Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2013, 5(1):24-27
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Simultaneous spectrophotometric estimation of vildagliptin and metformin in bulk and tablet dosage form

Baokar Shrikrishna[1]*, Mulgund S. V.[2] and Ranpise N. S.[3]

[1]Department of Pharmaceutical Chemistry, Shivnagar Vidya Prasarak Mandals College of Pharmacy, Malegaon (Bk.), Tal- Baramati, Dist- Pune, Maharashtra, India
[2]Department of Pharmaceutical Analysis, Sinhgad College of Pharmacy, Vadgaon (Bk.), Off Sinhgad Road, Pune, Maharashtra, India
[3]Department of Pharmaceutics, Sinhgad College of Pharmacy, Vadgaon (Bk.), Off Sinhgad Road, Pune, Maharashtra, India

---

ABSTRACT

A simple, precise, accurate, cost effective and reproducible spectrophotometric method has been developed for simultaneous estimation of Vildagliptin (VIDA) and Metformin (MET) in combined tablet dosage form. The method employs measurement of absorbance at the wavelength of maximum absorptions of VIDA and MET using 0.1 N NaOH as a solvent. The calibration curve was linear in concentration range of 30-70 µg/ml for VIDA with correlation coefficient of 0.999 and 5-25 µg/ml for MET with correlation coefficient of 0.999. Accuracy of proposed method was confirmed by performing accuracy studies which showed the accepted results. Precision of proposed method was confirmed by performing intraday and inter day precision. All the results were well within acceptance criteria which indicates the method has excellent scope for simultaneous estimation of VIDA and MET in combined dosage form.

Keywords: Vildagliptin, Metformin, Simultaneous estimation, Hyperglycaemic agents.

INTRODUCTION

Vildagliptin (VIDA) chemically ((s)-1-{2-(3-Hydroxyadamantan1ylamino) acetyl] pyrrolidine-2-carbonitrile; 1-[(3-hydroxyadamant-1ylamino)-acetyl}-pyrrolidine-2(s)-carbonitrile) belongs to class of medicines called 'Islet enhancers'. Metformin (MET) chemically 1, 1-dimethlybiguanide hydrochloride, belongs to the 'Biguanide' class. It is an oral anti hyperglycaemic agent. VIDA inhibits the inactivation of GLP-1[1-2] and GIP by DPP-4, allowing GLP-1 and GIP to potentiate the secretion of insulin in the beta cells and suppress glucagons release by the islets of langerhans in the pancreas. VIDA has been shown to reduce hyper glycaemia in type 2 diabetes mellitus [1]. The drug is still not approved for use in the US, it was approved in Feb 2008 by European Medicines Agency for use within the EU [3] and is listed on the Australian PBS with certain restrictions [4]. MET is the first-line drug of choice for the treatment of type 2 diabetes, in particular, in overweight and obese people and those with normal kidney function. It is used in the treatment of polycystic ovary syndrome and has been investigated for other diseases where insulin resistance may be an important factor. MET works by suppressing glucose production by the liver.

The present work describes the development and validation of a new simultaneous spectrophotometric method for estimation of VIDA and MET in bulk and in tablets.

MATERIALS AND METHODS

Instrumentation
A double beam spectrophotometer (Shimadzu UV–VIS 1700), weighing balance (Afcoset FX-300), Sonicator (Ultrapure) were used for experimentation.

Chemicals and Reagents
Reference standard of VIDA and MET gifted by Fortune Health Care Pvt. Ltd, Vadodara (Gujrat), India and Novartis Pharmacutical Pvt. Ltd., Hyderabad, (A.P.) India respectively and they were used as such without further purification. All the chemicals and reagents were of AR grade.

Determination of λ_{max} of VIDA and MET
Solutions of VIDA and MET were prepared from stock solution and scanned in range 400-200 nm.

Preparation of Standard Stock Solution
10 mg of VIDA was weighed accurately and dissolved in 10 ml of 0.1N NaOH to obtain stock solution of 1000 µg/ml. Similarly 1000 µg/ml of MET was prepared.

Preparation of Calibration Curve
From stock solution of VIDA 30 - 70µg/ml and from stock solution of MET 5 - 25µg/ml concentrations were prepared. Each drug solution of VIDA and MET were scanned three times. Mean peak absorbance was plotted against the concentration to construct calibration curve. The regression equation was established.

Analysis of Tablet Formulation
20 tablets were weighed and ground to a fine powder. Tablet powder equivalent to 100 mg of MET was weighed and transferred to a 100 ml volumetric flask and volume was made with diluents to obtain concentration of 1000 µg/ml. Resultant solution was filtered through Whatmann filter paper No.1. Suitable aliquots from the solution were taken and it was diluted with diluents to obtain sample solution of 50µg/ml. Absorbance of the sample solution was measured at 233 nm and 216 nm. The concentration of drugs in the sample solution was determined by using Vierodt's formula. The contents were calculated using the following equations,

$$C_X = (A_2\, ay_1 - A_1\, ay_2) / (ax_2\, ay_1 - ax_1\, ay_2)$$
$$C_Y = (A_1\, ax_2 - A_2\, ax_1) / (ax_2\, ay_1 - ax_1\, ay_2)$$

Where C_X and C_Y are the concentrations of VIDA and MET respectively, ax_1 and ax_2 are the absorptivity values of VIDA and MET at 233 nm and at 216 nm respectively, ay_1 and ay_2 are the absorptivity values of VIDA at 233 nm and at 216 nm respectively. A_1 and A_2 are the absorbances of the diluted sample at 233 nm and at 216 nm respectively. The result of analysis of tablet are given in Table No. 1

Table 1: Assay of VIDA and MET in Tablet Formulation

Brand Name	MET		VIDA	
	Label Claim (mg)	% Purity	Label Claim (mg)	% Purity*
Galvumet	500	100.1	50	99.8

**Denotes average of five determinations*

VALIDATION [5-10]
The method was validated according to ICH Q2B guidelines (ICH 1996) for validation of analytical procedures in order to determine the linearity, accuracy, precision of the analyte.

Table 2: Optical Parameter of VIDA and MET

Sr. No.	Parameters	VIDA	MET
1.	λ_{max}	233.0 nm	216.0 nm
2.	Beer's law limit	30-70 µg/ml	5-25 µg/ml
3.	Regression Equation	Y = 0.011x - 0.029	Y = 0.080 x + 0.088
4.	Slope	0.011	0.080
5.	Corel. Coeff. (r^2)	0.990	0.990
6.	Molar Absorptivity (L mol^{-1} cm^{-1})	0.0462 X 10^{-4}	1.334 x 10^{-4}
7.	Sandell's Sensitivity µg/ml	0.00358 x 10^{-4}	0.440 x 10^{-4}

Linearity

The linearity of an analytical procedure is its ability to obtain test results which are directly proportional to the concentration of analyte in the sample [10]. For linearity studies, five different concentrations of VIDA (30 - 70µg/ml) and MET (5 - 25µg/ml) were prepared. Calibration curves were plotted and regression equations were constructed. The optical parameters are discussed in Table No. 2.

Accuracy

The accuracy of an analytical method is the closeness of test results obtained by the method to the true value [11]. In order to ensure reliability of proposed method, accuracy was carried out [12] and confirmed by recovery studies as per ICH norms [13] at three different concentration levels 80%, 100% and 120% by replicate analysis. Here to a pre analyzed sample solution, standard drug solutions were added and then percentage of drug content was calculated [14] (standard addition method). Results are discussed in Table No. 3.

Table 3: Results of Recovery Studies

Level of Recovery (%)	Drug	% Recovery	Standard Deviation*	% RSD*
80	**VIDA**	99.96	0.450	0.451
	MET	99.37	0.625	0.628
100	**VIDA**	100.3	0.624	0.622
	MET	100.0	1.000	1.000
120	**VIDA**	99.88	0.196	0.196
	MET	99.97	0.455	0.455

**Denotes average of three determinations*

Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions [11]. The precision of the method was evaluated by checking repeatability, inter day, intra day variation studies.

Repeatability

To check the degree of repeatability of the method, suitable statistical evaluation was carried out [16]. Repeatability was performed for six times with tablet formulation [17]. The Standard Deviation was calculated and results of statistical evaluation are shown in Table No. 4.

Table 4: Repeatability Data of Tablet Formulation

Drug	Label claim mg/tab	Amount found Mg/tab	Label claim (%)	S.D.	% RSD
VIDA	50	49.50	99.00	0.007	0.001
MET	500	499.99	99.72	0.777	0.194

Intermediate Precision

The inter day and intra day precisions were determined by assay of the sample solution on the same day and on different day at different time intervals respectively [16]. In intra day studies, working solution of standard and sample were analysed within same day and percentage relative standard deviation (%RSD) were calculated [15]. The % RSD values were found to be 0.49 and 0.81 for VIDA and MET respectively for intraday precision. For Inter day precision it was 1.155 and 0.373 respectively.

RESULTS AND DISCUSSION

The present work describes the, simultaneous equation method (Vierordt's method) for the simultaneous spectroscopic estimation of VIDA and MET in tablet dosage form. Linearity range for VIDA and MET was 30-70 µg/mL and 5-25 µg/mL at respective selected wavelengths. The coefficient of correlation for VIDA at 233 nm and for MET at 216 nm was 0.990 and 0.990 respectively. Percentage estimation of VIDA and MET from tablet dosage form by this method is 100.10 and 99.80 with standard deviation < 2. The validity and reliability of proposed methods were assessed by recovery studies. Sample recovery for both the methods is in good agreement with their respective label claims, which suggest non interference of formulation additives in estimation (Table 3). Precision was determined by studying the repeatability and intermediate precision. Repeatability result indicates the precision under the same operating conditions over a short interval of time. The standard deviation, coefficient of correlation, slope and molar absorptivity were calculated for VIDA and MET. Intermediate precision study expresses within laboratory variation in different days. In both intra and inter day precision study for both the methods % RSD are not more than 2.0% which indicates good repeatability and intermediate precision.

CONCLUSION

The Vierordt's method permits simple, rapid and direct determination of VIDA and MET in commercially available tablet dosage form without previous separation. The results of analysis of two drugs from tablet formulation using method was found close to 100%, Standard deviation was satisfactorily low indicating accuracy and reproducibility of the method. Recovery studies were satisfactory which showed that there is no interference of excipient.

Acknowledgement
The authors wish to thanks Principal and Management of Shivnagar Vidya Prasarak Mandals College of Pharmacy, Malegaon (Bk), Tal- Baramati, Dist-Pune for providing required lab facilities with enthusiastic environment.

REFERENCES

[1] Ahren, B.Landin Olsson, M.Jansson, *J. Clin. Endocrinol. Metab*., (**2004**), 89 (5), pp 2078–84.
[2] Mentlein R., Gallwitz B., Schmidt, *Eur. J. Biochem.*, (**1993**), 214 (3), pp 829–35.
[3] EU approves Novartis diabetes drug Galvus. Reuters, February 01, (**2008**).
[4] NPS better medicines, better health, Vildagliptin for type 2 diabetes. Retrieved 27 August **2010**.
[5] Hokanson G.C., *Pharm. Tech*., (**1994**), pp 92-100.
[6] Green J.M., A practical guide to analytical method validation, *Anal. Chem. News and Features*, (**1996**), pp 305A-309A.
[7] Wegscheider, validation of analytical methods in acrediation and quality assurance in analytical chemistry, H. Guenzler, *Springer*, Berlin, (**1996**).
[8] Vessman J., *J. Pharm and Biomed. Anal.*, (**1996**), 14, pp 867-869.
[9] Arun R. and Anton Smith, *Int. J. Res. Pharm. Sci.*, (**2010**), 1(3), pp 321-324.
[10] Neetu sachan, Phool Chandra, Mayank Yadav, Dilipkumar Pal and Ashok Ghosh, *Journal of Applied Pharmaceutical Science*, (**2011**), 01(06), pp 191-193.
[11] Shrikrishna Baokar, Vinod Pawar, R. N. Patil, et.al., *Research J. Pharm and Tech.*, (**2012**), 5(2), pp 214-218.
[12] A. Patel, U. Sahoo, N. Patel, A. K. Senand, A. K, Seth, *Current Pharma Research*, (**2011**), 1(2), pp 140-144.
[13] Ilangovan Ponnilavarasan, Chebrolu Sunil Narendra kumar and P. Asha, *Int J of Pharm. Bio. Sci.*, (**2011**), 2(2), pp 334-338.
[14] Ramesh Sawant, Lokesh Bhangale, Rupali Joshi and Prashant Lanke, *Chem. Metrol.*, (**2010**), 4(1), pp 21-27.
[15] Rekha Gangola, Narendra Singh, Anand Gurav, *Pharmacia globale*, (**2011**), 2(4), pp 1-3.
[16] Ramesh Sawant, Rupali Joshi, Deepali Kawade and Varsha Sarode, *Der Pharmacia Lettre*, (**2010**), 2(2), pp 471-478.
[17] Rupali Joshi, Nilima Pawar, Sameer Katiyar, *Der Pharmacia Sinica*, (**2011**), 2(3), pp 164-171.