Of Sumatriptan In Rat Plasma By UPLC-MS. International Journal Of Pharmacy And Pharmaceutical Sciences, 5(3): D2013, 78-82.
10. Pharne AB, Santhakumari b, Ghemud aS, Jain hK, Kulkarni mJ, bioanalytical method development and validation of vildagliptin a novel dipeptidyl peptidase iv inhibitor by RP-HPLC method, int j pharm pharm sci, 2011; 4(3): 119-123.
11. Rao DN, Chinnappadu B, Sujana DL, Method Development and Validation of Forced Degradation Studies of Vildaglipin by Using UV Spectroscopy. World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(4): 1272-1281.
12. Ishaq BM, Prakash KV, Mohan GK, RP-HPLC Method for Simultaneous Estimation of Metformin and Vildagliptin In Bulk and Its Tablet Formulation. Journal of Global Trends in Pharmaceutical Sciences, 2012; 3(3): 747-754.
13. Butle SR, Deshpande PB, Validated Stability-Indicating Hptlc Method Development for Determination of Vildagliptin As Bulk Drug and In Tablet Dosage Form. European Journal of Pharmaceutical and Medical Research, 2015; 2(6): 234-237.
14. Sultana R, Bachar SC, Rahman F. Development and validation of stability indicating assay method of Vildagliptin in bulk and tablet dosage form by RP-HPLC. International journal of pharmacy and life sciences, 2013; 4(4): 2530-2534.
15. Pharne AB, Santhakumari B, Ghemud AS, Jain HK, Kulkarni MJ. A novel bioanalytical method

development and validation of Vildagliptin dipeptidyl peptidase IV inhibitor by RP-HPLC method. International Journal of Pharmacy and Pharmaceutical Sciences, 2012; 3(4): 119-123.
16. Gundala U, Bhuvanagiri CS, Nayakanti D. Simultaneous Estimation of Vildagliptin and Metformin in bulk and pharmaceutical formulations by UV Spectrophotometry. American Journal of PharmTech Research, 2013; 3(1): 338-345.
17. Moneeb MS. LC-UV determination of Vildagliptin either alone or simultaneously with metformin in pharmaceutical preparations. AZ Journal of Pharmaceutical Sciences, 2011; 44: 90–99.
18. ICH draft Guidelines on Validation of Analytical Procedures: Definitions and Terminology, Federal Register, 60, IFPMA, Switzerland, 1995; 1227.
19. Beckeet.A.H, Stenlak.J.B, "Practical pharmaceutical chemistry edn 4th CBS Publisher & Distribution, New Delhi, 2004; 275-337.
20. United States Pharmacopoeia. In Validation of Compendial Methods. 26th edn: Pharmacopoeial Convention Inc., Rockville, 2003; 2439-2442.
21. Indian Pharmacopoeia. Volume II. Ministry of Health and Family Welfare Government of India: Published by Indian Pharmacopoeia Commission, Ghaziabad, 2007; 692- 693.