International Journal of Drug Development & Research | January-March 2012 | Vol. 4 | Issue 1 | ISSN 0975-9344 | Available online http://www.ijddr.in
Covered in Official Product of Elsevier, The Netherlands
SJR Impact Value 0.03,& H index 2

UV Spectrophotometric methods for estimation of Ramipril in Pharmaceutical dosage form by absorption maxima method and area under curve

Syed Iftequar[1] ,Lahoti Swaroop [1] , Zahid Zaheer[1] , Mirza Shahid[1], Sayad Imran[*1], M H Dehghan
[1]Dr. Rafiq Zakaria Campus, Maulana Azad Educational Trust`s, Y. B. Chavan College of Pharmacy, Post Box No. 33, Rauza Bagh, Aurangabad (Maharashtra) India

Abstract

A new, simple, rapid and novel spectrophotometric method has been developed for estimation of Ramipril (RAM). For this Absorption maximum Method (method A) and Area under Curve Method (Method B) is used. The method involved measurement of absorbance at wavelengths 210 nm for method A and method B involved measurement of area under curve in the wavelength range 202 to 237.5 nm for RAM. Beer's law obeyed in concentration range of 0.1 to 3.5 µg/ mL by both the methods. The proposed methods are recommended for routine analysis since they are rapid, simple, accurate and also sensitive and specific. The results obtained are reproducible with a coefficient of variation less than 2%. These methods were validated for precision, reproducibility, linearity and accuracy as per ICH guidelines.

*Corresponding author, Mailing address:
Sayad Imran*
E-mail:-imranwsayad@gmail.com
Fax No. 0240-2381307
Mobile No. +919860923394

Key words:
Ramipril, Absorption Maxima Method, Area under curve.

How to Cite this Paper:
Syed Iftequar ,Lahoti Swaroop , Zahid Zaheer , Mirza Shahid, Sayad Imran* , M H Dehghan "UV Spectrophotometric methods for estimation of Ramipril in Pharmaceutical dosage form by absorption maxima method and area under curve", Int. J. Drug Dev. & Res., Jan-March 2012, 4(1): 286-290

Article History:----------
Date of Submission: 03-02-2012
Date of Acceptance: 11-02-2012
Conflict of Interest: NIL
Source of Support: NONE

1. Introduction

Ramipril is an angiotensin-converting enzyme (ACE) inhibitor. It acts on the renin–angiotensin aldosterone system. It inhibits the conversion of the inactive angiotensin-I to the highly potent vasoconstrictor angiotensin-II, and also reduces the degradation of bradykinin. Ramipril is

chemically2-[N-[(S)-1-(ethoxycarbonyl)-3-phenylpro pyl)] -L-alanyl]-(1S,3S,5S)-2-azabicyclo[3-3-0] octane carboxylic acid [1]. The drug is official in British Pharmacopoeia, which describes a potentiometric titration procedure for its assay in bulk and dosage form [2]. Publications concerning with determination Ramipril, viz: The estimation of ramipril along with hydrochlorothiazide in binary mixture was performed by derivative compensation technique [3] as well as zero crossing derivative technique [4, 5]. Chromatographic method involves GC [6, 7], HPLC [8, 9], enzymatic assay with GC or HPLC [10], and radioimmunoassay [11]. All the reported methods are laborious, time-consuming and require highly sophisticated instrumentation [2-11]. Among the various methods available for the determination of drugs, spectrophotometry continues to be very popular, because of their simplicity, specificity and low cost. This study presents new spectrophotometric methods for the determination of ramipril in tablets.

2. Material and Methods

2.1 Instrumentation

A Double beam UV-Visible spectrophotometer (Jasco V 530) with 10mm matched quartz cells was used. All weighing were done on single pan balance (Shimadzu).

2.2 Reagents and chemicals

RAM reference standards were kindly provided by Emcure Pharmaceuticals Pvt. Ltd, Pune. Analytical grade methanol was purchased from Merck Specialities Private Ltd., Mumbai. All the reagents were of analytical grade. Glass double distilled water was used throughout the experiment. Tablets were purchased from local market each containing 2.5 mg of RAM.

2.3 Preparation of standard stock solutions and calibration curve

Standard stock solution of pure drug containing 50 µg mL-1 of RAM prepared in methanol distilled water system. The working standard solutions of the drug were obtained by dilution of the stock solution in the distilled water. Series of solutions with conc. 0.1-4 µg mL-1 of RAM were used to prepare calibration curve. Solutions were scanned and proposed methods were applied.

2.4 Preparation of sample stock solution and formulation analysis

A quantity of powder from twenty tablets equivalent to 50mg of RAM was weighed and transferred to a flask containing 10 ml of methanol and ultrasonicated for 15 min and solution was filtered through Whatman paper No. 41 into a 100 mL volumetric flask. Volume was made up with distilled water. The solution was further diluted with distilled water to get 2.5 µg mL-1 of RAM.

2.5 Method A: Absorption Maxima Method

For the selection of analytical wavelength, 2.5 µg mL-1 of RAM was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. From the spectra figure 2 of drugs λmax of RAM 210 nm was selected for the analysis. The calibration curve was prepared in the concentration range of 0.1 4 µg/ mL at 210 nm. By using the calibration curve, the concentration of the sample solution was determined. The result shown in table no. 2.

2.6 Method B: Area under curve

For the determination using the area under curve (AUC) method, suitable dilutions of the standard stock solutions of RAM were prepared in methanol distilled water system. The solution of drugs was scanned in the range of 200-400 nm. From the spectra figure 3 of drugs λmax for estimation of RAM 202- 237.5nm was selected for the analysis. The calibration curve was plotted in the concentration range of 0.1 4 µg/ mL. This showed linear response with increasing concentration hence the same wavelength range was used for estimation of tablet formulations. The result shown in table no. 2.

3. Result:

3.1 Method validation

The Method was validated as per ICH guidelines using different parameter.

3.1.1 Linearity:

The linearity was evaluated by analyzing different concentration of standard solution of RAM. The Beer Lambert's law was obeyed in the concentration range of 0.1 4 µg/ mL for both method with regression coefficient of 0.9991 and 0.9998 for method A and method B respectively.

3.1.2 Limit of Detection and Limit of Quantitation:

LOD and LOQ were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the six replicate determinations, y intercept was calculated and the standard deviation of the y intercept was computed. From these values, the parameters Limit of Detection (LOD) and Limit of Quantitation and (LOQ) were determined on the basis of response and slope of the regression equation. The result was given table no 1.

3.1.3 Precision:

Six replicate analyses of tablets by the proposed method were done. The results of the precision study indicate that the method is reliable. The intermediate precision (inter-day precision) of the method was also evaluated using two different analysts in different days in same laboratory. Results are shown in table 3. Intraday and interday precision was carried out with 99.67% results.

3.1.4 Accuracy (Recovery studies)

Accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts of the drugs. The recovery was performed at three levels, 80%, 100% and 120% of the label claim of the tablet. The result shown in table no. 4.

4. Discussion

The proposed methods for estimation of RAM in pharmaceutical dosage form were found to be accurate, simple and rapid. Hence it can be used for routine analysis of these drugs in pharmaceutical dosage forms. There was no interference from tablet excipients was observed in these methods. The values of % RSD and correlation of coefficient were found to be (% RSD 0.49- 1.08) and correlation coefficient was 0.9991 and 0.9998 for RAM. The result of recovery studies for tablet was found to be in the range of 98.40 -100.96% for method A, 99.02-100.89 for method B. Values are reported in Table 4. It indicates that there is no interference due to excipients present in the formulation. It can be easily and conveniently adopted for routine quality control analysis. Both methods are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic and are validated as per ICH guidelines.

5. Conclusion

The results of our study indicate that the proposed UV spectroscopic methods are simple, rapid, precise and accurate. The developed UV spectroscopic methods were found suitable for determination of RAM in bulk drug and in marketed solid dosage formulation without any interference from the excipients. Statistical analysis proves that, these methods are repeatable and selective for the analysis of RAM. It can therefore be concluded that use of these methods can save much time and money and it can be used in laboratories with accuracy.

Acknowledgement:

The authors are very much thankful to the Chairman, Pdmashree Mrs. Fatma Rafiq Zakaria, Maulana Azad Educational Trust, for providing necessary facilities for the project work.

Table 1: Spectrophotometric characteristics and statistical data of the regression equations

Parameter	Method A	Method B
Beer`s range (µg/ mL)	0.1- 4.0	0.1- 4.0
Estimated on wavelength (nm)	210	202- 237.5
Limit of detection(µg/ mL)	0.08	0.12
Limit of quantitation(µg/ mL)	0.83	1.2
Intercept(a)	0.8×10^{-3}	4.9×10^{-3}
S.D. of intersept(Sa)	2.2×10^{-3}	3.2×10^{-3}
Slope(b)	4.7×10^{-3}	6.5×10^{-3}
S.D. of Slope(Sb)	5.1×10^{-2}	4.6×10^{-2}
Correlation coefficient(r)	0.9991	0.9998

Table No. 2: Results of Analysis of Tablet Formulation

Method	Label claim(mg/tab)	Amount of drug estimated(mg/tab)	%Label claim+ S.D.	% Recovery
A	2.5	2.40	99.96± 0.1316	99.99
B	2.5	2.49	99.96± 0.1238	100.00

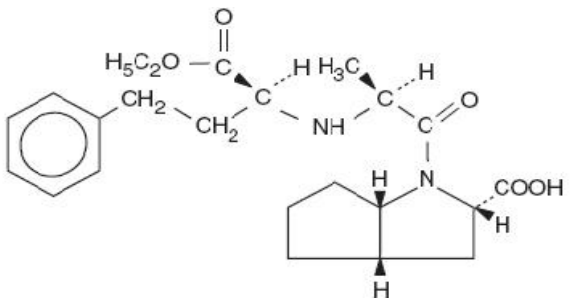
Table 3: Intra and interday Precision

Method	Label claim(mg/tab	Interday Precision(% Recovery)	Interday Precision(% Recovery)	
			Day 1	Day 2
Method A	2.5	99.89	99.94	99.96
Method B	2.5	99.92	99.93	99.88

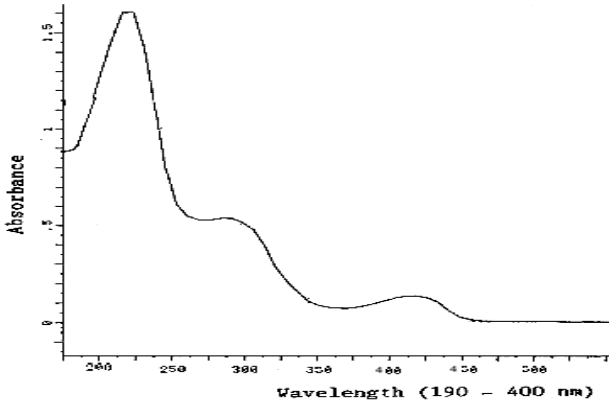
Table No. 4 Recovery data of Ramipril

Method	Level of % Recovery	Concentration Taken (µg/ mL)	Concentration estimated(µg/ mL) (±SD)	% Analytical Recovery
Method A	80	4.5	4.48±0.014	99.55
	100	5	4.92±0.024	98.40
	120	5.5	5.47±0.016	99.45
Method B	80	4.5	4.49±0.0024	99.77
	100	5	5.12±0.025	102.40
	120	5.5	5.47±0.021s	99.45

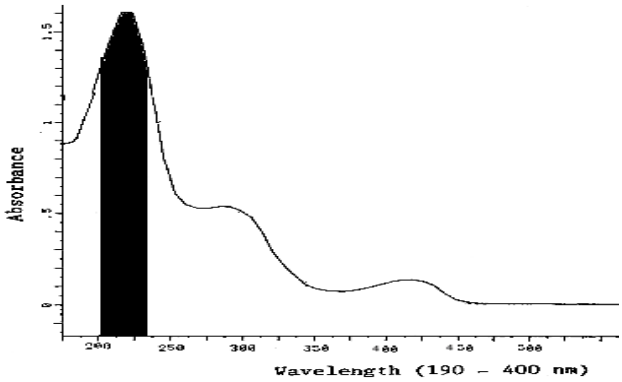
Fig.1. Chemical Structure of Ramipril



Figer 2: Absorption spectrum of the Ramipril



Figer 3: UV spectra of the Ramipril showing Area Under Curve.



Reference:

1) Warner TG, Perry MC. Ramipril: a review of its use in the prevention of cardiovascular outcomes. Drugs 2002: 62:1381-1405.

2) British Pharmacopoeia, vol. II. London, Royal Pharmaceutical Society, 2000, pp.1331-1333.

3) Abdine HH, El-Yazbi FA, Shaalan RA, Blaih SM. Direct differential solubility and compensatory-derivative spectrophotometric methods for resolving and subsequently determining binary mixtures of some anti hypertensive drugs. S. T. P. Pharm Sci., 1999:9:587-591.

4) Salem H. Derivative spectrophotometric determination of two component mixtures. Chin. Pharm. J., 1999:51: 123-142.

5) Erk N. Ratio-spectra-zero-crossing derivative spectrophotometric determination of certain drugs in two component mixtures. Anal. Lett., 199:32:1371-1388.

6) Sereda KM, Hardman TC, Dilloway MR, Lant AF. Development of a method for the detection of

angiotensin-converting enzyme [peptidyl-deipeptidase A] inhibitors using electron-capture gas chromatography detection. Anal. Proc. 1993:30:371–372.

7) SchmidtD, Keller A. Sensitive determination of the acetylcholine-esterase inhibitor HOE 498 and its metabolites in human urine by capillary GC. Anal. Chem. 1985:320:731.
8) Aboul-Enein HY, Thiffault C. Determination of ramipril and its precursors by reversed phase high performance liquid chromatography. Anal. Lett. 1991:24: 2217–2224.
9) Aboul-Enein HY, Bakr A. High-performance liquid chromatographic identification of ramipril and its precursor enantiomers using a chiralpak OT (+)-column, Drug Develop. Ind. Pharm. 1992:18:1013–1022.
10) Hajdu P, Schmidt D, Bomm M, Hack L, Keller A. Determination of 2-zeta-N-[(s)-1-ethoxycarbonyl-3-phenylpropyl]-Lalanyl, IOTA.-(1S, 3S, 5S)-2-azabicyclo[3.3.0]octane-3-carboxylic acid (Hoe 498) and its hydrolysis product in serum and urine. Arzenium. Forsch. 1984:34:1431–1435.
11) Eckert HG, Muenscher G, Oekonomopulos R, Strecker H, Urbach H, Wissmann H. Radio-immunoassay for the angiotensin-converting enzyme [dipeptidylcarboxypeptidase] inhibitor ramipril and its active metabolite. Arzeneim. Forsch. 1985:35:1251–1256.