Original Article

Development and Validation of Spectrophotometric Method for the Determination of Perindopril Erbumine in Bulk Dosage Form

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ABSTRACT

A simple, accurate, cost effective and reproducible spectrophotometric method has been developed for the estimation of perindopril erbumine in bulk and pharmaceutical dosage form. UV spectrophotometric method, which is based on measurement of absorption at maximum wavelength 213nm. The developed method was validated with respect to accuracy, linearity, precision, limit of detection, limit of quantification and Sandell's sensitivity. Beers law was obeyed in the concentration range of 4-16µg/ml having line equation Y=0.01350X+0.05879 with correlation coefficient of 0.998. Results of the analysis were validated statistically.

Keywords: UV spectrophotometry, Perindopril Erbumine, Method validation.

INTRODUCTION

Perindopril Erbumine Tert-butylammonium (2S, 3a S, 7a S)-1-N-[(S)-1-ethoxycarbonyl butyl]-(-alanyl) perhydroindole-2-carboxylate is a dipeptide monoester with perhydroindole group. It is an Angiotensin Converting Enzyme inhibitor[1]. Perindopril Erbumine is used in treatment of hypertension and heart failure, it is also used to reduce proteinuria and renal diseases in patients with nephropathies, prevent myocardial infarction, stroke and cardiac death in high risk patients. Perindopril Erbumine is converted to Perindoprilat in liver. The overall bioavailability of Perindopril is about 66% following absorption approximately 38% of the systemically available perindopril is hydrolysed to perindoprilat (active metabolite) which has mean bioavailability of about 27%. Peak plasma concentration of Perindoprilat is attained in 3-7 hours after administration of Perindopril. Perindopril is extensively metabolized following oral administration with only 4-12% of the dose recovered unchanged in urine[2,3]. Literature survey revealed that Perindopril is official in British pharmacopoeia[4]. It was also observed that Perindopril has been analysed by different methods either individually or in combination with other drug. The methods include HPLC, RP-HPLC, Microcalorimetry, Immunoassay,

Spectroflurometry, Densitometry, biosensor methods, LC-MS/MS, capillary gas chromatographic method, spectrophotometric method and electrochemical methods[5-13].

The objective of the current study was to develop a simple, precise and accurate UV spectrophotometric method. The newly developed method was validated as per ICH guidelines to confirm the reproducibility and application of the method[14].

MATERIALS AND METHODS

Instrumentation

The instrument used for the current study was UV-VIS Spectrophotometer (SHIMADZU-1800).

Chemicals

Perindopril Erbumine was generously gifted by Hetero drugs Pvt Ltd. distilled water was used as diluent.

Selection of λmax

Preparation of stock solution

An accurately weighed 10 mg of perindopril erbumine was transferred in a 100ml volumetric flask. To the flask distilled water was added in small proportion so as to dissolve perindopril erbumine. The volume was made up to 100ml with distilled water to get a concentration of 100µg/ml.

Determination of λmax

20µg/ml solution of Perindopril Erbumine was prepared in diluent. The resulting solution was scanned in UV-Vis spectrophotometer from 400-200nm to determine the λmax. The λmax of Perindopril Erbumine was found to be 213 nm.

Preparation of calibration curve for Perindopril Erbumine

Aliquots (0.2-2.0ml) from standard stock solution were pipette out in series of ten 10 ml volumetric flask and the volume was made up with distilled water. The absorbance was measured in triplicate at 213 nm against blank. The calibration curve data and summary of analytical parameters are presented in table 1 and 3.

Method validation[14]

Accuracy, Precision, linearity. Limit of detection and limit of quantification were studied to validate the Spectrophotometric method for determination of perindopril erbumine.

RESULTS & DISCUSSION

Accuracy

The accuracy of the method was established by using recovery experiments i.e. by external dilution method. The known amount of standard was added at three different levels of 80%, 100% and 120% of sample. The percentage recoveries were calculated from calibration curve. The data is summarised in table 2.

Precision

The precision of analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurement obtained from multiple sampling of the same homogenous sample under the prescribed condition. Precision was determined by repeatability (intra-day) and intermediate precision (inter-day). Repeatability was evaluated by 3 determinations of 3 different concentrations during the same day. Intermediate precision was determined during 3 different days. Precision (intra-day and inter-day) were expressed as relative standard deviation.

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.

Calibration curve was constructed by plotting absorbance versus concentration which showed linearity over the concentration range of 4-16µg/ml.

Detection and quantification limits

Limit of detection

The limit of detection of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected it was calculated using the following formula

$$LOD = 3.3\sigma/S$$

Where, = the standard deviation of the response, S = the slope of the calibration curve (of the analyte)

Limit of quantification

The limit of quantification of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined. It was calculated using the following formula

$$LOQ = 10\sigma/ S$$

Where σ, =the standard deviation of the response, S=the slope of the calibration curve (of the analyte).

CONCLUSION

The developed method was found to be simple, sensitive, and accurate and can be used for routine quality analysis of perindopril erbumine in bulk dosage form.

REFERENCES

1. Sweetman S.C. In Martindale: The complete Drug Reference. Pharmaceutical Press.London. 2002; 33: 953.
2. O'Neil M. J., Smith A., Heckelman P. E. and Kinneary J. F. The Merk Index, an Encyclopedia of Chemicals, Drugs and Biologicals. Merck & Co. Inc., White House Station, New Jersey. 1996; 12: 1234.
3. Hai Lu Zaho, Qian Chen, Wilson Ys Leung, G Neil Thomas and Brian Tomlinson. Perindopril: Along acting angiotensin converting enzyme inhibitor with new clinical trial data. Drug Profile medical progress. 2003: 40-48.
4. British Pharmacopoeia. British Pharmacopoeial Commission office, London,U.K. 2007; vol. II: 1609 – 1611.
5. Z. Simoncic, R. Roskar, A. Gartner, K. Kogej and V. Kmetec. The use of microcalorimetry and HPLC for determination of degradation kinetics and thermodynamic parameters of perindopril erbumine in aqueous solution. *Int. J. Pharm*. 2008; 356 (1-2): 200-05.
6. V Bhaskara Raju and A. Lakshmana Rao. Development and validation of new HPLC method for estimation of perindopril in tablet dosage form. RJC. 2011; 4(1):113-116.
7. Bharadwaj V, Gulecha B, Madgulkar A, Damle M. Reverse phase high performance liquid chromatographic method for simultaneous estimation of perindopril and indapamide in tablet formulation. Indian *Drugs* 2007; 44(7): 504-07.
8. Chaudhary AB, Patel RK, Chaudhary SA. Determination of Losartan Potassium and Perindopril Erbumine in Tablet Formulations by Reversed-Phase HPLC. *Int. J. Chem Tech Res* 2010; 2 (2): 1141-46.
9. Van den Berg et al., A New Radioimmunoassay for the Determination of the Angiotensinconverting Enzyme Inhibitor Perindopril and its Active Metabolite in Plasma and Urine: Advantages of a Lysine Derivative as Immunogen to Improve the Assay Specificity. *J.Pharm. Biomed. Anal*. 1991; 9: 517-24.
10. Van Staden J. F., Stefan R. I., Aboul-Enein H. Y., Amperometric biosensor based on D aminoacid oxidase for the R-perindopril assay Fresen *J Anal Chem*.2000;367: 178-180.
11. Deepak S. Jain, Gunta Subbaiah, Mallika Sanyal, Umesh C. Pande and Pranav Shrivastav. First LC–MS/MS electrospray ionization validated method for the quantification of perindopril and its metabolite perindoprilat in human plasma

and its application to bioequivalence study. *J. Chromatogr*. B 2006; 837: 92-100.
12. Lin S. J., Wu H. L., Chen S. H., Wen Y.H.,Derivatization-GAS Chromatographic Determination of Perindopril, *Analytical Letters* 1996; 29: 1751 – 62.
13. Erk N. Comparison of spectrophotometric and LC method for determination of perindopril and indapamide in pharmaceutical formulation. *J. Pharm. Biomed Anal.* 2001; 26: 43-52.
14. ICH, Q2B. Validation of Analytical Procedure: Methodology. International Conference on Harmonization, IFPMA, Geneva. 2005

Table 1. Calibration curve data for perindopril erbumine

Sr.no	Concentration	Absorbance	Standard deviation	% RSD
1	4	0.111	0.001	0.892857
2	6	0.142	0.001732	1.202813
3	8	0.167	0.002	1.212121
4	10	0.198	0.004726	2.431809
5	12	0.215	0.001	0.465116
6	14	0.248	0.003606	1.471654
7	16	0.275	0.005033	1.834711

Table 2. Determination of accuracy by percentage recovery method

Ingredient	Tablet amount µg/ml	Level of addition (%)	Amount added	Drug found µg/ml	% Recovery	Average
Perindopril erbumine	4.44	80%	3.55	7.93	99.24	99.2533
	4.44	100%	4.44	8.73	98.30	
	4.44	120%	5.38	9.80	100.12	

Table 3. Summary of validation parameters of perindopril erbumine

Parameters	Perindopril erbumine
Absorption maxima	213nm
Linearity range	4-16µg/ml
Std regression equation	Y=0.01350X+0.05879
Correlation coefficient	0.99861
Molar absorptivity	0.04982
$A^{1\%}_{1CM}$	206.42
Accuracy	99.2533%
Precision	Intra-day: 1.142829
	Inter-day: 1.238583
Limit of detection	1.04435
Limit of quantification	3.1647
Sandell's sensitivity	0.04982

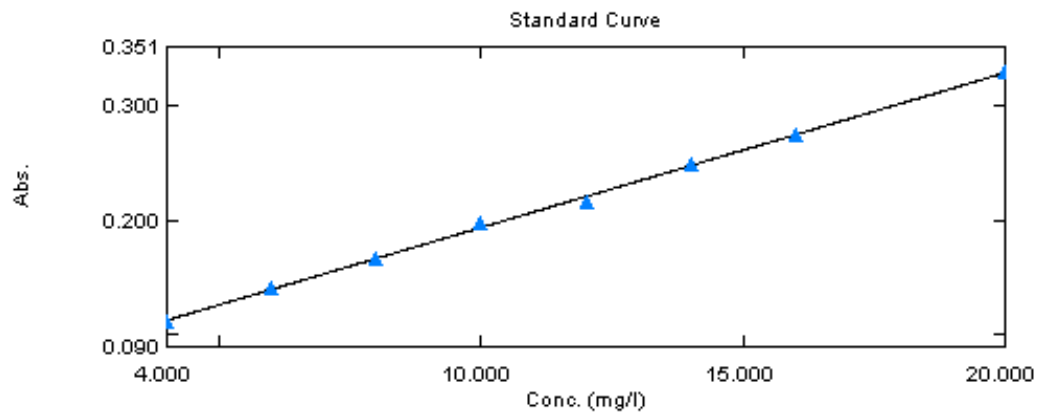

Figure.1. Calibration curve for perindopril erbumine.