

Research Article



New Derivative Spectrophotometric Methods for the Determination of Epalrestat – An Anti Diabetic Drug

Sharath Chandra. Seelam*, Dhanalakshmi.K, Nagarjuna reddy

Department of Pharmaceutical Analysis, KLR Pharmacy College, New Paloncha, Khammam Dist, Andhra Pradesh, India.

*Corresponding author's E-mail: sharathpharma99@hotmail.com

Accepted on: 13-05-2013; Finalized on: 30-06-2013.

ABSTRACT

A simple, efficient and reproducible derivative spectrophotometric method was developed for the drug Epalrestat in bulk and tablet dosage forms. First derivative spectrophotometric estimation is used for the elimination of irrelevant absorption. Epalrestat was determined at 388 nm, 366nm for zero, and first order derivatives respectively using methanol as solvent. Linearity was obtained within the range of 1-7 µg/ml with correlation coefficient of 0.999, and 0.998 for zero and first order derivatives. The %recovery for the proposed method was found to be 100.04-131.06, 102.31-129.34% indicating no interferences from the tablet excipients. The result of analysis was validated statistically and recovery studies confirmed the accuracy and precision of the proposed method.

Keywords: Epalrestat, First Order Derivative Spectroscopy, Zero Order Derivative Spectroscopy, Derivative spectroscopy.

INTRODUCTION

Epalrestat is an aldose reductase inhibitor is used in the treatment of peripheral neuropathy chemically known as 5-[(Z,E)-β-Methylcinnamylidene]-4-oxo-2-thioxo-3- thiazolidine acetic acid and The recommended dosage of oral epalrestat is 50mg 3 times daily before meals. Epalrestat is particularly recommended for use in patients with high glycosylated haemoglobin levels (indicating failure to control hyperglycaemia), despite standard pharmacological and non pharmacological intervention.

The methods for Epalrestat in bulk and pharmaceutical dosage forms was determined by RP-HPLC¹⁻² but only few are reported the zero order and area under curve in pharmaceutical formulations Epalrestat³.

Derivative spectroscopy involves in the conversion of the normal spectrum into its derivatives⁴. Derivatives minimises the interaction of matrix interferences which results in accurate estimation of the API in the dosage form unlike zero order⁵. As the order of derivatives increase there will be decrease in interferences⁶.

The literature reports do not show any Derivative spectrophotometric method for Epalrestat in bulk and pharmaceutical formulation, hence there is a need to develop and validate an analytical method for the Epalrestat in bulk and dosage form. Hence the present study aims to develop and validate a method Epalrestat in bulk and tablet dosage form by Derivative spectrophotometrically. The structure of Epalrestat is given under Figure 1.

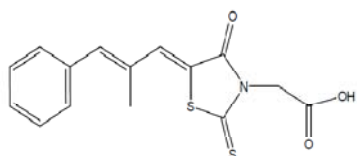


Figure 1: Structure of Epalrestat

MATERIALS AND METHODS

Chemicals and Materials

Epalrestat standard supplied by IDEAL ANALYTICAL AND RESEARCH INSTITUTION Puducherry-605 110 as a gift sample Analytical grade solvent Methanol was purchased from local market, Milli-Q Water obtained from all glass double distillation apparatus. Eparel50 (Micro labs Ltd), India tablets was purchased from local market.

Instrumentation

Spectral and absorbance measurements are done on UV Spectrophotometer with software UV Win, lab India make 3092. 10mm path length quartz cells were used. Digital analytical balance Shimadzu make AUX 220 was used for weighing.

Preparation of standard stock solution

Weigh accurately and transfer about 25.00mg of Epalrestat working standard into a 50mL volumetric flask. Add about 5mL of methanol and sonicate to dissolve. Make up the volume with methanol and mix well.

From the above solution transfer 5mL to 25mL volumetric flask and make up the volume with methanol, mix well.

Preparation of test solution

A quantity of powder equivalent to 25.00mg (78.50mg) of Epalrestat dosage form was transfer carefully into 50mL volumetric flask and dissolves in 10mL methanol and make up the volume with methanol. From the above solution transfer 5ml to 25mL volumetric flask and make up the volume.

Method Validation

Linearity

Aliquots of solutions 0.1-0.7ml were taken from the standard stock solution in to 10ml volumetric flasks. The

volume is made up to 10 ml using methanol to obtain the concentrations of 1,2,3,4,5,6,7 (mcg/ml). The absorbance was measured at 388nm, 366nm, against a blank. The linearity curve for zero order and first order derivatives were plotted was given in Figure 2 and 3. The all spectra for standard Epalrestat solution in zero order were given in Figure 4 and higher concentration of first order was given in Figure 5.

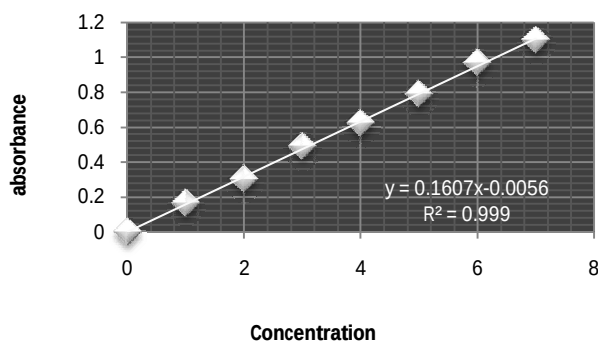


Figure 2: Linearity for zero order

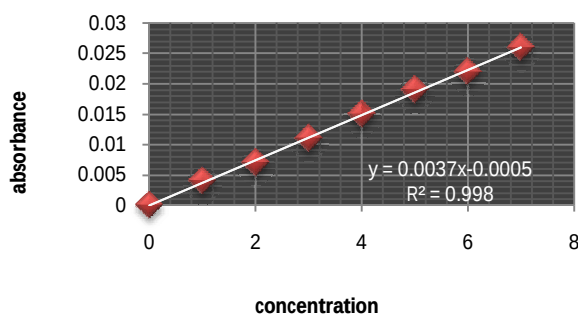


Figure 3: Linearity for First order

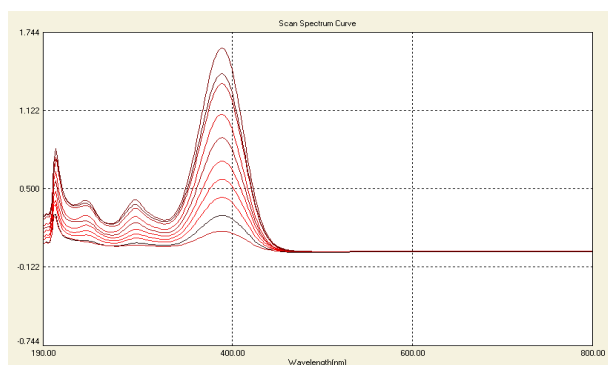


Figure 4: All Spectra of Zero order

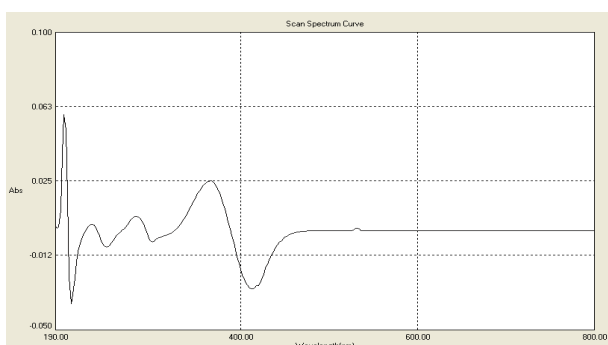


Figure 5: First Order Derivative spectra (7 mcg)

Precision (as per USP)

Preparation of Precision sample solution (Prepare in six replicates)

Transfer carefully different concentrations of tablet content into 6 different 50mL volumetric flask and dissolve in 5mL methanol and make up the volume with methanol from the above solution transfer 5ml to 25mL volumetric flask and make up to 25mL. Record the absorbance at 388 and 366 nm against blank. The results are tabulated in table 1.

Accuracy (as per USP)

Accuracy can be done by measuring the absorbance of three replicate samples at 100% dilution and three replicate samples each at other levels prepared by spiking Epalrestat API Sample solution at 10%, 20%, 30%, to test stock solution of target concentration level.

Preparation of sample solution (100% Dilutions) Prepare in triplicate

A quantity of powder equivalent to 25.00mg (78.50mg) of Epalrestat transfer carefully into 50mL volumetric flask and dissolve in 5mL methanol and make up the volume with methanol, from the above solution transfer 5ml to 25mL volumetric flask and make up the volume.

Preparation of sample solution (10% standard spiked) Prepare in triplicate

From the above sample stock solution transfer carefully 5ml into 25ml volumetric flask, to this add 0.5ml of standard stock solution and make up the volume with methanol.

Preparation of sample solution (20% standard spiked) Prepare in triplicate

From the above sample stock solution transfer carefully 5ml into 25ml volumetric flask, to this add 1.0ml of standard stock solution and make up the volume with methanol.

Preparation of sample solution (30% standard spiked) Prepare in triplicate

From the above sample stock solution transfer carefully 5ml into 25ml volumetric flask, to this add 1.5ml of standard stock solution and make up the volume with methanol.

All the above solutions are filter through 10µm filter and measure the absorbance at 388 and 366nm. The results are tabulated in table 2.

Detection Limit

The Detection Limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

The detection limit (LOD) may be expressed as:

$$\text{LOD} = 3.3\sigma / S$$

Where

σ = Relative standard deviation of the response.

S = the slope of the calibration curve (of the analyte).

Quantitation Limit

The Quantitation limit of an analytical procedure is the lowest amount of analyte in a sample, which can be quantitatively determined with suitable precision and accuracy.

Quantitation Limit (LOQ) may be expressed as:

$$LOQ = 10\sigma/S$$

Where

σ = Relative standard deviation of the response.

S = the slope of the calibration curve (of the analyte).

The results are tabulated in table 3.

Assay

The proposed method was applied to the determination of Epalrestat in a brand name Eparal50. The spectra for Zero order and first order derivatives were obtained. The results are tabulated in table 3.

RESULTS

Accuracy

The accuracy solutions were prepared individually at 100%, 110%, 120%, and 130%. They were analysed and % recovery obtained is tabulated in table 2.

Assay, LOD and LOQ data

Observations of Assay, LOD and LOQ data are provided in table 3.

Table 1: Precision data of Epalrestat

Sample Id	Standard Absorbance		Sample Absorbance		Mg/Tablet	% of Drug
	Zero order	First order	Zero order	First order		
1	0.622	0.014	0.623	0.014	50.01	100.02
2	0.622	0.014	0.627	0.015	50.05	100.10
3	0.622	0.014	0.628	0.015	50.06	100.12
4	0.622	0.014	0.618	0.013	49.96	99.92
5	0.622	0.014	0.621	0.014	49.99	99.98
6	0.622	0.014	0.622	0.014	50.00	100.00
Mean	0.622	0.014	0.623	0.0141	-----	100.02
SD	-----	-----	0.0037	0.0075	-----	-----
%RSD	-----	-----	0.0593	-----	-----	-----

Table 2: Accuracy data of Epalrestat

Sample Id	No Of Replicates		Absorbance		Average		% Recovery	
	Zero order	First order	Zero order	First order	Zero order	First order	Zero order	First order
1	100%-1		1.135	0.027	1.135	0.027	100.04	102.31
	100%-2		1.135	0.027				
	100%-3		1.135	0.027				
2	110%-1		1.263	0.029	1.262	0.029	111.7	110.03
	110%-2		1.264	0.029				
	110%-3		1.262	0.030				
3	120%-1		1.372	0.032	1.372	0.032	121.4	121.6
	120%-2		1.372	0.033				
	120%-3		1.373	0.032				
4	130%-1		1.480	0.034	1.480	0.034	131.06	129.34
	130%-2		1.480	0.035				
	130%-3		1.481	0.034				

Table 3: Assay, LOD and LOQ data of Epalrestat

Sample Id	Zero order	Mg/tab	First order	Mg/tab	LOD For Zero order	LOQ For Zero order
1	102%	0.051	104%	0.052	0.554mcg/ml	0.230mcg/ml



DISCUSSION AND CONCLUSION

The method was validated and found to be simple, sensitive, accurate and precise as per ICH guidelines. Zero order, first order derivative spectrophotometric methods were developed for the determination of Epalrestat in bulk and tablet dosage form. Epalrestat can be directly determined in tablets in presence of excipients without sample pre treatment procedures by using spectrophotometric methods. The apparatus and reagents used seem to be accessible even for the simple laboratories. Also, no significant difference was found between the proposed spectrophotometric methods. Therefore, developed methods can be recommended for routine and quality control analysis of epalrestat pure drugs and their pharmaceutical formulations.

REFERENCES

1. Janaki pathi.P, Appala Raju.N; Analytical Development and Validation of RP-HPLC method for the estimation of Epalrestat in tablet dosage form. Asian J. Pharm. Ana, 2(2), 2012, 49-51.
2. Shirkhedkar.A, Chetan Nankar.S, Sanjay Surana.J; Quantitative determination of Epalrestat (EPL) by RP-HPLC method. Eurasian J Anal Chem, 7(1), 2012, 49-55.
3. Dr.shirkhedkar.A, Nankar Chetan, Patil Amod; The Zero order and area under curve Spectrophotometric methods for determination of Epalrestat in Pharmaceutical Formulation. Internationale pharmaceutica sciencia, 2(2), 2012, 8-12.
4. Kalpesh Patel.N, Jayvadan Patel.K, Ganesh Rajput.C, Naresh Rajgor.B; Derivative spectrometry method for chemical analysis: A review. Der Pharmacia Lettre, 2(2), 2010, 139-150.
5. Sivakumar Ch.V, Chandrakala Gunturu, Meera Indrakanti; Second and third order derivative spectrophotometric estimation of ofloxacin in bulk and pharmaceutical dosage form. International Journal Of Pharmacy & Technology, 3(3), 2011, 3083-3091.
6. Bilal YILMAZ; Determination of Atenolol in Pharmaceutical Preparation by Zero-, First, Second and Third Order Derivative Spectrophotometric Methods. FABAD J. Pharm. Sci, 3, 2008, 119–129.

Source of Support: Nil, Conflict of Interest: None.

