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Research Article

Method development of Perindopril using UV spectrophotometer

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ABSTRACT
Perindopril is chemically (2S, 3aS, 7aS)-1-[(S)-N-[(S)-1-carboxybutyl] alanyl] hexahydro-2-indolinecarboxylic acid 1-ethyl ester2. It is an angiotensin-converting-enzyme inhibitor (ACE inhibitor). In this method measurement of absorbance at the wavelength of maximum absorptions of Perindopril using water as a solvent is done . The calibration curve was linear in concentration range of 12.5-200 µg/ml for Perindopril with correlation coefficient of 0.9991. The accuracy and precision of the method was determined and validated statically. The method showed good recovery with % RSD less than 2 and good reproducibility. Method was found to be rapid, specific, precise and accurate. This method can be successfully applied for the routine analysis of perindopril Accuracy of proposed method was confirmed by performing accuracy studies which showed the accepted results. Precision of proposed method was confirmed by performing intraday and inter day precision. The method for the determination of perindopril was validated according to ICH guidelines.
Keywords: Perindopril accuracy, linearity, regression equation , precision.

INTRODUCTION

Perindopril is an angiotensin-converting-enzyme inhibitor (ACE inhibitor). It is used in the treatment of heart failure and hypertension. Perindopril is prodrug,it is converted in the body into its active form perindoprilat[1]. Perindopril is chemically (2S, 3aS, 7aS)-1-[(S)-N-[(S)-1-carboxybutyl] alanyl] hexahydro-2-indolinecarboxylic acid 1-ethyl ester[2]. The elimination half life perindopril is more than 30 hours in human beings following oral administration[3]. In rats, significant inhibition of angiotensin-converting-enzyme in lung tissue and pulmonary artery persists 24 h following a single oral dose of perindopril (1, 4 or 8 mg kg^{-1}), at this time inhibition of plasma angiotensin-converting-enzyme can no longer be detected[4,5].

Literature survey showed that, perindopril active pharmaceutical ingredient (API) is official in British Pharmacopoeia[6] This Drug is determined by many methods, only two HPLC methods, The HPLC method may be considered more specific than other methods, but also more expensive, requiring sophisticated chromatographic instrumentation for its performance.Therefore, it was thought worthwhile to develop simple, precise, accurate UVspectrophotometric method for determination of perindopril .Validation was done with respect to various parameters, as required under ICH guideline Q2B12[7]. Darshana K. Modi et al in 2010 developed a method for simultaneous determination of estimation of perindopril and indapamide in pharmaceutical dosage form using UV spectrophotometer[8]. Erk.NA reported a reversed-phase high performance liquid chromatographic (HPLC) and two spectrophotometric methods for resolving binary mixture of perindopril and indapamide in the pharmaceutical dosage forms[9]. Spectrophotometric and atomic absorption spectrometric procedures are reported to develop for the determination of ramipril and perindopril (Abdellatef HE)[8]. Abdellatef HE. In his another study Also reported spectrophotometric method based on the reaction of perindopril as n-electron donor with 2,3-dichloro-5,6-dicyano-p-benzoquinone(DDQ)-7,7,8,8- tetracyanoquinodimethane (TCNQ), chloranil (CL) , tetracyanoethylene (TCNE), and p-chloranilic acid (p-CA) as pi-acceptors to givecoloured complex species[10].

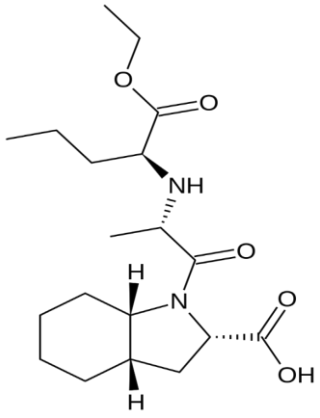

Fig-1 Structure of Perindopril

Our objective of study is to develop a precise, simple, cost effective, accurate and reproducible spectrophotometric method.

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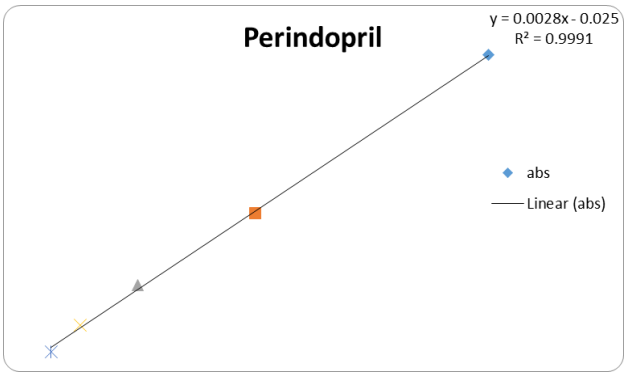

Fig-2 Linearity of Perindopril

MATERIALS AND METHOD

Material and reagents: Standard bulk drug sample of Perindopril were supplied by Martin Dow Laboratories (Pvt.)

Instrumentation: UV visible 1601 Shimadzu double beam spectrophotometer was used to measurement of spectra. The solvent used for the assay was water.

Wavelength Selection: About 200 ppm of Perindopril solution was accurately prepared by dissolving the active in water. The Perindopril solution was scanned in the 200-400 nm UV regions. The wavelength maximum (λmax) was observed at 210 nm and this wavelength was adopted for absorbance measurement.

Standard Stock solution: Accurately weighed 20 mg of Perindopril standard was transferred to a volumetric flask and dissolved in small amount of water then add sufficient water to produce 100 ml. This solution was used for preparation of working solutions which were prepared by diluting the stock solutions of Perindopril with water.

Procedure: After preparation of standard solution of 200 ppm in 100 ml, different dilutions were made (100ppm, 50ppm, 25ppm and 12.5ppm). At the wavelength of maximum absorbance about 210nm, the absorbance of the dilutions and standard preparation in 1cm cell was measured using a spectrophotometer. Calculate the quantity in mg, of Perindopril.

RESULTS AND DISCUSSION

This study has been designed to develop a precise, simple, rapid, and accurate method.

Method validation: The validation of developed method was done by various parameters which include linearity, accuracy test and precision.

Linearity: In the range 12.5-200 µg mL^{-1} linearity was determined. Peak area versus concentration of Perindopril was subjected to least square linear regression analysis. A linear regression line was obtained with correlation coefficient (R2 > 0.9991). The regression equation for active is displayed in fig-2.

Table 2: Accuracy of Perindopril

mg mL−1	%RSD	%Recovery
40	0.23	100
50	0.25	101
60	0.26	100.5

Accuracy: Accuracy of the method was determined as the percentage of recovery of known amounts of Perindopril.It is performed at spike concentration that was 40, 50 and 60 mg mL−1.Every sample was taken 5 times and result range was 100%-101%,Mentioned in table-2, high recovery indicated that the method has a high degree of accuracy.

Table 3: Inter day and intraday precision of Perindopril

Inter-day		Intra- day	
%RSD	%Recovery	%RSD	%Recovery
0.00	99.44	0.89	100.7
0.01	100.5	1.07	101.5
0.03	99.87	1.29	99.05
0.09	99.2	0.06	101.8
0.02	100	0.05	101

Precision: Repeatability (i.e. intra-day precision and inter day precision) of The proposed method was determined. It was defined as relative standard deviation % RSD. Five different concentrations of Perindopril (100ppm, 50ppm, 25ppm and 12.5ppm) in the linear range were analyzed in the same day (intra-day precision) and two consecutive days (inter-day precision); every sample was taken five times. Both intra- and inter-day %RSD values were in the range 0.00-1.29% confirming good precision (Table 1).The results were insignificant and do not indicate remarkable deference in Inter-day and intra-day precision.

CONCLUSION

Calibration curve was linear in concentration range of 12.5-200 µg/ml for Perindopril with correlation coefficient of 0.9991. The accuracy and precision of the method was determined and validated statically. The

Table 1: Descriptive Statistics

	N	Mean	Std. Error	Std. Deviation
200 ppm	5	0.5438	0.000734847	0.001643168
100 ppm	5	0.2514	0.002891366	0.006465292
50 ppm	5	0.1242	0.000374166	0.00083666
25 ppm	5	0.054	0.000707107	0.001581139
12.5 ppm	5	0.00246	5.09902E-05	0.000114018
Valid N (listwise)	5	-	-	-

method showed good recovery with % RSD less than 2 and good reproducibility. Method was found to be rapid, specific, precise and accurate. This method can be successfully applied for the routine analysis of perindopril Accuracy of proposed method was confirmed by performing accuracy studies which showed the accepted results. Precision of proposed method was confirmed by performing intraday and inter day precision. The method for the determination of perindopril was validated.

The according to ICH guidelines.This method can be adapted for routine assay. The intra-run and inter-run variability and accuracy results were in acceptable limit according to ICH guidelines. The short analysis time (< 5min) enables its application in routine and quality control analysis of finished products.

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