Research Article

Spectrophotometric Method for the Determination of Vildagliptin in Bulk and Pharmaceutical Dosage Forms

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ABSTRACT

Vildagliptin, a dipeptidyl peptidase-4 inhibitor, is one of the potent oral antidiabetic agent. vildagliptin is considered as new drug. There has been no monograph for it in pharmacopeia. So, the objective of the present work was to develop a new simple, accurate and precise spectrophotometer method as per ICH guideline for estimation of Vildagliptin in bulk. and Vildaglptin has absorbance at the wavelength of maximum λmax = 202.5 in 0.5 M HCl, Proposed method was precise with RSD less than 2%. Linearity test was approved within range of 10-40 µg/ml for with correlation coefficient (R2) of 0.999. Accuracy was 100.17%. LOD and LOQ were 0.055 µg/ml and 0.166 µg/ml, respectively. The spike recovery of vildagliptin in tablet was 99.96%, so this method has been successfully applied on national pharmaceutical product.

Keywords: UV, vildagliptin, precicion, accuracy, LOD, LOQ, assay, ICH.

INTRODUCTION

Vildagliptin chemically (S)-1-[N-(3-hydroxy-1-adamantyl) glycyl] pyrrolidine-2-carbonitrile[1], it has one adamantane backbone containing three condensed cyclohexane rings and a heterocyclic ring containing nitrogen[2].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 (GLP-1) and regulates blood glucose levels[3]. It is well tolerated and improves glycaemic control in patients with type 2 diabetes when given as monotherapy or in combination with metformin[4,5], thiazolidinediones, sulfonylureas or insulin[6,7]. Many papers have reviewed its pharmacokinetics which are out of scope[8].

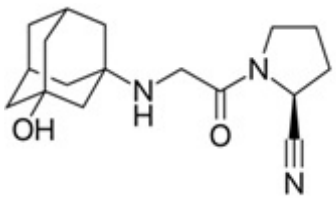

Figure 1: chemical structure of vildagliptin

A few methods were reported for the determination of vildagliptin, in plasma[9,10], in bulk and in tablet dosage form[11-13].

spectrophotometer method is important for quality control of pharmaceutical industry and Uv methods still using in pharmacopeia for detection and determination active compound because of it is simple, easy to use and cost effective[14-16].

To our best knowledge, VILD is not approved till now in any Pharmacopoeia monographs. That why it is of high importance to develop analytical methods to answer pharmaceutical industry requirements either to quantify VILD in its bulk or brand So, this paper present simple, accurate and precision method for determination Vildagliptin in bulk.

MATERIALS AND METHODS

Chemicals and reagents

Working standard of vildagliptin with a potency of 99.8% was given as a gift from Medico Lab Homs. Hydrochloric acid fuming 37% was procured from Merck (Darmstadt, Germany), Water used was generated by double distillation.

Equipment

The method was performed on an ultraviolet visible (UV-VIS) spectrophotometer (Shimadzu model 18001 (Shimadzu, Kyoto, Japan)).

Procedure for pure drug

About 25 mg of Vildagliptin was weighed accurately, transferred into a 100 ml volumetric flask, dissolved in 25 ml of 0.5 M HCl shacked and sonicated for 10 minutes, then the volume made up with solvent to give the stock concentration of 250 µg/ml.

5 ml of above solution Transferred into the 50 ml volumetric flask, dilute and made up to the volume with the solvent mixture to get a standard concentration of 25 µg/ml. This solution scanned against a blank over the

entire UV wavelength of 190 to 400. Based on the spectrum, a λ_{max} of 202.5 nm selected for further analysis.

Procedure for commercial tablets

Twenty tablets of (50 mg of Vildagliptin in each) were weighed accurately. An average weight of each tablet was determined, Tablet powder equivalent to 25 mg of vildagliptin, was weighed and transferred to a 100 ml volumetric flask and mixed well then sonicated for 10 min. The solution was filtered using Whatman paper and the 5ml was made up to 50 ml using the same solvent obtain the final concentration of 25 µg/ml.

Method validation

The optimized chromatographic conditions were validated by evaluating linearity, precision, accuracy, limit of detection (LOD) and limit of quantification (LOQ), parameters in accordance with the ICH guideline Q2 (R1)[17].

Linearity

Standard stock solutions of Vildagliptin were diluted in the concentration range of 10–35 µg/mL for the determination of linearity. 3 sets of such solutions were prepared. Each set was analysed to plot a calibration curve. Standard deviation (SD), slope, intercept and coefficient of determination (R^2) of the calibration curves were calculated to ascertain linearity of the method.

Accuracy

The accuracy is the measure of how close the experimental value is to the true value. The recovery study was carried out as 80%, 100% and 120% of the test concentration as ICH guidelines. The recovery study was performed three times at each level. Accuracy was determined and expressed as percent recovery.

Precision

Method repeatability was determined by six times repetitions of assay procedure. Precision of analyst was determined by repeating study by another analyst working in the laboratory. Standard deviation and percent RSD were determined.

Limit of detection (LOD) and Limit of quantification (LOQ)

The LOD and LOQ for VLG was estimated by using following formula:

LOQ = 3.3*σ/S and LOD = 10*σ/S, where σ is the standard deviation of the response and S is the slope of the calibration curve

RESULTS AND DISCUSSION

Vildagliptin shows maximum absorption at 202.5 nm using 0.5 M HCL as a solvent (Figure 2).

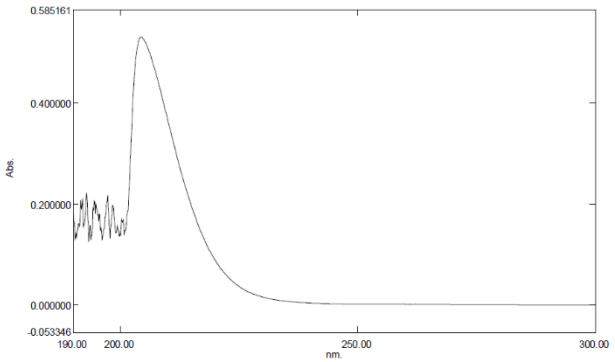

Figure 2: Vildagliptin spectra using 0.5 M HCL

The analytical curves constructed for Vildagliptin was found linear in the 10–40 µg/mL range. The value of correlation coefficient calculated (R^2 = 0.999, y = 0.216x−0.0062), where x is concentration and y is absorbance) were shown in Figure 3.

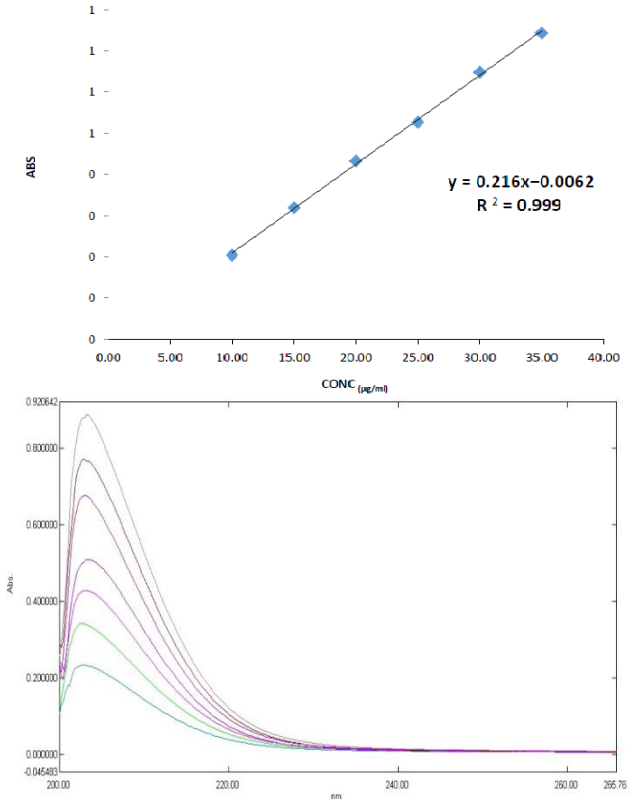

Figure 3: Calibration graph for Vildagliptin

Precision

The precision evaluated at the repeatability of the method was studied by calculating the relative standard deviation (RSD) for 6 determinations of 25 µg/mL performed on the same day and under the same experimental conditions. The RSD value for was 0.479. The inter-day precision was assessed by analyzing 6 samples on 3 different days. The RSD values obtained was 0.497. These results were summarized in Table 1.

Table 1: Intra-day Precision and Inter-day precision

Precision type	Intraday precision	Interday precision
Mean± SD	100.07±0.045	99.17±0.712
RSD%	0.479	0.497

*n=6, SD=standard deviation, RSD=Relative standard deviation

Accuracy

Accuracy was evaluated by determining the analyte in solutions prepared according to the standard addition method and expressed in terms of percentage recovery Vildagliptin from the real samples. The mean recovery data was 100.17 % Table 2m demonstrating that the method is accurate within the desired range.

Table 2: Recovery study results for Vildagliptin; (n = 6).

S. No	Excess drug added to the analyte (%)	Percentage recovery	% RSD
1	80	100.1	0.98
2	100	100.2	0.87
3	120	100.21	0.89

Limits of detection and quantitation

This method has high sensitivity by obtain low LOD and LOQ:

LOD = 3:3*SD/Slope =3:3*0.003583/0.216=0.055 µg/ml,
LOQ = :10*SD/Slope =3:3*0.003583/0.216= 0.166 µg/ml.

APPLICATION

Twenty tablets of formulation were weighed and finely powdered. The powder equivalent to 25 mg of Vildagliptin was accurately weighed. It was then transferred to volumetric flask of 100 ml capacity containing 25 ml of 0.5 M HCl and sonicated for 10 min. The flask was shaken and the solution was filtered through Whatmann filter paper into 100 ml volumetric flask. Volume was made up to the mark with 0.5 M HCl to give a solution of 250 µg/ml (Stock solution). From this solution 5 ml was taken and placed in 50 ml volumetric flask. The volume was made up to the mark using 0.5 M HCl to give a solution of 25 µg/ml. last solution was further used for the estimation of Vildagliptin. The result was reported in Table 3.

The reference method was khatun'sone[18] and Statistical analysis (t- and F-tests) showed there was no significant difference between the proposed method and reference method at the 95% confidence Level, results illustrated in Table 3.

Table 3: Analysis data of Tablet formulation by UV

	Drug	Label claim mg/tab	Amount found mg/tab	Label claim %	*SD	RSD%
Present method	Vildacross	50	49.8	99.96	0.11	0.06
Reference method	Vildacross	50	49.4	99.45	0.17	0.09

CONCLUSION

It can be concluded that the proposed newly developed method is a rapid, economical, accurate and precise method for the routine determination of Vildagliptin in bulk; economically alternative to HPLC and better than UV-spectrophotometric simultaneous equation methods.

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REFERENCES

1. 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.
2. Chaphekar MM, Hamrapurkar PD, Development and Validation Of RP-HPLC Assay Method for Vildagliptin Using Qbd Approach and Its Application to Forced Degradation Studies, International Journal of Pharmaceutical Sciences and Drug Research, 8, 2016, 157-165
3. Baig FA, khan S, Naeem MA, khan GJ, Ansari M.T, Vildagliptin Loaded Triangular DNA Nanospheres Coated With Eudragit For Oral Delivery And Better Glycemic Control In Type 2 Diabetes Mellitus. Biomedicine & Pharmacotherapy, 24, 2018, 1250-1258.
4. El-Bagary sRI, Elkady EF, Ayoub BM, Spectrophotometric methods for the determination of Sitagliptin and Vildagliptin in bulk and dosage forms, Int J Biomed Sci, 7(1), 2011, 55–61.
5. Dejager S, Razac S, Foley JE and Schweizer, A, Vildagliptin In Drug-Naïve Patients With Type 2 Diabetes: A 24-Week, Double-Blind, Randomized, Placebo-Controlled, Multiple-Dose Study, Hormone and metabolic research, 39(3), 2007, 218-23.
6. Keating GM, Vildagliptin: A review of its use in type 2 diabetes mellitus, Drugs, 70, 2010, 2089-112.
7. Bosi E, Camisasca RP, Collober C, Rochotte E and Garber AJ, Effects of Vildagliptin On Glucose Control Over 24 Weeks In Patients With Type 2

Diabetes Inadequately Controlled With Metformin. Diabetes Care, 30(4), 2007, 890-895.

8. He H, Tran P, Yin H, Smith H, Batard Y, Wang L, Einolf H, Gu H, Mangold JB, Fischer V, And Howard D. Absorption, Metabolism, And Excretion Of [14c]Vildagliptin, A Novel Dipeptidyl Peptidase 4 Inhibitor, In Humans, Drug Metabolism And Disposition, (37), 2008, 536-544.

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, 4(3), 2011, 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, 3(4), 2014, 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, 3(3), 2012, 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, 2(6), 2015, 234-237.

14. Ola Mahmoud Younes, Joumaa Al- Zehouri, HabibAbboud, Spectrophotometric Method for the Determination of Vildagliptin in Bulk and Pharmaceutical Dosage Forms, Int. J. Pharm. Sci. Rev. Res, 29(1), 2014, 33-36.

15. 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 & life sciences, 4(4), 2013, 2530-2534.

16. 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, Int J Pharm PharmSci, 3(4), 2012, 119-123.

17. ICH harmonized tripartite guideline, validation of analytical procedures: text and methodology, Q2R1, International Conference on Harmonization of Technical requirements for Registration of Pharmaceuticals for Human use, 2005.

18. khatun R, Mirazunnabi Md. A Validated Reversed-Phase HPLC Method for the determination Of Vildagliptin From Tablet Dosage Form. International Journal of Pharmaceutical and Life Sciences, 2, 2013, 90-98.

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