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PharmTech
International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.2, No.1, pp 411-416, Jan-Mar 2010

Development and Validation of Spectrophotometric Method for Simultaneous Estimation of Perindopril and Indapamide in Combined Dosage Form by Absorbance Correction Method.

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ABSTRACT: A new sensitive, simple, rapid and precise two spectrophotometric method has been developed for simultaneous estimation of perindopril and indapamide in pharmaceutical dosage form. This method was based on UV-spectrophotometric determination of two drugs, using absorbance correction method. It involves measurement of absorbances at two wavelengths 210.4nm (λmax of perindopril) and 285.8nm (λmax of indapamide) in methanol for the simultaneous quantitative determination of perindopril and indapamide in the binary mixture without previous separation. The linearity was observed in the concentration range of 24 – 56 µg mL^{-1} for perindopril and 7.5 – 17.5 µg mL^{-1} for indapamide. The accuracy and precision of the method was determined and validated statically. The method showed good reproducibility and recovery with % RSD less than 2. Method was found to be rapid, specific, precise and accurate, can be successfully applied for the routine analysis of perindopril and indapamide in bulk, and combined dosage form without any interference by the excipients. The method was validated according to ICH guidelines.
Keywords: Perindopril, Indapamide, Simultaneous estimation, Absorption correction method.

INTRODUCTION

Perindopril is an ACE inhibitor. It is used in the treatment of hypertension and heart failure. Perindopril is converted in the body into its active metabolite perindoprilat[1]. Perindopril is chemically (2S, 3aS, 7aS)-1-[(S)-N-[(S)-1-carboxybutyl] alanyl] hexahydro-2-indolinecarboxylic acid 1-ethyl ester[2]. The structure of perindopril is shown in Fig 1.

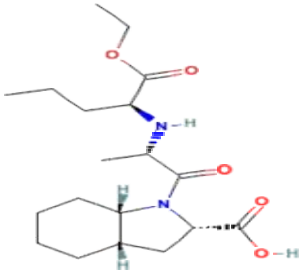

Fig 1. Structure of perindopril

Indapamide is a diuretic with actions and uses similar to those of thiazide diuretics, even though it does not contain a thiazide ring system. It is used for hypertension and also for oedema, including that associated with heart failure[3]. Indapamide is chemically 3-(amino sulfamoyl)-4-chloro-N-(2, 3-dihydro-2-methyl-1H-indol-1-yl) benzamide[4]. The structure of indapamide is shown in Fig 2.

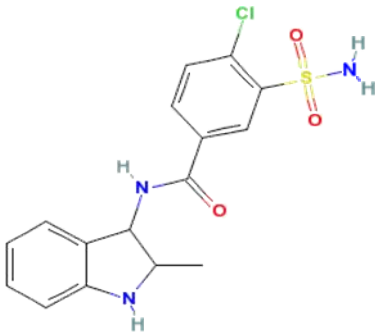

Fig 2. Structure of indapamide

Recently, perindopril has been marketed in combination with indapamide in tablets for the treatment of essential hypertension. This combination is advised in patients whose blood pressure is not adequately controlled by alone drug.

Literature survey revealed that, perindopril active pharmaceutical ingredient (API) is official in British Pharmacopoeia[5]; indapamide active pharmaceutical ingredient (API) is official in British Pharmacopoeia[6] and United States Pharmacopoeia[7], while indapamide tablets are official in British Pharmacopoeia[8] and United States Pharmacopoeia[9]. However, the combination is not official in any pharmacopoeia. On detailed literature survey, it was found that through individually these drugs have been analyzed by many methods, only two HPLC methods and two spectrophotometric methods were reported for this combination[10,11]. 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 simultaneous determination of perindopril and indapamide in tablets.

The proposed method was applied to the determination of both analytes in synthetic mixtures and pharmaceutical preparations, with satisfactory results in both cases. Validation was done with respect to various parameters, as required under ICH guideline Q2B[12].

MATERIAL AND METHODS

Apparatus:

Spectrohotometric analysis was carried out on a Shimadzu 1700 double beam spectrophotometer with fixed slit width (2 nm) and 10 mm matched quatz cells using UVProbe software version 2.01.Other apparatus used included analytical balance model ALC 210.4 (Acculab).

Chemicals and Reagents:

Perindopril and indapamide were kindly supplied by Torrent Research Centre (Gandhinagar, India). A pharmaceutical preparation (label claim perindopril 4 mg and indapamide 1.25 mg) and placebo (Batch No. - A/036) were manufactured and supplied by Torrent Research Centre (Gandhinagar, India). Methanol was analytical-reagent grade (S.D. Fine Chemicals Ltd., Mumbai).

Preparation of calibration curve:

Stock solutions were prepared by dissolving perindopril and indapamide in methanol to obtain a concentration of 0.8 mg mL^{-1} and 0.25 mg mL^{-1}, respectively. The standard solutions were prepared by dilution of stock solutions in methanol to reach concentration ranges of 24.0 – 56.0 and 7.5 – 17.5 µg mL^{-1} for perindopril and indapamide, respectively.

Assay procedure for tablets:

Ten tablets were accurately weighed and transferred into 200 mL volumetric flask and 10mL of methanol was added. The volumetric flask was sonicated to disperse tablets completely and about 150 mL methanol was added and sonicated for 15 minutes with intermittent shaking. The solution was cooled to the room temperature and made up to volume with methanol. The solution was filtered through whatman filter paper no.41. The aliquot portion of filtrate was further diluted with methanol to get final concentration 40µg mL^{-1} and 12.5 µg mL^{-1} of perindopril and indapamide, respectively.

Amount of each drug was determined by using formula as following:

$$Cy = \frac{A_{285.8nm}}{A\ (1\%, 1\ cm)_{285.8nm\ of\ Indapamide}} \quad .. (1)$$

$$Ay_{210.4nm} = Cy \times A\ (1\%, 1\ cm)_{210.4nm\ of\ Indapamide}$$

$$CAx_{210.4nm} = A_{210.4nm} - Ay_{210.4nm}$$

$$Cx = \frac{CAx_{210.4nm}}{A\ (1\%, 1\ cm)_{210.4nm\ of\ Perindopril}} \quad .....(2)$$

Where,
Cx = Concentration of Perindopril in gm/100ml
Cy = Concentration of Indapamide in gm/100ml
$A_{210.4nm}$ = Absorbance of mixture at 210.4nm
$A_{285.8nm}$= Absorbance of mixture at 285.8nm
$CAx_{210.4nm}$= Corrected absorbance of Perindopril at 210.4nm
$Ay_{210.4nm}$ = Absorbance of Indapamide at 210.4nm.
The percentage of each drug in laboratory mixture was calculated by using following formula:

$$\% \text{ Estimation of drug} = \frac{C}{Cs} \times 100 \quad \ldots..(3)$$

Where, C=Cx or Cy
Cs = Concentration of standard in gm/100ml

RESULTS AND DISCUSSION

The stability of working solutions of perindopril and indapamide was studied by recording their absorption spectra. At first these spectra were measured. No changes in the spectra were observed for at least 48 hours when the solutions were stored at room temperature in the dark.

The aliquot portions of standard stock solutions of perindopril and indapamide were diluted appropriately with methanol to obtain a concentration 40 µg mL-1 of perindopril and 12.5 µg mL^{-1} of indapamide. They were scanned in the wavelength range of 400−200 nm and the overlain spectrum was obtained (Fig 3).

Fig 3 shows the absorption spectra of perindopril (40 µg mL^{-1}) with a maximum at 210.4 nm and indapamide (12.5 µg mL^{-1}) with a maximum at 241.2 nm. Indapamide also shows λmax at 285.8 nm, where perindopril was not showing any absorbance. Hence 285.8 nm was selected as detection wavelength for indapamide and 210.4 nm was selected as detection wavelength for perindopril, where absorption of indapamide is corrected in absorption correction method. The wavelengths 210.4 nm and 285.8 nm were chosen for the simultaneous determination of perindopril and indapamide, respectively.

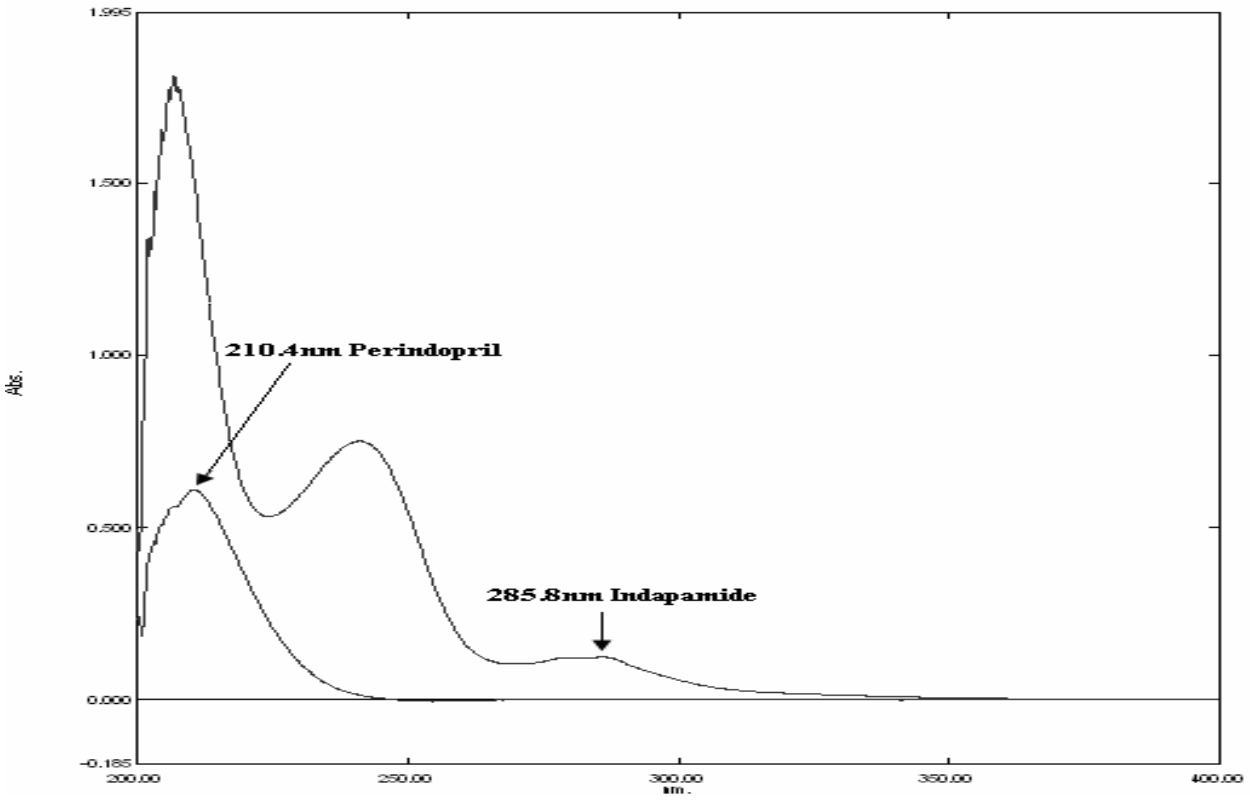

Fig. 3 Overlain spectra of perindopril (40 µg mL^{-1}) with a maximum at 210.4 nm and indapamide (12.5 µg mL^{-1}) with a maximum at 285.8 nm in methanol taken on UV – Vis spectrophotometer (SHIMADZU 1700)

Table 1: Statistical analysis of calibration graph in the determination of perindorpil and indapamide

Parameters	Perindopril	Indapamide
Range (µg mL^{-1})	24 – 56	7.5 – 17.5
Regression equation(y)[a]		
Slope (m)	0.0211	0.0012
Intercept (c)	0.0152	0.0053
Correlation coefficient (r^2)	0.9998	0.9997

[a] y = mx + c where x is concentration in µg mL^{-1} and y in absorbance unit.

Under the described experimental conditions, the graphs were obtained by absorbance of each drug in this mixture versus concentration, in the range stated in Table 1, show linear relationship. A critical evaluation of the proposed method was performed by statistical analysis of data, where slopes, intercepts and correlation coefficients were shown in Table 1.

Intra-day precision was performed by using same procedure as under tablet formulation analysis and absorbance recorded at 2 hours interval within day. Inter-day precision was assessed by analyzing the same samples on different days. The data obtained were within 2% RSD indicating reasonable repeatability of the proposed method which is shown in Table 2.Thus, it was concluded that there was no significant difference on the assay, which was tested on an intra – day and inter – day basis.

The placebo was added to the drug for recovery studies according to manufacture's batch formula for per tablets. The results are summarized in Table 3.

The validated method was applied to the determination of perindopril and indapamide in tablet dosage from. The results are summarized in Table 4. The results of assay indicate that the method is selective for the analysis of both perindopril and indapamide without interference from the excipients used to formulate and produce these tablets.

CONCLUSION

A simple, rapid, accurate and precise spectrophotometric method has been developed and validated for the routine analysis of perindopril and indapamide in API and tablet dosage forms. The spectrophotometric method is suitable for the simultaneous determination of perindopril and indapamide in multi-component formulations without interference of each other. The absorbance correction method is rapid, simple and sensitive. The developed method is recommended for routine and quality control analysis of the investigated drugs in two component pharmaceutical preparations.

Table 2.: Intra- and inter-assay precision data

Parameters	Perindopril		Indapamide	
	*Mean ± S.D.	% R.S.D.	Mean ± S.D.	% R.S.D.
Intraday Precision	100.2 ± 0.7548	0.7533	99.5 ± 0.4619	0.4644
Interday Precision	101.2 ± 1.8448	1.8229	99.2 ± 0.8000	0.8065

Results are mean of three replicates

Table 3.:Data indicating recovery studies of perindorpil and indapamide in presence of placebo

Level of recovery	Amount added (µg mL^{-1})	Amount found (µg mL^{-1})	*Recovery (%)	Mean ± % R.S.D.
Perindopril				
60 %	24	23.70	98.8	99.5 ± 0.8160
100 %	40	40.20	100.4	
140 %	56	55.68	99.4	
Indapamide				
60 %	7.5	7.44	99.2	99.3 ± 0.1435
100 %	12.5	12.43	99.4	
140 %	17.5	17.38	99.3	

* Recovery is mean of three estimations.

Table 4.: Analysis data of tablet formulations

Parameters	Perindopril	Indapamide
Label Claim (mg)	4	1.25
*Drug content	100.3	99.6
± S.D.	0.6580	0.4382
% R.S.D.	0.6563	0.4399

* Value for Drug content (%) are the mean of five estimations; S.D. is standard deviation and R.S.D. is relative standard deviation

ACKNOWLEDGEMENTS

The authors are thankful to Torrent Research Centre, Gandhinagar, Gujarat for providing drug samples and Shri Sarvajanik Pharmacy College, Mehsana, for providing facilities to carry out this work.

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