Research Article

Simultaneous Estimation of Perindopril Erbumine and Indapamide in Combined Dosage form using Derivative Spectrophotometric Method

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ABSTRACT

A first-order derivative spectrophotometric method for the simultaneous determination of Perindopril erbumine and Indapamide in pharmaceutical dosage forms is described. Methanol was used as a solvent. First order derivative spectroscopy method was adopted to eliminate spectral interference, using 215nm and 241nm zero crossing points for Perindopril Erbumine and Indapamide respectively. The linear dynamic ranges were 1-5 µg ml^{-1} for Perindopril Erbumine and 2-20 µg ml^{-1} for Indapamide, the correlation coefficient for the calibration graphs were near to 0.9998, n=5, the precision (%RSD) was better than 1.43% and the accuracy was satisfactory (E_r<0.99%). The detection limits were found to be 0.45 and 0.35 µg ml^{-1} for Perindopril Erbumine and Indapamide, respectively. The method was applied in the quality control of commercial tablets and proved to be suitable for rapid and reliable quality control. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method.

Keywords: First order derivative spectroscopy, indapamide, perindopril erbumine. zero-crossing point.

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INTRODUCTION

A simple, accurate, and reproducible UV spectrophotometric method for simultaneous estimation of two component drug mixture of Perindopril Erbumine and Indapamide in combined dosage form has been developed. Perindopril Erbumine is 2-Methyl Propane-2-amine (2S, 3As, 7As)-1-[(2S)-2-2[[(1S)-1- (ethoxycarbonyl) butyl] amine] propanoyl] octahydro-1H-indol-2-carboxylate (**Fig. 1**) which is best known as an antihypertensive drug (1). Indapamide is 4-chloro- N-(2-methyl-2,3-dihyrro-1H-indol-1-yl)-3- sulfamoylbenzamide (**Fig. 2**) and it is used as antihypertensive and diuretic drug (3).

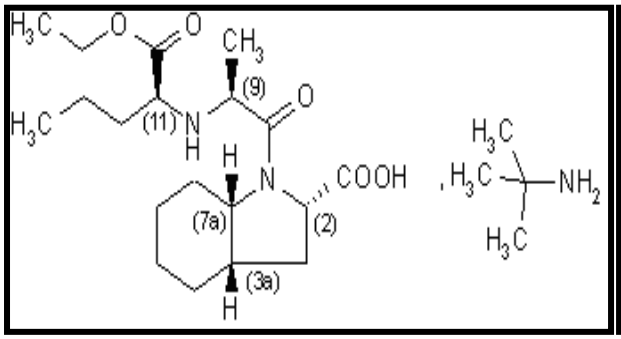

Fig: 1 Structure of Perindopril Erbumine

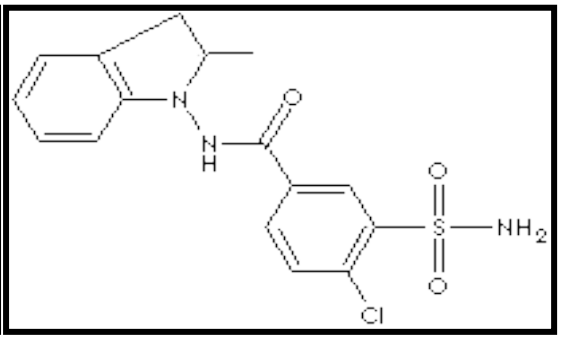

Fig: 2 Structure of Indapamide

Need of study: There is no First order Derivative method developed on perindopril Erbumine and Indapamide in combination.

MATERIALS AND METHODS Perindopril Erbumine 4 mg and 1.25 mg of Indapamide is available in market (COVERSYL PLUS). A survey of literature revealed that few chromatographic, HPTLC and Spectro-photometric and methods are reported for determination of Perindopril Erbumine and Indapamide individually or in combination with other drugs. However there is no method reported so far its simultaneous determination of Perindopril Erbumine and Indapamide from combined dosage form (6). The present work describes a validated, simple, precise and accurate spectro-photometric method for simul-taneous estimation of Perindopril Erbumine and Indapamide from combined tablet dosage form.

Materials: Reference Standards of Perindopril Erbumine and Indapamide were obtained as gift samples from the Apotex Reserch Pvt LTD, Bangalore. The drug sample, COVERSYL PLUS was procured from local market. All other reagents were of analytical grade for Spectrophotometric method.

Preparation of Standard Solution: Accurately weighed Perindopril Erbumine (10 mg) and Indapamide (10 mg) standards were transferred to a10 ml volumetric flask, dissolved in and diluted to the mark with methanol to obtain standard stock solution for Perindopril Erbumine (1000mg/ml) and Indapamide (1000 mg/ml) (5). Aliquot ofthe solution (10 ml) was transferred to a 10ml volumetric flask, and diluted to the mark with methanol to obtain working standard solution for Perindopril Erbumine (100 mg/ml) and Indapamide (100 mg/ml).

Selection of analytical wavelength: Solution of Perindopril Erbumine (20µg/ml) was prepared in methanol and spectrum was recorded between 200-400 nm. First-derivative spectrum for above concentration was obtained. Similarly, Solution of Indapamide (6µg/ml) was prepared in methanol and spectrum was recorded between 200-400 nm and first derivative spectrum was obtained. The overlain derivative spectrum of Perindopril Erbumine (20µg/ml) and Indapamide (6µg/ml) show the zero crossing point (ZCP) 215 nm and 241 nm, respectively, which were selected for measurement of Perindopril Erbumine and Indapamide respectively (2).

Preparation of calibration curve: From the working standard solution appropriate volume of aliquots were transferred to different volumetric flask of 10 ml capacity. The volume was adjusted to the mark with methanol to obtain the concentration of 1,2,3,4,5µg/ml Perindopril Erbumine and 2,4,6,8,10µg/ml for Indapamide.(1). The samples were scanned between 200-400 nm using JASCO V-630 UV/Visible double beam spectrophotometer with 1cm matched quartz cells. And spectrums were converted into first order derivative form. Absorbances of Perindopril Erbumine and Indapamide solutions were measured at 215 nm and 241 nm, respectively using first order derivative spectrophotometricn method. The graph of absorbance versus respective concentration was plotted. (4).

Methods: Twenty tablets were accurately weighed and average weight per capsule was calculated. Powder equivalent to 10 mg Perindopril erbumine and 3.12mg Indapamide was accurately weighed and transferred to a 10 ml volumetric flask containing methanol (10 ml).(1). The flask was sonicated for 5 min. The flask was shaken and the volume was diluted to the mark with methanol. The above solution was filtered through Whatman filter paper no. 41. The aliquot 1 ml was transferred to 10 ml volumetric flask and volume adjusted to the mark with methanol. The first derivative response of this solution was measured at 215 nm and 241 nm for quantification of Perindopril erbumine and Indapamide, respectively. First order derivative absorbances at these wavelengths were substituted in regression equationre presenting the calibration curves for Perindopril erbumine and Indapamide, with correction for dilution, to calculate the amounts of drug present.

RESULTS AND DISCUSSION

Selection of wavelength for simultaneous estimation of Perindopril Erbumine and Indapamide:

UV spectra of Perindopril erbumine completely overlaps that of Indapamide so, absorbance effect of Indapamide is suppressed in the mixture. Therefore

simultaneous estimation in zero order spectra was not successful. So it was thought of interest to develop the first order derivative spectrophotometric method for simultaneous estimation of Perindopril erbumine and Indapamide from capsule dosage form. Individual first order derivative spectra were recorded for both drugs and zero crossing points were selected. First order derivative spectrum for Perindopril erbumine was taken and it showed zero crossing point 215 nm, was selected for determination of Indapamide in the mixture. Similarly, first order derivative spectrum for Indapamide was taken and it showed zero crossing point 241 nm, was selected for estimation of Indapamide in mixture since it showed adequate absorbance at this wavelength (3).

Validation of the proposed Method: The method is validated as per ICH (International conference on harmonization) Guidelines as follows:

Linearity and Range: The linearity range for both Perindopril erbumine and Indapamide was found to be in the range of 1-5µg/ml and 2-10 µg/ml respectively (**Fig. 5**). Correlation co-efficient for calibration curve of Perindopril erbumine and Indapamide was found to be 0.997 and 0.996 respectively. The regression line equation for Perindopril erbumine and Indapamide are as following,

YPERI = 0.018x + 0.002…… (1)

YIND = 0.2108X-0.0328..... (2)

Table 1: Linear Regression data of the calibration plots for Perindopril Erbumine and Indapamide

Parameter	PERINDOPRIL	INDAPAMIDE
Linearity range (µg/ml)	1-5	2-10
Correlation coefficient (r)	0.997	0.996
Slope	0.018	0.2108
Intercept	0.002	0.0328

Accuracy (% Recovery):

The accuracy of the method was determined by calculating recoveries of Perindopril erbumine and Indapamide by the standard addition method. Known amount of standards of Perindopril erbumine (02, 04µg/ml) and Indapamide (4.8, 6µg/ml) were spiked to a prequantified sample (10 and 6 µg/ml for Perindopril erbumine and Indapamide, respectively) and the mixtures were analyzed again. The amounts of Perindopril erbumine and Indapamide were determined by measuring the absorbances and by fitting these values into the regression equation of the calibration plots. The % recovery was found in the range of 98.00 - 100.42 % for Perindopril erbumine and 98.60 – 101.15 % for Indapamide (**Table 2**).

Table 2: Results of recovery studies for PERI

Amount of PERI in sample (µg/ml)	Amount of Std PERI added (µg/ml)	Total amount of PERI (µg/ml)	Spicked amount of PERI (µg/ml) (n=3)	% Recovery Mean ± SD
10	8	18	7.56	
	8	18	7.66	95.23±0.2
	8	18	7.64	
10	10	20	9.86	
	10	20	9.70	
	10	20	9.80	97.86±0.8
10	12	22	11.58	
	12	22	11.60	96.43±0.2
	12	22	11.55	

(n=3)

Table 3: Results of recovery studies for INDA

Amount of INDA in sample (µg/ml)	Amount of Std INDA added (µg/ml)	Total amount of INDA (µg/ml)	Spicked amount of INDA (µg/ml) (n=3)	% Recovery Mean ± SD
10	8	18	7.80	
	8	18	7.70	
	8	18	7.75	96.8±0.6
10	10	20	9.86	
	10	20	9.80	
	10	20	9.86	98.4±0.3
10	12	22	11.83	
	12	22	11.89	
	12	22	11.85	98.8±0.2

(n=3)

Precision

Repeatability: The repeatability of measurement of absorbance was checked by repeatedly measuring (n = 7) absorbance of same concentration of Perindopril erbumine (2µg/ml) and IND (10µg/ml). The relative standard deviations for the same are 0.47 for Perindopril erbumine ; and 0.96 for Indapamide, respectively

Intermediate precision:

The Intermediate precision of the proposed method was assessed by estimating the corresponding responses (n = 3) for 5 different concentrations (1,2,3,4,5µg/ml) for Perindopril erbumine and (2,4,6,8,10 µg/ml) for Indapamide on the same day (Intraday) and on the different days (Interday). The results are reported in terms of relative standard deviation.

Table 4: Intraday precision data for PERI and INDA

Concentration(µg/ml)		% C.V.(n=3)	
PERI	**INDA**	**PERI**	**INDA**
1	2	0.55	1.02
2	4	0.60	0.58
3	6	0.89	0.59
4	8	1.02	0.80
5	10	0.80	0.75

Table 5: Interday Precision data for PERI and INDA

Concentration(µg/ml)		% C.V.(n=3)	
PERI	**INDA**	**PERI**	**INDA**
1	2	0.58	0.89
2	4	0.86	0.81
3	6	0.59	0.75
4	8	0.75	0.62
5	10	0.60	0.85

LOD and LOQ: The limits of detection (LOD) and quantification (LOQ) were calculated from the standard deviation (SD) of y-intercepts and slope (S) of the calibration plots using equations LOD = 3.3 × SD/S and LOQ = 10 × SD/S as per International Conference on Harmonization (ICH) guidelines. The detection and quantification limits obtained by this method were 0.208 and 0.622µg for

Perindopril erbumine; while 0.301 and 0.325µg for Indapamide, respectively, which indicates the sensitivity of the method (**Table 6**).

Table 6: LOD and LOQ

PERI	INDA
LOD=3.3 x (SD/Slope) 0.45µg/ml.	LOD=3.3 x (SD/Slope) 0.35µg/ml.
LOQ=10 x (SD/Slope) 0.85µg/ml.	LOQ=10 x (SD/Slope) 0.98µg/ml

Simultaneous estimation of PERI and IND in pharmaceutical dosage form:

The proposed method was applied to analyze the combined capsule dosage form of Perindopril erbumine and Indapamide. Marketed preparation was analyzed by the proposed method. The amount of Perindopril erbumine and Indapamide was found to be 99.84 ± 0.2666 and 99.41 ± 0.4055% of the labeled amount respectively. Thus, the developed first order derivative spectrophotometric method is simple, rapid, precise, accurate and economical. It can be applied for routine analysis of PERI and INDA combined dosage forms.

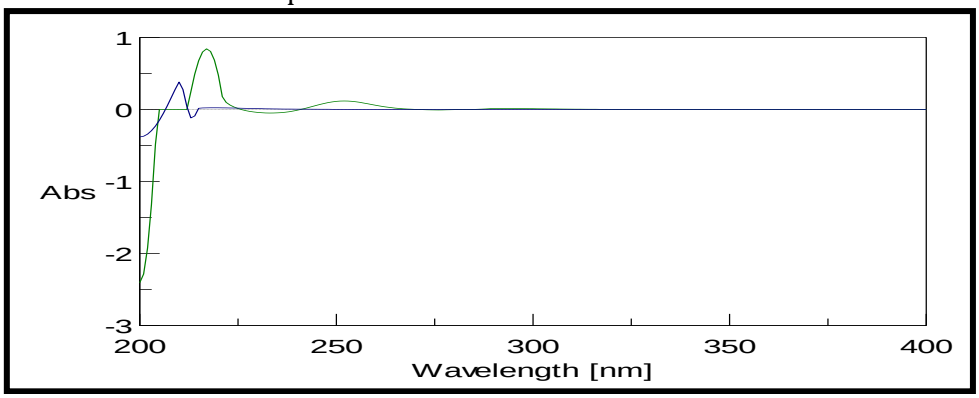

Fig 3: Overlain first order spectra of PERI (4 g/ml) and INDA (4µg/ml) in methanol

CONCLUSION

The proposed first order derivative Spectrophotometric method is accurate, simple, rapid and selective for simultaneous estimation of Perindopril erbumine and Indapamide in Tablet dosage form. Hence it can be conveniently adopted for routine quality analysis of the Tablet.

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