



# Development of New Spectrophotometric Methods for the Determination of Perindopril in Pharmaceutical Dosage Forms

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## Abstract

Three simple and sensitive Spectrophotometric methods have been developed for the determination of Perindopril (PDL) in pure and pharmaceutical dosage forms. Method A is based on the formation of Ion-association complex of the drug with Bromothymol Blue ( $\lambda_{\max}$ : 415 nm). Method B is based on the formation of charge transfer complex of the drug with chloranilic acid ( $\lambda_{\max}$ : 580 nm). Method C is based on oxidation of the drug under alkaline conditions by oxidizing agents like potassium permanganate and subsequent formation of cherry red colored chromogen ( $\lambda_{\max}$  : 609 nm). These methods have been statistically evaluated and found to be precise and accurate.

## INTRODUCTION

Perindopril (PDL)<sup>1-3</sup> is chemically (2S,3aS,7aS)-1-[(2S)-2-[[[(2S)-1-ethoxy-1-oxapentan-2-yl]amino]propanoyl]-octahydro-1H-indole-2-carboxylic acid, with selective clinical activity against hypertension. A literature of survey revealed that there are a few analytical methods have been reported, which include immunoassay<sup>4</sup>, spectrophotometric<sup>5,6</sup>, HPLC<sup>7</sup>, biosensor method<sup>8-10</sup>, LC-MS/MS<sup>11,12</sup> and capillary gas chromatographic methods<sup>13</sup> for the estimation of the drug in biological fluids and pharmaceutical formulations. Only few visible Spectrophotometric methods have been reported for its quantitative determination in its pure form and pharmaceutical formulations. In the present investigation, three simple and sensitive Spectrophotometric methods have been developed for the determination of PDL. Method A is based on the formation of Ion-association complex of the drug with Bromothymol Blue (BTB). Method B is based on the formation of charge transfer complex of the drug with chloranilic acid. Method C is based on oxidation of the drug under alkaline conditions by oxidizing agents like potassium permanganate and subsequent formation of cherry red colored chromogen. Beer's law is obeyed and results of analysis for the three methods have been validated statistically and by recovery studies.

## MATERIALS AND METHODS

### Instrument

A Systronics Model 2201 UV-VIS spectrophotometer was used for the measurements.

### Reagents:

All the chemicals used were of analytical grade. BTB (0.2%w/v), Sodium hydroxide (20%w/v), Chloranilic acid (0.1%w/v) and KMnO<sub>4</sub> (0.05 M) were prepared.

## Standard drug solution

The stock solution (1 mg/ ml) of Perindopril was prepared by dissolving 100 mg of the drug in 100ml of water and sonicated for about 10 minutes. This stock solution was further diluted to get 1000  $\mu$ g/ml (for method B) and 100  $\mu$ g/ml of working standard solution (for methods A and C).

## Sample solution

Twenty tablets of PDL were weighed and powdered. A quantity of powder equivalent to 100mg was dissolved in 100 ml of distilled water. The solution was sonicated for 15min, filtered and made up to the mark with water. This stock solution was further diluted with sufficient volume of water to get 1000  $\mu$ g/ml (for method B) and 100  $\mu$ g/ml of working standard solution (for methods A and C).

## ASSAY PROCEDURES

### Method A

Aliquots of the drug solution representing 20-100  $\mu$ g of PDL was transferred into a series of 125 ml separating funnels and equalized with water. To these flasks added 4 ml of pH 2 buffer and 1 ml of Bromothymol blue (0.2% w/v) and the solution was saturated with aqueous phase up to 10 ml and the mixture was shaken for 10 min. The drug-dye complex was then extracted with 10 ml chloroform. The absorbance of the separated yellow colored chloroform layer was measured after 5 min at 415 nm against reagent blank. The amount of PDL was computed from its

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**Table 1.** Optical characteristics, Precision and Accuracy of the proposed methods

PARAMETER	METHOD A	METHOD B	METHOD C
$\lambda_{\max}$ (nm)	415	580	609
Beer's law limit( $\mu\text{g}/\text{mL}$ )	2-10	80-400	1-5
Sandell's sensitivity ( $\mu\text{g}/\text{cm}^2/0.001$ abs. unit)	0.0256	0.8695	0.0069
Molar absorptivity (litre.mole <sup>-1</sup> .cm <sup>-1</sup> )	$1.70 \times 10^4$	$1.90 \times 10^5$	$6.36 \times 10^4$
Regression equation (Y*)			
Slope(b)	0.0834	0.0024	0.1221
Intercept(a)	0.0001	0.0043	0.0018
Correlation coefficient(r)	0.9995	0.9992	0.9991
%Relative standard deviation**	0.1308	0.2750	0.6407
%Range of error			
0.05 significance level	0.1372	0.2886	0.5187
0.01 significance level	0.2152	0.4526	0.8513

**Table 2.** Estimation of Perindopril in Pharmaceutical dosage Forms

Formulation	Labeled Amount (mg/tablet)	Amount found* by proposed methods (mg)			% recovery** by proposed methods		
		Method A	Method B	Method C	Method A	Method B	Method C
Tablet 1	8	7.91	8.02	7.94	99.89	99.86	100.23
Tablet 2	8	8.09	7.96	7.93	99.92	100.54	99.87

\* Average of six determinations

\*\*Recovery of amount added to the pharmaceutical formulation (Average of three determinations)

calibration graph.

#### Method B

Aliquots of standard PDL solution ranging from 0.8-4 ml (1000 $\mu\text{g}/\text{ml}$ ) were taken into a series of 10 ml volumetric flasks. To this added 1 ml of 0.1 % w/v chloranilic acid solution and allowed to stand at room temperature for 5 min. The final volume was made up to the mark with chloroform. The absorbance of the resulting solution was measured at 580 nm against the reagent blank. The amount of PDL was computed from its calibration graph.

#### Method C

To a series of 50 ml volumetric flasks aliquots of standard drug solution (100  $\mu\text{g}/\text{ml}$ ) ranging from 0.1 to 0.5 ml were transferred and 1 ml of Potassium Permanganate (0.05 M) solution, 7.5 ml of 0.5 M sodium hydroxide were added and subjected to constant heating for 30 min at 70<sup>o</sup>C in a water bath. The contents were cooled to room temperature and the solution in each volumetric flask was made up to the mark with water. The absorbance of the Cherry red colored chromogen was measured at 609 nm against the corresponding reagent blank within 30 minutes of maximum color development. The amount of PDL was calculated from the corresponding Beer-Lambert's plot.

### RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation and percent range of error (0.05 and 0.01 confidence limits) were calculated for all the three methods. The

results are summarized in Table 1. The precision and accuracy were performed by analyzing six replicate samples containing known amount of drug and the results were summarized in Table 1. The values obtained for the determination of PDL in pharmaceutical formulations (tablets) by the proposed methods are presented in Table 2. Studies reveal that the common excipients and other additives usually present in the tablets did not interfere in the proposed methods.

### CONCLUSION

The proposed methods are applicable for the assay of PDL and have an advantage of wider range under Beer's law limits. The proposed methods are simple, selective and reproducible and can be used in the routine determination of PDL in pure form and formulations with reasonable precision and accuracy.

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