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Research Article

SPECTROPHOTOMETRIC METHOD DEVELOPMENT OF RAMIPRIL AND HYDROCHLOROTHIAZIDE IN BULK AND MARKETED FORMULATION BY VIERORDT'S METHOD

Ananda Thangadurai*, Munusamy Jambulingam, Dhanapal Kamalakannan, Ramachandran Sundaraganapathy and Chennakesavalu Jothimanivannan
Department of pharmaceutical Analysis, Swamy Vivekanandha College of Pharmacy, Elayampalayam, Tiruchengode, India

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*Dr. S. Ananda Thangadurai, Head, Dept. of Pharmaceutical Analysis, Swamy Vivekanandha College of Pharmacy, Elayampalayam, Namakkal (Dt)-637 205 Tamil Nadu, India E-mail-anands17@rediffmail.com

ABSTRACT
This paper describes a simple, accurate, specific and validated method for quantitative determination of Ramipril and Hydrochlorothiazide in bulk and marketed dosage formulation by Vierordt's method. This method a involves simultaneous equation at 219.52 nm (λ max of Ramipril) and 270.54 nm (λ max of Hydrochlorothiazide).A study was carried out all the parameters established as per ICH, i.e. accuracy, precision, linearity, LOD, LOQ. Method was found to be linear in the range of 10-80µg/ml and 1.7-6.7µg/ml for Ramipril and Hydrochlorothiazide respectively with a correlation co-efficient 0.9945 for Ramipril, and 0.9976 for Hydrochlorothiazide. The percentage recovery is 94% for Ramipril, 102% Hydrochlorothiazide which reflect that the method is free from the interference of impurities and other additives during estimation of drug in formulation. The results of analysis have been validated by the recovery studies and were found satisfactory.

Key words: Ramipril, Hydrochlorothiazide, Validation, Vierordt's Method

INTRODUCTION

Cardace-H tablet (Sanofi Aventis) which contain Ramipril and Hydrochlorothiazide, used commonly for the treatment of high blood pressure when monotherapy is not sufficiently effective. Ramipril-(2s,3as,6as)-1-[(s)-N-[(s)-1-carboxy-3-(phenylpropyl)-alanyl]-octahydro cyclopenta-6-pyrazole-2-carboxylic acid-1-ethylester is an angiotensin converting enzyme inhibitor. It belongs to the class of cardiovascular drug. Hydrochlorothiazide 6-chloro-3,4 di hydro-2H-1,2,4 benzothiadiazine-7-sulfonamide-1,1 dioxide is an thiazide diuretic. The literature survey reveal RP-HPLC method for Ramipril with other drugs also reported.[1,2] Spectrophotometeric method for simultaneous estimation of hydrochlothiazide with other drugs also reported.[3-8] The RP-HPLC method for Hydrochlorothiazide with other drugs has been reported.[9-12] The simultaneous estimation of present work describes a simple, accurate, rapid and economical method for simultaneous estimation of Ramipril and Hydrochlorothiazide in bulk and in marketed formulation. The method has been successfully used for quality control analysis of the drugs and for other analytical purposes.

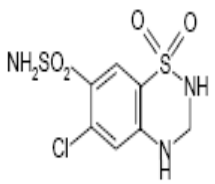

Fig. 1 : Chemical structure of Hydrochlorothiazide

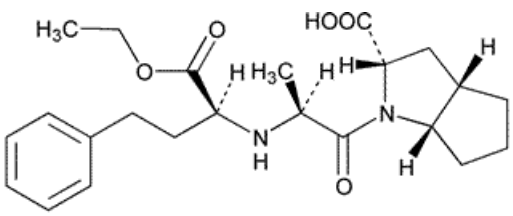

Fig. 2 : Chemical structure of Ramipril

MATERIALS AND METHODS

MATERIAL

Reference standards of Ramipril and Hydrochlorothiazide were obtained from Tristar formulation, puddhucherry as a gift sample. All the reagents and chemical used were AR grade. The commercially available tablet with brand name of Cardace-H tablet (Sanofi Aventis). It contains 12.5 mg of Hydrochlorothiazide; 5 mg of Ramipril. Analytical grade methanol was used in the preparation of samples.

Apparatus and Instruments

A Perkin Elmer – lamda-25UV-vis Double beam spectrophotometer and Elico UV-vis Double beam spectrophotometer –SL-164 with wavelength accuracy ± 0.1nm. And pair of quartz cells (1 cm) were used for measuring the absorbance.

Preparation of Standard Solutions

Standard stock solutions of Ramipril (10µg/ml) and Hydrochlothiazide (10µg/ml).Were prepared by using Analytical grade methanol.

METHOD[13]

Simultaneous Equation method (or) Vierordt's method

The simultaneous equation method of analysis is based on the absorption of the drugs Ramipril and Hydrochlorothiazide at their wave length maximum. Two wave lengths are elected for this method 219.52 nm and 270.54 nm.

A set of two simultaneous equations obtained by using mean absorptivity values are given below

At λ1 A1= ax1 bcx + ay1 bcy ---------- (1)
At λ2 A2= ax2 bcx + ay2 bcy ---------- (2)

Rearranging equations (1) and (2),

$$Cx = \frac{A1\ ay1 - A1\ ay2}{ax2\ ay1 - ax1\ ay2}$$

$$Cy = \frac{A1\,ax2 - A2\,ax1}{ax2\,ay1 - ax1\,ay2}$$

Where

Cx – concentration of Ramipril

Cy – concentration of Hydrochlorthiazide

A1 – absorbance of diluted mixture at λ1

A2 – absorbace of diluted mixture at λ2

ax1- absorptivity of the x (Ramipril) at λ1

ax2 - absorptivity of the y (Hydrochlorthiazide) at λ2

ay1 - absorptivity of the y (Hydrochlorthiazide) at λ1

ay2 - absorptivity of the y (Hydrochlorthiazide) at λ2

VALIDATION OF DEVELOPED METHODS

The following parameters are considered under the ICH guidelines for the validation of the method .

Linearity

Linearity of the method was anlyzed by using eight different concentrations in the range of 10 - 80µg/ml for Ramipril.and for Hydrochlorthiazide six different concentrations were used from 1.7 – 6.7 µg/ml.The correlation co efficint for Ramipril 0.9945, for Hydrochlorthiazide 0.9976.The linearity data presented in **Table 1.**

Precision

The interday and intra day precision was performed by the assay of the sample solution on the same dat and on different time intervals respectively.Percentage RSD is reported for Ramipril and Hydrochlorthiazide.The results are indicated in **Table 2.**

Accuracy

The accuracy of the method was determined by recovery studies at 75% level.The % recovery for Ramipril and Hydrochlorthiazide was calculated and reported.The accuracy data displayed in **Table 3.**

Limit of detection and limit of quantitation

The limit of detection (LOD) and limit of quantitation (LOQ) of Ramipril and Hydrochlorthiazide was determined by linearity curve.LOD and LOQ were calculated by using the formula 3.3 x SD / S and 10 x SD / S respectively,where S is the slope of the linearity curve and SD is the standard deviation.The results are showed in **Table 4.**

RESULTS AND DISCUSSION

The linearity range for Ramipril 10-80 µg/ml and for a Hydrochlorthiazide 1.7 – 6.7 µg/ml.The correlation co efficient for Ramipril at 219.52 nm and for Hydrochlorthiazide 270.54nm is 0.9945 and 0.9976 respectively (Fig 3 & 4).It shows the good regression values and the results of precision studies shows good repetability of the method.In the intra day precision three repeated standard dilution for three consecutive days were made and % of RSD were 0.3 % for Ramipril and 0.3% for Hydrochlorthiazide.In inter day precision three repeated standard dilution for three consecutive days were made and % of RSD were 0.2% for Ramipril and 0.3 % for Hydrochlorthiazide.It shows good repeatability and precision.

The accuracy of this method calculated by percentage of recovery. The percentage recovery for Ramipril 94 % and Hydrochlorthiazide 102 % were obtained by this method. It describes any small change in drug concentration in the solution coulde be accurately dtermined by reported method.

The LOD and LOQ values for Ramipril105.10 µg/ml and 0.000617 µg/ml respectively and for Hydrochlorthiazide 318.49 µg/ml and 0.018724 µg/ml it indicates good sensitivity of reported method.

CONCLUSION

The reported method very simple, accurate, rapid, economical and validated i.e accuracy, precision linearity, LOD, LOQ, can be used sucesfully for routine analysis of Ramipril and Hydrochlorthiazide in bulk and marketed dosage forms.

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Table 1: Linearity

Parameters	Ramipril	Hydrochlorothiazide
Beers law limit	10-80µg/ml	1.7-6.7µg/ml
Concentration	10-80µg/ml	1.7-6.7µg/ml
Regression coefficient	0.9945	0.9976
Regression equation	Y=0.0126x-0.027	Y=0.2013x+0.0107

Table 2: Precision

Drug	Concentration (µg)	Intra-day precision % RSD
Ramipril	10	0.45
	20	0.17
Hydrochlorthiazide	2	0.35
	5	0.21

Table 3: Accuracy

Drug	Amount present	Amount recovered	% Recovery
Ramipril	5mg	4.7 mg	94
Hydrochlorothiazide	12.5 mg	12.6 mg	102

Table 4: Optical characteristics

Parameters	Ramipril	Hydrochlorothiazide
Beers law limit	10-80µg/ml	1.7-6.7µg/ml
Concentration	10-80µg/ml	1.7-6.7µg/ml
Regression coefficient	0.9945	0.9976
Regression equation	Y=0.0126x-0.027	Y=0.2013x+0.0107
Precision Intra day	0.3%	0.3%
Inter day	0.2%	0.3%
Limit of quantification	318.49µg/ml	0.018724µg/ml
Limit of detection	105.10µg/ml	0.000617µg/ml
Slope	0.0126	0.2013
Recovery studies	94%	102%

Table 5. Result of analysis of tablet

Sample	Label claim	Amount of drug in formulation	Absorbance*		Absorptivity*		% purity
			219.52nm	270.54nm	219.52nm	270.54nm	
Ramipril &	10 mg	11.23 mg	0.05027	0.00235	0.5027	0.0235	112.3
Hydrochloro thiazide	12.5mg	3.45mg	0.00028	0.00727	0.0028	0.0727	107.6

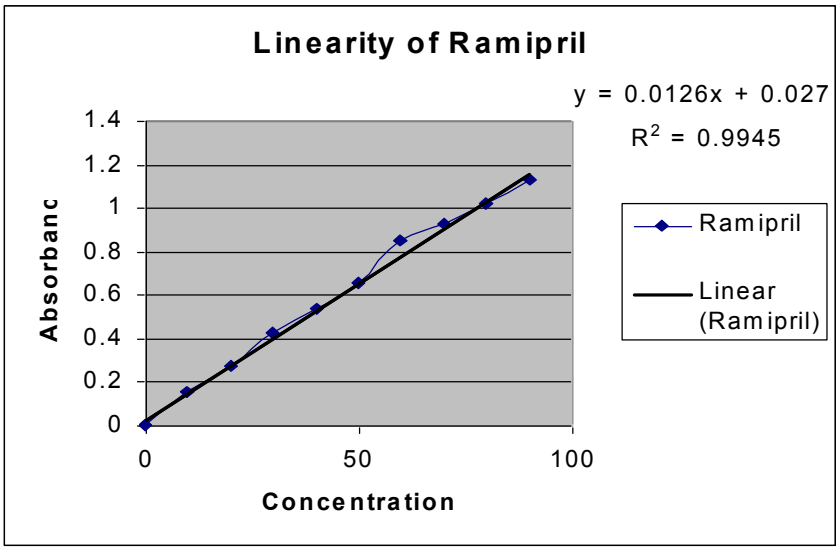

Fig 3. Linearity curve for the Ramipril

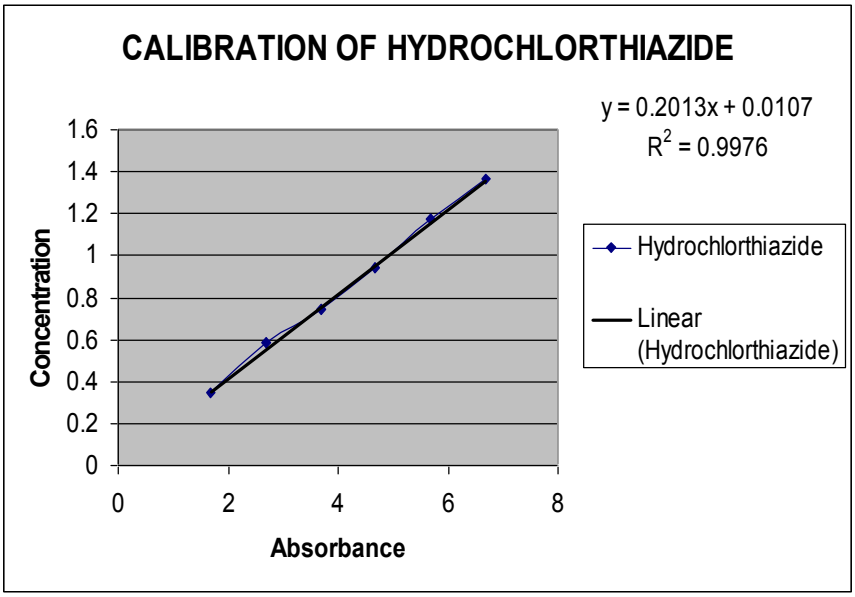

Fig 4. Linearity curve for the Hydrochlorthiazide

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