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Original Research Article

Development and Validation of UV Spectrophotometric Method for Alogliptin Benzoate in Bulk Drug and Tablet Formulation.

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Abstract

A simple, precise and economical spectrophotometric method has been developed for the estimation of Alogliptin benzoate in bulk and pharmaceutical formulations. The quantitative determination of the drug was carried out using the first order derivative method. Alogliptin benzoate shows a sharp peak at 278.0 nm in first order derivative spectrum with n =1. The drug follows Beer-Lambert's law in the concentration range of 2-16µg/ml with correlation coefficient of 0.9996. Results of the analysis were validated statistically and found to be satisfactory. The method was validated as per ICH guideline.

Keywords: Alogliptin benzoate, Derivative spectroscopy, UV spectrophotometry, Validation**.**

Introduction

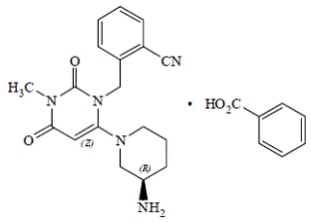

Fig. 1: Structure of Alogliptin.

Alogliptin (ALG), 2-({6-[(3*R*)-3-aminopiperidin-1-yl]-3-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)- yl}methyl) benzonitrile (Fig. 1) is a novel hypoglycemic drug that belongs to dipeptidyl-peptidase-4 inhibitor class which stimulates glucose-dependent insulin release. DPP-4 inhibitors represent a new therapeutic approach to the treatment of type 2 diabetes that functions to stimulateglucose-dependent insulin release and reduce glucagons levels. This is done through inhibition of the inactivation of incretins, particularly glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP), thereby improving glycemic control. Recently, DPP-4 inhibitors have been recommended in the treatment of diabetes mellitus to improve glycemic control and it is effective in controlling the metabolic syndrome and resulted in significant weight loss, a reversal of insulin resistance, islet and adipocyte hypertrophy, and alleviated hepatic steatosis. Thus, the aim of the present work was to develop a UV spectroscopic method for the determination of Alogliptin benzoate in bulk and pharmaceutical preparation. Derivative spectroscopy uses first or higher derivatives of absorbance with respect to wavelength for qualitative and quantitative analysis. This technique has various advantages over other spectrophotometric methods in which broad peak are observed due to solvent and excipients interference which are eliminated by taking the first derivative spectra of drug at respective wavelength. Scattering of radiation and matrix means interference from excipients are common problem in biological analysis in other methods of drug estimation. By first derivative method we can improve the accuracy of quantification of a narrow band component in the presence of a broad band component and to reduce error caused by scattering and matrix. The introduction of microcomputers is made it generally practicable to use mathematical methods to generate derivative spectra quickly, easily and reproducibly. This significantly increased the use of the derivative technique. A derivative spectrum shows better resolution of overlapping bands than the fundamental

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spectrum and may permit the accurate determination of λmax of the individual bands. These advantages of derivative spectroscopy, enhanced resolution and band width discrimination, permit the selective determination of certain absorbing substance in samples in which non-specific interference may prohibit the application of simple spectrophotometric methods [13].

Experimental

Materials

Pure sample of Alogliptin benzoate was purchased from Swapnroop drugs pvt. Ltd. Aurangabad. The 0.1M HCl (analytical reagent grade, Merck) prepared in distilled water and used as solvent. JASCO V-630 UV/VIS spectrophotometer was used with 1cm matched quartz cells.

Method

Accurately about 10mg of the pure drug was weighed and dissolved in 25ml of 0.1M HCl and volume made up to 100ml with double distilled water to give standard stock solution (0.1 mg/ml).Aliquots of standard stock solution were pipette out and suitably diluted with double distilled water to get final concentration of 2-16 µg /ml of standard solution .The solution were scanned in the spectrum mode from 400 nm to 200 nm wavelength range and the first order derivative spectra were obtained at n =1 a sharp peak was obtained at 222.0 nm(Figure-2). The absorbance difference at n=1 (dA/dλ) was calculated by the inbuilt software of the instrument which is directly proportional to the concentration of the standard solution .A calibration curve was plotted taking the absorbance difference (dA/dλ) against the concentration of the standard solutions (Figure-3). The method was applied for the sample solution of known concentration and was found be satisfactory for analysis of tablet formulation. Optical characteristics of Alogliptin indicated in Table 2.

Analysis of Pharmaceutical Dosage Forms

To determine the content of Alogliptin benzoate (label claim: 25 mg of Alogliptin benzoate) twenty tablets were weighed, their average weight determined and. The weight equivalent to 10 mg of Alogliptin benzoate was taken and amount of powder was dissolved in 25ml of 0.1M HCl by stirring for 30 min. The excipients were separated by filtration. After filtration, an appropriate amount of internal standard was added and diluted up to mark with double distilled water. Appropriate aliquots were subjected to above methods and the amount of Alogliptin benzoate was determined. The results are reported in Table 3.

Validation

Validation of proposed method was done by ICH guidelines [14] by means of the following parameters:

Linearity study

The calibration curves were constructed at optimum experimental conditions using absorbance values versus concentration in the range of 2-16 µg/ml. High values of correlation coefficient for Alogliptin benzoate (r =0.9996) indicated good linearity to Beer-Lambert's law. The results are reported in Table 1.

Recovery Study

To study the validity and reproducibility of the proposed method, recoveries were carried out by adding a known amount of drug to pre-analyzed sample at three different levels and the percentage recoveries were calculated. The results are reported in Table 4 and 5.

Ruggedness study

Intra-day precision of the method was determined by analyzing the drug sample three times a day. Inter-day precision of the method was determined by analyzing the drug sample by three different days. The results are reported in Table 6.

Results and Discussion

The developed method for estimation of Alogliptin benzoate in bulk and tablet dosage form was found to be simple, accurate, reproducible, sensitive and economic. For projected method we used easily available and cheep solvent like 0.1M HCL and double distilled water (AR grade), derivative method not required any expensive and satisfactory apparatus in contrast to chromatographic

methods and proposed method required less time for estimation of drug because generation of derivative spectra is quick, so it shows first derivative spectroscopy method is simple, economic and rapid for estimation of Alogliptin benzoate. Precision was calculated as repeatability (±S.D. and %R.S.D) values of Inter-day and Intra-day were closes to standard value(Table 5). Beer-Lambert's law obeyed in the concentration range of 2-16 µg/ml and correlation coefficient observed at 0.9996 it shows good sensitivity and selectivity of method for given concentration of drug .The values of standard deviation were satisfactory and recovery studies (Table 3 and 4) were close to 100 %, it shows accuracy of the developed method and also eliminates the interference caused by the excipients and the degradation product present, if any, in the formulation. First derivative spectrum (Figure 2) of Alogliptin benzoate shows sharp λmax at 222.0 nm with better resolution of overlapping bands. Hence the developed method for estimation of Alogliptin benzoate can be useful in the routine analysis of Alogliptin benzoate in bulk drugs and formulations.

Conclusion

The developed and validated UV estimation method reported here is rapid, simple, accurate, sensitive and specific. The method was also successfully used for quantitative estimation and analysis of Alogliptin benzoate from formulation. Thus the reported method is of substantial importance and has great industrial applicability for quality control and analysis of Alogliptin benzoate from bulk drug and formulations. The first derivative spectroscopy method is significant and beneficial over other reported chromatographic methods due to it does not shows problems of Scattering of radiation, matrix interference from excipient and overlapping in bands. By observing validation parameter and statistical data, the proposed method was found to be satisfactory over other reported spectroscopic and chromatographic methods.

Acknowledgement

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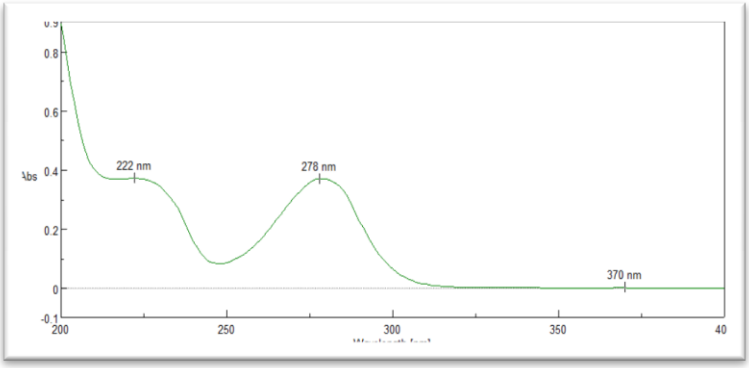

Fig. 2: Spectra of Alogliptin.

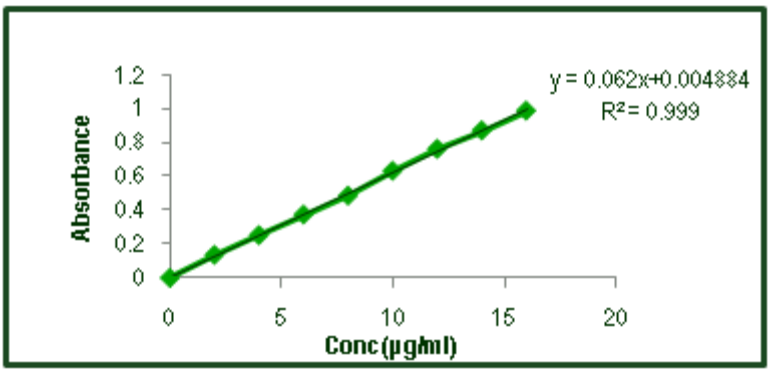

Fig. 3: Calibration curve of Alogliptin at 222 nm Method.

Table 1: Standard calibration Table for Alogliptin Benzoate.

conc. of Alogliptin (µg/ml)	Absorbance at 222 nm	SD*	% RSD*
0	0.000	0.000000	0.00000
2	0.1362	0.003033	0.22139
4	0.2437	0.0002653	0.10456
6	0.3754	0.0006801	0.1805
8	0.4873	0.0001673	0.03437
10	0.6343	0.00231	0.0348
12	0.7638	0.00027	0.035557
14	0.8734	0.0001	0.01621
16	0.9902	0.0001	0.139
	Avg. SD	**0.0002646**	
	Avg. % RSD		**0.357313**

***average of six estimations.

Table 2: Optical Characteristic and Other Parameters.

Parameters	Alogliptin
Slope	0.062
Intercept	0.004884
Correlation coefficient (R2)	0.999
Range	2-16 µg/ml

Table 3: Estimation of Alogliptin benzoate in tablet Formulation.

Alogliptin benzoate	Amount present (mg)	Amount found (mg)	% Estimated	±S.D*	%RSD*
1	25	24.98	99.92	0.5717	0.5746

***average of six estimations.

Table 4: Recovery Study Data for Alogliptin benzoate.

Level of % Recovery	Amount present	Amount added	% Recovery
50	10	5	100.81
	10	5	99.46
	10	5	99.53
100	10	10	100.14
	10	10	100.86
	10	10	99.88
150	10	15	100.16
	10	15	99.62
	10	15	99.62

Table 5: Statistical data of recovery Study for Alogliptin benzoate.

% Recovery level	Alogliptin	
	%Recovery ± SD*	% RSD *
50%	99.76 ± 0.03785	0.03794
100%	99.99 ± 0.756 301	0.7596
150%	99.44 ± 0.05686	0.5718

***average of six estimations.

Table 6: Intra-day and Inter-day precision data for Alogliptin benzoate.

Alogliptin conc.(µg/ml)	Intra-day precision			Inter-day precision		
	Mean % of Estimated	± SD*	% RSD*	Mean % of Estimated	± SD*	% RSD*
5	99.573	0.15177	0.15246	99.45	0.1345	0.1354
10	99.61	0.28658	0.28775	99.74	0.1205	0.1208
15	99.74	0.20408	0.20468	99.63	0.62002	0.61888

***average of six estimations.