Method development and validation of Vildagliptin using UV spectrophotometer

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Abstract—

Vildagliptin is an antidiabetic agent, belongs to the dipeptidyl peptidase IV (DPP-4) inhibitors. The method employs measurement of absorbance at the wavelength of maximum absorptions of vildagliptin using water as a solvent. Calibration curve was linear in the concentration range of 12.5-200 microgram per ml µg/ml for vildagliptin with the correlation coefficient of 0.985. Accuracy of proposed method was confirmed by performing accuracy studies which showed the results within the range. Precision of proposed UV method was confirmed by performing intraday and inter day precision. Results were well within acceptance criteria which indicate the method has excellent scope for the determination of Vildagliptin in bulk.

Keywords: Vildagliptin, accuracy, linearity, regression equation , precision.

Introduction

Vildagliptin is a novel antidiabetic agent. It belongs to the dipeptidyl peptidase IV (DPP-4) inhibitors. It acts on the incretin system [1]. An incretin hormone Glucagon-like peptide 1 (GLP-1) is released in the gut wall after food ingestion from the L-cells. This hormone inhibits glucagon secretion and stimulates insulin secretion and rapidly eliminated by DPP-4 [2]. Vildagliptin inhibits DPP-4 therefore results in increased GLP-1 concentrations and decreased glucose concentrations [3]. This drug is a potent and selective inhibitor of dipeptidyl peptidase-IV (DPP-4). It is a orally active drug and improves glycemic control in patients with type 2 diabetes (T2DM) by increasing pancreatic (α and β) islet function. Thus vildagliptin suppress the inappropriate glucagon secretion seen in patients with T2DMand improves insulin secretion in them. It also reduces HbA_{1c} when given as a single drug, without weight gain and with a little hypoglycemia, in combination with the other commonly prescribed classes of oral hypoglycemic drugs: a thiazolidinedione, a sulfonylurea or insulin. [4] Vildagliptin is rapidly absorbed when administered orally. 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. Food ingestion does not alter the pharmacokinetics of the drug [5]. 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) [6] [7]. The pharmacokinetics of vildagliptin is not affected by Age, gender, BMI, and race. [8]

Our objective of study is to develop a simple, precise, accurate, cost effective and reproducible spectrophotometric method.

Experimental

Material and reagents

Standard bulk drug sample of vildagliptin were supplied by Martin Dow (Pvt.)

Instrumentation

UV visible 1601 Shimadzu double beam spectrophotometer was used to measurement of spectra. The solvent which are used for the assay was water.

Wavelength Selection

About 100 ppm of vildagliptin solution was accurately prepared in water. These solutions were scanned in the 200-400 nm UV regions. The wavelength maxima (λmax) were observed at 244 nm and this wavelength was adopted for absorbance measurement.

Standard Stock solution

Accurately weighed 20 mg of vildagliptin standard was transferred to a volumetric flask and add sufficient water to produce 100 ml. This solution was used for preparation of working solutions which were prepared by diluting the stock solutions with the same solvent.

Procedure

After preparation of standard solution of 200 ppm in 100 ml, different dilutions are made i.e. 100ppm, 50ppm, 25ppm and 2.5ppm. The absorbance of the dilutions and standard preparation in 1cm cell at the wavelength of maximum absorbance at about 244nm, using a spectrophotometer, using the blank solution. Calculate the quantity in mg, of vildagliptin.

Results and Discussion

This work has been designed to develop a simple, rapid, precise and accurate method.Baokar Shrikrishna et al in 2013 reported a spectrophotometric method for simultaneous estimation of Vildagliptin and metformin in combined tablet dosage form. [9]Our research group has done these type of assay for different formulation which are very useful for pharmacist [10-19].

Method validation

The developed method was validated by various parameters which include linearity, accuracy test and precision.

Linearity

Linearity was determined in the range 12.5-200 µg mL^{-1}. Concentration of vildagliptin versus peak area was subjected to least square linear regression analysis. A linear regression line was obtained with correlation coefficient (R2 > 0.985). The regression equation for active is displayed in fig-1.

Accuracy

Method accuracy was evaluated as the percentage of recovery of known amounts of vildagliptin.It is performed at spike concentration that was 80%, 100% and 120%.Each sample was taken five times and result range was 99.69-100%,Compiled in table-2, high recovery indicated that the method has a high degree of accuracy.

Precision

Precision of the proposed method was determined by repeatability i.e. intra-day precision and intermediate precision i.e. inter-day precision. It was expressed as relative standard deviation RSD. Five different concentrations of vildagliptin in the linear range were analyzed in the same day (intra-day precision) and two consecutive days (inter-day precision); every sample was taken five times. Both intra- and inter-day RSD values were in the range 0-2 confirming good precision (Table 1).The results were insignificant and indicated no remarkable deference in

Inter-day and intra-day precision.

Conclusion

A simple and reliable Uv spectrophotometric method for determining in bulk has been successfully developed. This method can be adapted for routine assay. The intra-run and inter-run variability and accuracy results were in acceptable limit according to ICH guidelines. The short analysis time (< 5min) enables its application in routine and quality control analysis of finished products.

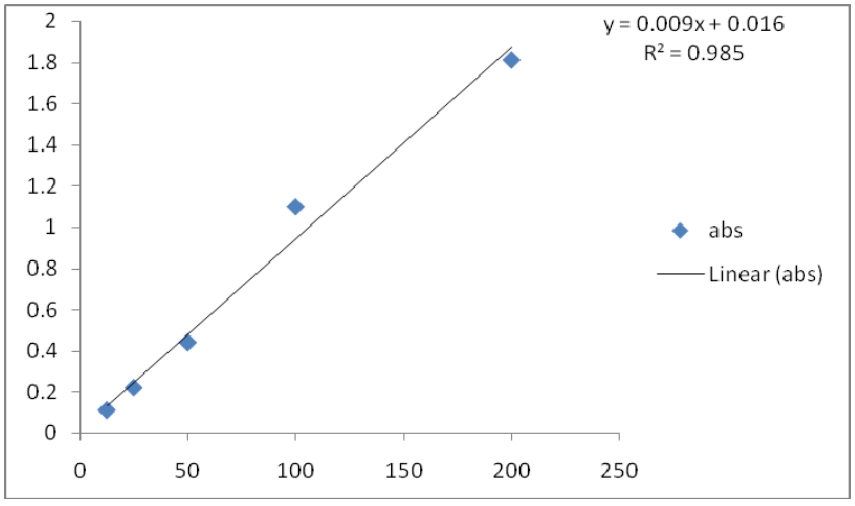

Fig-1 Linearity

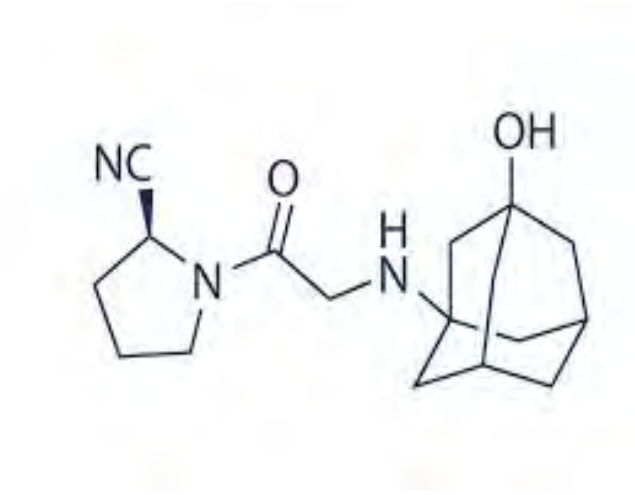

Fig-2 Structure of vildagliptin

Table-1 absorbance at different concentration

Conc. µg mL^{-1}	**abs**
200	1.814
100	1.1
50	0.44
25	0.22
12.5	0.11

Table-2 Accuracy of vildagliptin

Accuracy			
Drugs	**Conc.**	**%RSD**	**% Recovery**
Vildagliptin	80%	0.01	99.96
	100%	0.00	100.00
	120%	0.01	99.98

Table-3 Precision of vildagliptin

Inter day and intraday precision of Vildagliptin					
	Conc.				
	µg mL^{-1}	**Inter-day**		**Intra-day**	
Drugs		%RSD	%Recovery	%RSD	%Recovery
	200	0.55	99.00	0.5	98.00
	100	0.9	100.90	0.9	100.00
	50	1.2	102.30	2	101.00
	25	1.6	98.40	15	98.40
Vildagliptin	12.5	1.9	97.20	2	98.00

REFRENCES:

[1] Kleppinger EL, Helms K. The role of vildagliptin in the management of type 2 diabetes mellitus. Ann Pharmacother. 2007; 41:824–32.
[2] Baggio LL, Drucker DJ. Biology of incretins: GLP-1 and GIP. Gastroenterology. 2007; 132:2131–57.
[3] Idris I, Donnelly R. Dipeptidyl peptidase-IV inhibitors: a major new class of oral antidiabetic drug. Diabetes Obes Metab. 2007; 9:153–65.
[4] 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.
[5] 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.
[6] Ayalasomayajula SP, Dole K, He YL, et al. Evaluation of the potential for steady-state pharmacokinetic interaction between vildagliptin and simvastatin in healthy subjects. Curr Med Res Opin. 2007; 23:2913–20.
[7] El Ouaghlidi A, Rehring E, Holst JJ, et al. The dipeptidyl peptidase 4 inhibitor vildagliptin does not accentuate glibenclamide-induced hypoglycemia but reduces glucose-induced glucagon-like peptide 1 and gastric inhibitory polypeptide secretion. J Clin Endocrinol Metab. 2007; 92:4165–71.
[8] He YL, Sabo R, Riviere GJ, et al. Effect of the novel oral dipeptidyl peptidase IV inhibitor vildagliptin on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects. Curr Med Res Opin. 2007a; 23:1131–8.
[9] Baokar Shrikrishna, Mulgund S. V.2 and Ranpise N. S. Simultaneous spectrophotometric estimation of vildagliptin and metformin in bulk and tablet dosage form. Der Pharma Chemica, 2013, 5(1):24-27
[10] Huma Dilshad, Safila Naveed and Baqir Naqvi (2013) *Assay of new formulations of isosorbide mononitrate by using uv spectrophotometer* : BPJ0000115 - World Research Journal of Medicine *Volume : 1 Issue : 1, pg9-10*
[11] Huma Dilshad, Safila Naveed and Ghulam Sarwar (2014) Simple spectrophotometric assay of available brands of Acetaminophen tablets and their comparative study Journal of pharmacy and pharmaceutical sciences Volume 2, Issue 1,1-4
[12] Safila Naveed, Fatima Qamar, Ghulam Sarwer., (2014) Percentage assay of metformin in different medium using UV-spectrophotometer BPJ0000130 - World Research Journal of Organic Chemistry Volume : 2 Issue : 1, *12-14* ISSN: 2320-3374 & E-ISSN: 2320-5679, http://www.bioinfopublication.org/jouarchive.php?opt=&jouid=BPJ0000130
[13] Safila Naveed (2014) Simple UV spectrophotometric assay of Atorvastatin API formulation and their comparative study, Global Journal of Medical Research .14(2):35-38. https://globaljournals.org/GJMR_Volume14/4-Simple-UV-Spectrophotometric-Assay.pdf
[14] Safila Naveed and Fatima Qamar (2014) A simple assay of Esomeprazole Using UV spectrophotometer The Global Journal of Pharmaceutical Research (TGJPR) 3(2); 1921-25,http://www.tgjpr.com/view-article.php?id=3433
[15] Safila Naveed and Fatima Qamar (2014) Simple UV spectrophotometric assay of Mefenamic acid International Journal of Pharma Sciences and Research (IJPSR) ,5(7):364-366 .http://www.ijpsr.info/ijpsr-v5n7.php
[16] Safila Naveed, Shabana Naz Shah, Fatima Qamar , Nimra Waheed, and Safeena Nazeer, (2014) simple uv spectrophotometric assay of new formulation gentamycin J App Pharm Vol. 6; Issue 4: 407-410
[17] Safila Naveed, Shabana Naz Shah, Fatima Qamar , Nimra Waheed, and Safeena Nazeer, (2014) Simple UV spectrophotometric assay of Lincomycin, IJPRDD, 1 (2),10-12.
[18] Safila Naveed* and Amber Nawab (2014) Assay of LVFX (levofloxacin) in different formulation by UV spectroscopy IJPRDD, 1 (2), 13-16.
[19] Safila Naveed and Fatima Qamar (2014) Simple UV spectrophotometric assay of Metronidazole Open Access Library Journal, 1