Print ISSN: 0974-2115
www.jchps.com Journal of Chemical and Pharmaceutical Sciences

First Derivative Spectrophotometric Methods for the Quantification of Epalrestat (An Aldose Reductase Inhibitor)

Mukthinuthalapati Mathrusri Annapurna*, Malineni Sushmitha and Kunala Anusha
Department of Pharmaceutical Analysis and Quality Assurance,
GITAM Institute of Pharmacy, GITAM University, Visakhapatnam, India
***Corresponding author: E-Mail: mathrusri2000@yahoo.com**

ABSTRACT

Epalrestat is a noncompetitive reversible inhibitor of aldose reductase. Three first derivative spectrophotometric methods have been developed for the estimation of Epalrestat in pharmaceutical formulations using phosphate buffer (pH 5.0), phosphate buffer (pH 7.0) and borate buffer (pH 9.0).and Beer-Lambert's law was obeyed 0.1-20, 0.1-25 and 0.1-20 µg/ml respectively. The three methods were validated and applied for the analysis of tablets.

KEY WORDS: Epalrestat, Tablets, Derivative spectroscopy, Validation.

1. INTRODUCTION

Epalrestat is used to treat diabetic neuropathy in patients with diabetes mellitus. Epalrestat is 2- [(5Z)- 5- [(E)- 3-phenil- 2- methylprop- 2- enylidene]- 4-oxo- 2-thioxo- 3- thiazolidinyl] acetic acid (Mo. Wt. 319.41g/mol). Epalrestat was analyzed by various techniques such as HPLC (Atul, 2012), UPLC (Sharath Chandra, 2013) and spectrophotometry (Patel Hiral, 2013; Sharath, 2013; Sharath Chandra, 2013; Patel Chandani, 2014). The authors have proposed three simple methods for the assay of Epalrestat in the present study and validated (ICH guidelines, 2005).

2. MATERIALS AND METHODS

Instrumentation: A UV-1800, Shimadzu (Japan) double beam UV-VIS spectrophotometer with spectral bandwidth of 1nm was employed for the spectral analysis and electronic balance (Shimadzu) was used during the weight measurements.

Reagents and chemicals: Analytical grade reagents were used. Pure samples of Epalrestat were supplied as gift sample from Zydus Cadila Healthcare Ltd., India. Epalrestat is commercially available as tablets and injections with brand name EPAREL ((Label claim: 50.0 mg/tablet, Micro labs Ltd., Bangalore) ALDONIL ((Label claim: 50.0 mg/tablet Zydus Cadila Healthcare Ltd., Gujarat).

Borate buffer (pH 9.0) was prepared by dissolving 6.2 g of boric acid in water followed by the adjustment of pH to 9.0 with 1M sodium hydroxide in 1 litre volumetric flask. Phosphate buffer (pH 5.0) can be prepared by dissolving 6.8 g of potassium di hydrogen phosphate in water followed by the adjustment of pH to 5.0 with 10M potassium hydroxide in 1 litre volumetric flask. Phosphate buffer (pH 7.0) can be prepared by dissolving 50.0 ml of 0.2 M potassium dihydrogen phosphate and 29.1 ml NaOH in water in a 1 litre volumetric flask.

Preparation of stock solutions: Epalrestat stock solution was prepared by dissolving 100 mg of the drug in methanol in 100 ml volumetric flask (1000 µg/ml) and further dilutions were made with the reagents mentioned for methods A, B and C respectively.

Validation:

Linearity and Range: A series of Epalrestat solutions 0.1-20, 0.1-25 and 0.1-20 µg/ml were prepared in phosphate buffer (pH 5.0), phosphate buffer (pH 7.0) and borate buffer (pH 9.0) for method A, B and C respectively and scanned in UV region against their reagent blank. The absorbance of these solutions were noted at λ_{max} from their absorption spectra in all the three methods A, B and C. Calibration curves were drawn by plotting the concentration on the x-axis and the derivative absorbance on y-axis in method A, B and C.

Precision and Accuracy: Precision studies were performed (5, 10 and 20 µg/ml) individually on the same day (Intra-day) for all the five methods A, B and C respectively and percentage RSD was determined. The inter-day precision study was also performed on three different days i.e. day 1, day 2 and day 3 at three levels (5, 10 and 20 µg/ml) individually for all the five methods A, B and C respectively. Accuracy was determined by spiking the pure drug solutions with the pre-analysed formulation solution. Epalrestat was extracted from the formulation (10 µg/mL) and spiked with pure drug solution (80%, 100% and 120%) and recovery was calculated.

Assay of tablets: EPAREL and ALDONIL tablets were procured from the local pharmacy store, and twenty of them were weighed and powdered. Powder which is equivalent to 25 mg of Epalrestat was transferred carefully in to two different 25ml volumetric flasks and extracted with methanol. The filtrate was diluted with the respective reagents separately for method A, B and C respectively and the percentage recovery was calculated.

3. RESULTS AND DISCUSSION

Three new spectrophotometric methods (D_1) were proposed for the assay of Epalrestat in all the reagents mentioned for method A, B and C respectively. The resulting overlay derivative spectra were shown in Figure 2. The zero crossing points were observed at 334.18, 399.37 and 498.73 nm for method A, 231.01, 267.20, 296.20, 329.11, 398.73 and 493.67 for method B and 227.84, 233.46, 267.75, 294.87, 333.76, 399.27 and 494.45 for method C respectively. The amplitude was chosen for method A, B and C for the linearity study. Epalrestat has shown maxima at 378.42 and minima at 428.48 nm in all the three methods A, B and C and therefore amplitude was selected for the spectral calculations.

Validation: Calibration graphs were drawn by plotting the Epalrestat concentration on x-axis and respective absorbance on y-axis for method A, B and C (Figure 3). The linear regression equations were found to be y = 0.0067x + 0.0014 (R^2=0.9994), y = 0.0047x + 0.0005 (R^2=0.9997) and y = 0.0065x - 0.0004 (R^2=0.9991) in method A, B and C respectively. The RSD in precision studies was less than 2% in all the method A, B and C that the methods are more precise. The recovery percentage in accuracy studies was ≤ 97.9 % in all the three methods emphasizing that the method is more accurate. The optical characteristics of Epalrestat were given in Table.1.

The methods were examined for the recovery studies of Epalrestat marketed formulations. The percentage recovery was 98.17-99.24, 97.57-97.85 and 98.45-98.84 for method A, B and C respectively (Table.2).

Table.1. Characteristics of Epalrestat

Parameters	**Method A**	**Method B**	**Method C**
Amplitude (nm)	378.42 - 428.48	378.42 - 428.48	378.42 - 428.48
Regression equation (y=mx + c)	y = 0.0067x + 0.0014	y = 0.0047x + 0.0005	y = 0.0065x - 0.0004
Correlation coefficient (R^2)	0.9994	0.9997	0.9991
Linearity range (µg/ml)	0.1-20	0.1-25	0.1-20
Accuracy (% Recovery) (%RSD))	98.15-99.20 (0.11)	97.9-99.18 (0.24)	98.3-99.25 (0.28)
Precision Intra-day (% RSD)	0.21-0.44	0.19-0.39	0.25-0.43
Inter-day (% RSD)	0.74-0.92	0.64-0.93	0.50-0.99

Table.2. Assay of Epalrestat tablets

Brand	**Labeled Amount (mg)**	***Amount obtained (mg)**			**% Recovery***		
		Method			**Method**		
		A	**B**	**C**	**A**	**B**	**C**
I	50.0	49.62	48.785	49.225	99.24	97.57	98.45
II	50.0	49.085	48.925	49.42	98.17	97.85	98.84

*Each value is average of three determinations

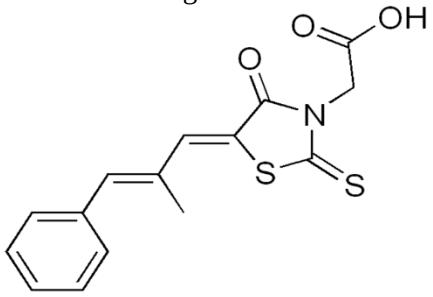
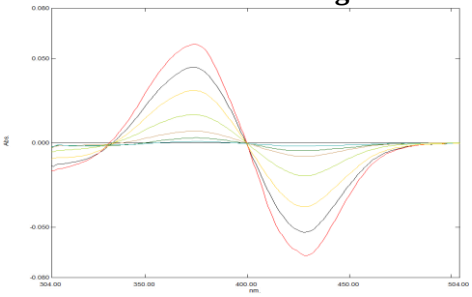
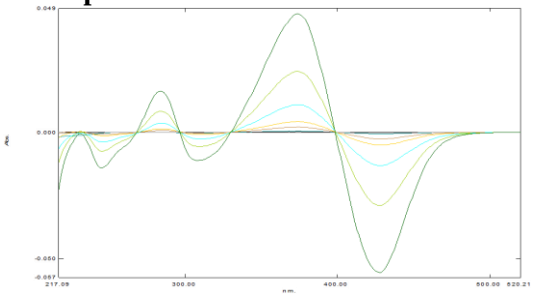


Figure.1. Chemical structure of Epalrestat





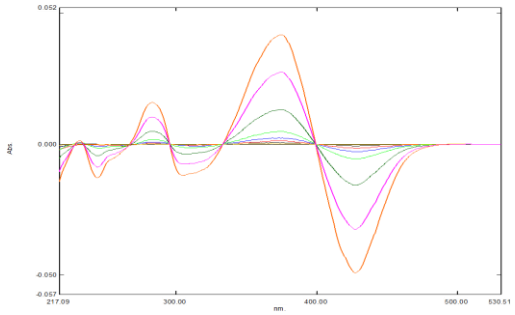


Figure. 2. Overlay first derivative spectrum of Epalrestat in Phosphate buffer pH-5.0 [A], Phosphate buffer pH- 7.0 [B] and Borate buffer pH-9.0 [C]

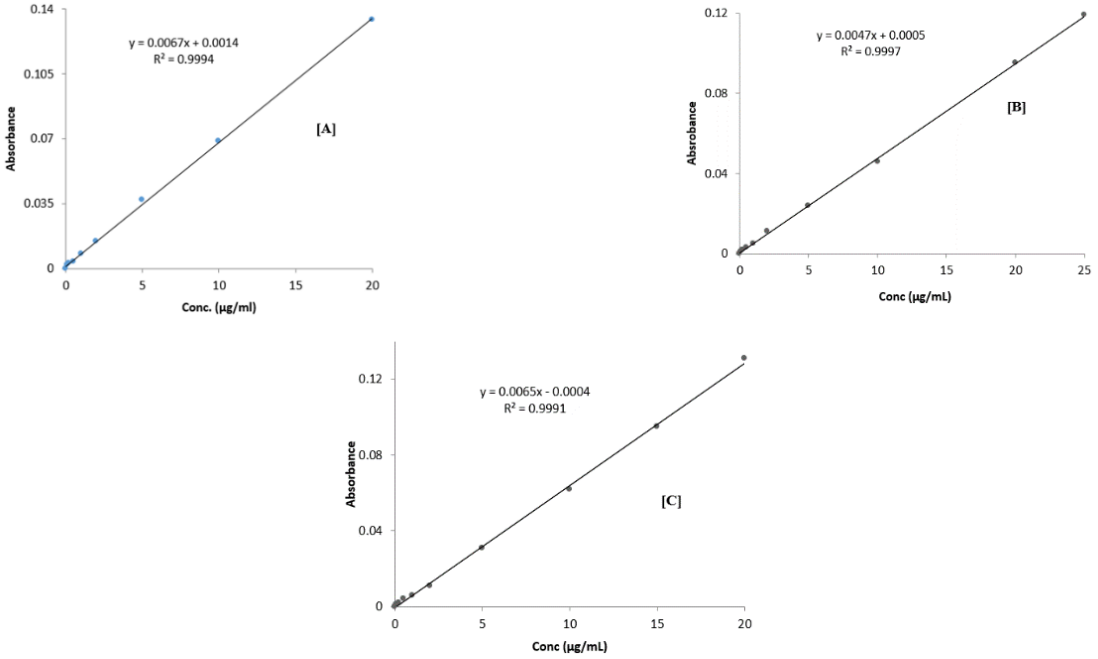


Figure.3. Calibration curves of Epalrestat in Phosphate buffer pH-5.0 [A], Phosphate buffer pH- 7.0 [B] and Borate buffer pH-9.0 [C]

4. CONCLUSION

The three spectrophotometric techniques so far suggested for the determination of Epalrestat are validated. The three methods are economical and suitable for assay of Epalrestat in pharmaceutical formulations.

5. ACKNOWLEDGEMENT

The authors are grateful to M/s GITAM University, Visakhapatnam for providing the research facilities. The authors do not have any conflict of interest.

REFERENCES

Atul Arun Shirkhedkar, Chetan Shantaram Nankar, Sanjay Javarilal Surana, Quantitative determination of Epalrestat using reversed – phase high-performance liquid-chromatography, Eurasian Journal of Analytical Chemistry, 7 (1), 2012, 49-55.

International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceutical for Human Use, Validation of Analytical procedures, Text and methodology - Q2 (R1), 2005.

Patel Chandani D, Patel Rajan J, Shah Shruti S, Mardia R.B, Chauhan S.P, Suhagia B.N, Simultaneous estimation of epalrestat and methylcobalamin in bulk and tablet formulation by UV spectrophotometery and liquid chromatography, Indo American Journal of Pharmaceutical Sciences, 4 (5), 2014, 2650-2656.

Patel Hiral M, Shaikh Farhatjahan, Bharucha Rinal, Kachhadiya Kruti, Development and validation of analytical methods for estimation of epalrestat and methylcobalamin in bulk and in tablet dosage by absorption ratio method. Inventi Rapid, Pharma Analysis & Quality Assurance, 2013.

Sharath Chandra Seelam, Dhana Lakshmi K, Nagarjuna Reddy G, Sreenivasa, Analytical method validation of Epalrestat an antidiabetic drug in bulk and tablet formulations by UPLC - A novel technique, Indo American Journal of Pharmaceutical Research, 3 (7), 2013, 5479-5187.

Sharath Chandra Seelam, Dhanalakshmi K, Nagarjuna Reddy New derivative spectrophotometric methods for the determination of epalrestat, an anti - diabetic drug, Int. J. Pharm. Sci. Rev. Res, 21 (1), 2013, 247-250.

Sharath Chandra Seelam, Swarna Mayuri R, Priyanka G, Priyanka M, Nidhi NK, UV spectrophotometric methods for estimation of epalrestat in bulk and dosage forms by difference and area under curve methods, Indo American Journal of Pharmaceutical Research, 3 (7), 2013, 5134-5140.

Sharathchandra Seelam, Dhanalakshmi K, Nagarjuna Reddy G Validation of derivative spectrophotometric and UPLC methods for Quantitative determination of epalrestat in bulk and pharmaceutical dosage form, International Journal of Pharmacy and Pharmaceutical Sciences, 5 (3), 2013, 341-346.