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Simultaneous Estimation of Vildagliptin and Metformin in Bulk and Pharmaceutical Formulations by UV Spectrophotometry

Usharani Gundala*[1], Chandra Shekar Bhuvanagiri [2], Devanna Nayakanti[3]

1. Research Scholar, JNTUA, Anantapur, A.P, India.

2. Professor, MLR Institute of Pharmacy, Hyderabad, A.P, India.

3. Director of OTRI, JNTUA, Anantapur, A.P, India.

ABSTRACT

A simple, accurate, precise and reproducible method has been developed for the simultaneous estimation of Vildagliptin and Metformin hydrochloride in combined tablet dosage forms. As there are no reported UV methods for the simultaneous estimation of Vildagliptin and Metformin hydrochloride in their combined dosage form, a need was felt to develop new methods to analyze the drugs simultaneously. The estimation was done by multi-wavelength technique, at wavelengths of 217 nm and 234 nm over the concentration ranges of 0.7µg/ml and 7 µg/ml with mean recovery 100% for both drugs Vildagliptin and Metformin hydrochloride respectively. The results of the analysis were validated statistically and recovery studies were carried out as per ICH guide lines. Thus the proposed method can be successfully applied for the simultaneous estimation of Vildagliptin and Metformin hydrochloride in routine analysis work.

Keywords: Vildagliptin, Metformin, Simultaneous, Multi-wavelength, spectro-photometric.

*Corresponding Author Email: usha.mpharm@gmail.com

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INTRODUCTION

Vildagliptin (Figure-1) is an oral anti-hyperglycemic agent (anti-diabetic drug[1]) of the new dipeptidyl peptidase-4 (DPP-4) inhibitor class of drugs. Chemically it is *S*)-1-[*N*-(3-hydroxy-1-adamantyl) glycyl] pyrrolidine-2-carbonitrile. Metformin (Figure-2) is an oral anti-diabetic drug in the biguanide class. It 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.[2,3,4] Chemically it is N, N-(Dimethylimidocarbonimidic) diamide.

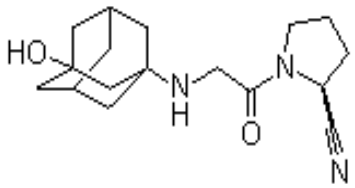


Figure-1

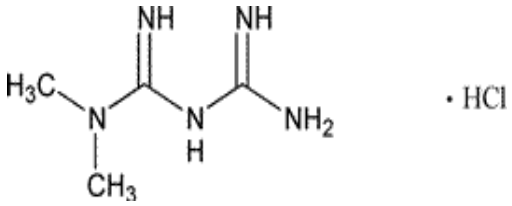


Figure-2

A combination of Vildagliptin and Metformin hydrochloride is indicated as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus whose diabetes is not adequately controlled on metformin hydrochloride or vildagliptin alone or who are already treated with the combination of vildagliptin and metformin hydrochloride, as separate tablets[2]. Literature survey reveals that there are reported HPLC and UV methods for vildagliptin[5-7] and metformin[8-12] separately, and reported HPLC methods[13, 14] for simultaneous estimation of both drugs, but no UV method is there for the simultaneous estimation of vildagliptin and metformin hydrochloride. As there are no reported UV methods for the simultaneous estimation of vildagliptin and metformin hydrochloride in their combined dosage form, a need was felt to develop new methods to analyze the drugs simultaneously. So here a successful attempt has been made to develop simple, accurate, sensitive, rapid and economic method for simultaneous estimation of Vildagliptin and Metformin hydrochloride from tablet dosage forms using UV – Visible spectroscopy.

MATERIALS AND METHODS:

The developed new method was carried out on LABINDIA spectrophotometer, with 1cm matched quartz cells was used for experiments. The absorption spectra of reference and test solution were carried out in a 1 cm quartz cell over the range of 200-400 nm. A Staurtover electronic balance was used for weighing the sample. An ultrasonic cleaner was used for sonicating the tablet sample solution.

Reagents and chemicals:

Analytical pure samples of Vildagliptin and Metformin hydrochloride were a kind gift from

Novartis limited, Hyderabad, Andhra Pradesh, INDIA. Distilled water was used as solvent. The pharmaceutical dosage form used in this study was Galvusmet 50/500 (Novartis limited, Hyderabad, Andhrapradesh, India) labeled to contain 50 mg of Vildagliptin and 500 mg of Metformin hydrochloride per tablet.

Experimental condition:

According to the solubility characteristics of the drug, distilled water was selected as the solvent for analysis. From scanning of both drugs by UV spectra, wavelengths were selected for estimation of Vildagliptin at 217 nm[15] and for Metformin at 234 nm[16].

Working standard solution:

Tablets of Vildagliptin and Metformin combinations are available in 1:10 and 1:20 ratios. Working standards was prepared in the ratio of 1:10 from standard stock solution 100 µg/ml.

Preparation of standard stock solution:

Accurately weighed 5 mg of Vildagliptin and 50 mg of Metformin hydrochloride, is transferred into 100ml volumetric flask and made up with diluents to get the concentrations 0.7µg and 7µg of Vildagliptin and Metformin respectively, sonicated for 30 minutes and filtered through 0.45µm filter paper.

Analysis of tablet formulation:

Twenty tablets were accurately weighed average and crushed to fine powder. An accurately weighed powder sample equivalent to 5 mg of vildagliptin and 50 mg of Metformin hydrochloride was transferred into a 100ml volumetric flask. Add 50 ml of distilled water and sonicated for 20 minutes. The resultant solution was filtered through 0.45 µ membrane filter and finally diluted the volume with distilled water. The solution was suitably diluted with diluent to obtain sample solutions containing Vildagliptin and Metformin in the concentrations ratio of 1:10 µg/ml respectively as in the tablet formulation.

Wavelength selection:

The standard solution of Vildagliptin and Metformin hydrochloride were separately scanned at different concentration in the range of 200-400 nm and the λ max was determined. The overlain spectrum of both the drugs was also run (figure 3).

Method Validation

Accuracy was determined by recovery study. Recovery experiment was carried out by spiking the already analyzed sample of the tablets with their different known concentration of standard Vildagliptin and Metformin. Precision for assay were determined by repeatability, inter day, intraday precision for both drugs (each in three replicate). The UV analysis results were

Indicated in table 1.

Accuracy

Accuracy of the procedure was determined by comparing the analytical amount determined Vs known amount spiked at 80%, 100% and 120% level of LOQ concentration with measurements for each concentration level achieved.

Limit of Detection and Quantitation

The LOD and LOQ of Cefixime Trihydrate were estimated from the standard deviation of the response and the slope of the calibration curve by using following formula.

$$LOD = 3.3 \times \sigma / S$$

$$LOQ = 10 \times \sigma / S$$

Where

σ = the standard deviation of the response

S = the slope of the calibration curve

LOD and LOQ were found to be 0.023 µg / ml and 0.225 µg / ml for Vildagliptin and 0.44 µg / ml and 1.35 µg / ml for Metformin respectively. And results are indicated in Table 3.

Precision

Precision of the method reported as % RSD, was estimated by repeatability, reproducibility and intermediate precision by measuring absorbance of six replicates of 0.7 µg / ml of Vildagliptin and 7 µg / ml of Metformin. % RSD values as in Table 4 are less than 2% that illustrate the good precision of the analytical method.

Linearity:

Vildagliptin and Metformin exhibited linearity with absorbencies in the range of 0.35-1.05 mcg ml^{-1} and 3.5-10.5 mcg ml^{-1} at their respective selected wavelengths i.e., 217 nm and 234 nm respectively. The calibration graphs of Vildagliptin and Metformin were shown in Figure 4.

RESULTS AND DISCUSSION:

The proposed new method for determination of Vildagliptin (Figure 1) and Metformin (Figure 2) showed molar absorptivity. Linear regression of absorbance on concentration gave the equation y = 0.004x+ 0.005 (Vildagliptin) and y =0.006x + 0.012 (for Metformin) with a correlation coefficient (r^2) 0.999 for Vildagliptin and 0.999 for Metformin (Figure 4). Result of UV analysis has been shown in Table 1.

The standard deviation and %RSD calculated for the method is low, indicating high degree of precision. The %RSD is also less than 2% as required by ICH guidelines and shown in Table 2.

The % recovery was between 98- 102% indicating high degree of accuracy and specificity of the proposed method. The results of the recovery study are shown in Table 2. The developed spectro-photometric method was validated for simultaneous estimation of Vildagliptin and Metformin using linearity, range, accuracy and precision and the results were interpreted in Table 3. The %RSD for all parameters was found to be less than two, which indicates the validity of method and assay results obtained by this method are in fair agreement.

Table-1: Result of UV Analysis:

Parameters	Vildagliptin	Metformin
Detection wavelength	217nm	234nm
Beers law limit	0.17 µg / ml -1.56 µg / ml	1.19 µg / ml -10.73 µg / ml
Regression equation	y = mx + c	y = mx + c
Slope	0.004	0.006
Intercept	0.005	0.012
Correlation Coefficient	0.999	0.999

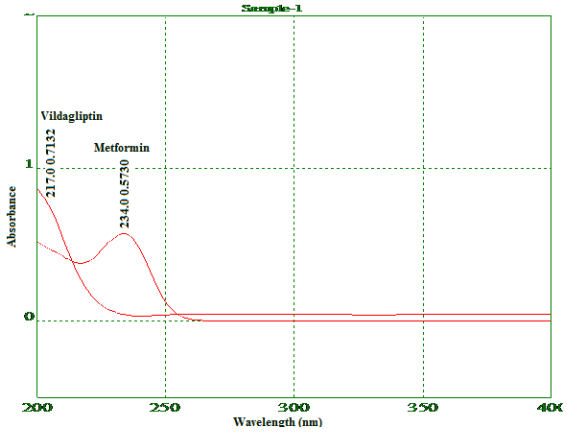
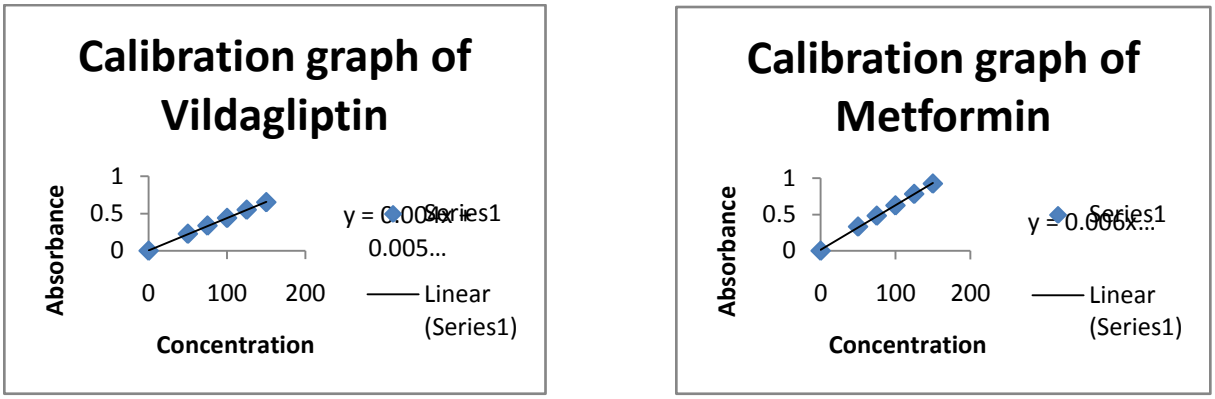


Figure 3: UV overlain spectra for Vildagliptin and Metformin:



(A) **(B)**

Figure 4: Calibration graph of Vildagliptin and Metformin:

Table-2: Recovery

Drug	Level of Recovery (in %)	Amount present (in µg / ml)	Amount found (in µg / ml)	%Recovery	%RSD
Vildagliptin	50%	0.35	0.3479	99.28	0.0966
	100%	0.7	0.7049	100.77	0.1321
	150%	1.05	1.0542	100.4	0.1443
Metformin	50%	3.5	3.498	99.94	0.1598
	100%	7	7.008	100	0.1072
	150%	10.5	10.507	100.06	0.1218

Table-3: Result of Validation parameters

S. No	Validation parameter	Result (Vildagliptin)	Result (Metformin)
1	Linearity	R^2=0.999	R^2=0.999
2	Precision	% RSD	% RSD
	Interday Precision	0.167	0.147
	Intermediate Precision	0.159	0.155
	Intraday Precision	0.136	0.132
3	Accuracy	%Recovery	%Recovery
	50%	99.28	99.94
	100%	100.77	100
	150%	100.4	100.06
4	LOD	0.074 µg / ml	0.44 µg / ml
5	LOQ	0.225 µg / ml	1.35 µg / ml
6	Beer-Lambert's limit	0.17 µg / ml -1.56 µg / ml	1.192 µg / ml -10.73 µg / ml

CONCLUSION:

The method is simple, economical, rapid, precise, accurate and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine estimation of Vildagliptin and Metformin in bulk drug & pharmaceuticals.

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