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Simultaneous estimation of Ramipril and Valsartan in pharmaceutical dosage form

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ABSTRACT

Simple spectrophotometric methods have been developed for simultaneous estimation of Ramipril (RAM) and Valsartan (VAL) in two component tablet formulation. The methods employed are Absorbance corrected for interference method and First order derivative spectroscopy method. For absorbance corrected for interference method the working wavelengths selected are 218 nm for RAM and 250 nm for VAL. Similarly for derivative spectroscopy method the working wavelength selected are 218 nm for RAM and 236 nm for VAL in 1:9 mixture of methanol and 0.1N HCl. For both the methods linearity was observed in the concentration range of 10-40 mg/ml for RAM and VAL. The recovery studies confirmed the accuracy of proposed method and the methods were validated as per ICH guidelines.

Key words: Ramipril, Valsartan, Absorbance corrected for interference, Derivative spectroscopy.

INTRODUCTION

Ramipril (RAM), [2S-[1[R*(R*)], 2α, 3aβ, 6aβ-1-[2-[[1-(Ethoxycarbonyl)-3 phenylpropyl] amino]-1-oxopropyl] octahydrocyclopenta [b] Pyrrole-2-carboxylic acid is a Antihypertensive drug[1]. Literature reveals, U.V. spectrosctroscopy[2], HPLC[3-6] and Liquid chromatography tandem mass spectrometry[7] have been reported for the estimation of RAM alone or in combination with other drugs.

Valsartan (VAT), N-(1-Oxopentyl)-N-[[2'-(1H-tetrazol-5-yl) [1, 1'-biphenyl]-4-yl] methyl]-L-valine, is a potent angiotensin receptor blocker[1]. Methods such as HPLC[8], Capillary electrophoresis[9], and UV- spectrophotometric methods[10,11] are reported for estimation of VAL alone or in combination with other drugs. But no method is developed so far for the combination of RAM and VAL. A successful attempt is made to estimate the two drugs simultaneously by spectrophotometric analysis. This paper describes simple, rapid, accurate, reproducible and economical methods for the simultaneous determination of RAM and VAL in tablet formulations using absorbance corrected for interference method and derivative spectroscopy method.

MATERIAL AND METHODS

Instrument

A dual beam Shimadzu UV-visible spectrophotometer 1700 was used in the study.

Reagents and chemicals

Doubled distilled water, methanol (analytical grade) and HCl were used in this work. Methanolic HCl was prepared by mixing methanol and 0.1 N HCl in 1:9 ratio. RAM and VAL are obtained as gift samples from Lupin Laboratories Ltd, Pune. Marketed formulation Valent R (Lupin Laboratories Ltd) of combined dosage form of RAM and VAL was procured from the local market.

Absorbance corrected for interference method[12]

If the identity, concentration and absorpitivity of the one of the absorbing component are known, it is possible to calculate their contribution to the total absorbance of a mixture. The concentration of other absorbing component is then calculated from the corrected absorbance (total absorbance minus the absorbance of the one of the component) in the usual way.

Solutions of 20 mg ml of RAM and VAL were prepared separately in methanolic HCl. Both the solutions were scanned in the spectrum mode from 400 nm to 200 nm. The wavelengths 218 nm and 250 nm for RAM and VAL were selected respectively (Fig. 1) where both drugs shows linearity in the concentration ranges of 10-40 µg/ml with regression coefficient (r^2) values 0.9984 and 0.9995 for RAM and VAL and respectively. The absorbances were taken at 218 nm and 250 nm for both the drugs. The absorpitivity (A1%, 1cm) values for RAM was 246.4 at 218 nm and 0 at 250 nm and for VAL was 701.9 at 218 nm and 306.0 at 250 nm. Mixed standard solutions of the two drugs were prepared in methanolic HCl and their absorbances were measured at the selected wavelengths and the concentrations of the two drugs in mixed standards and the sample solution were calculated.

Derivative spectroscopy method

Standard stock solutions (100 µg/ml) of both RAM and VAL were prepared by dissolving separately 10 mg of each drug in methanolic HCl and making up the volume upto 100 ml with the same.

The sampling wavelength selected for estimation of RAM and VAL are 218 nm and 236 nm where both drugs shows linearity in the concentration ranges of 10-40 µg/ml with regression coefficient (r^2) values 0.9996 and 0.9987 for RAM and VAL respectively. The absorbances were taken at 218 nm and 236 nm for both the drugs. The absorpitivity values for RAM was 2.55 at 218 nm and 0.389 at 236 nm and for VAL was 2.35 at 218 nm and 2.12 at 236 nm. Mixed standard solutions of the two drugs were prepared in methanolic HCl and their absorbances were measured at the selected wavelengths. The concentrations of the two drugs in mixed standards and the sample solution were calculated

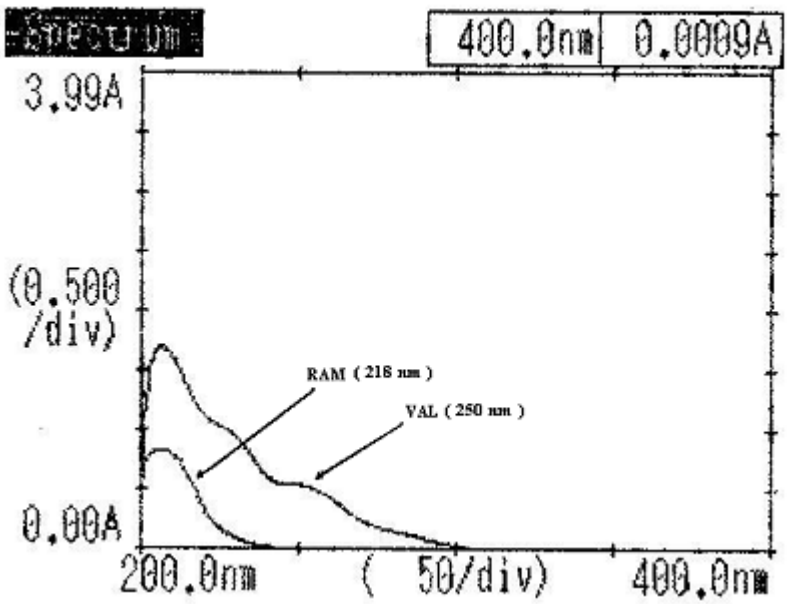

Fig. 1: Overlain spectra of Ramipril (RAM) and Valsartan (VAL)

using equations (1) and (2).

$A_1 = 2.55\ C_{RAM} + 2.35\ C_{VAL}$ ...(1)
at 218 nm

$A_2 = 0.389\ C_{RAM} + 2.12\ C_{VAL}$ ...(2)
at 236 nm

Where $-A_1$ and A_2 are the absorbances of mixed standard at 218 nm and 236 nm respectively.

C_{RAM} and C_{VAL} are concentrations of RAM and VAL respectively. Fig. 2 represents the overlain first order derivative spectra of RAM and VAL.

Analysis of the marketed formulation

A total of 20 capsules were uncapped and the contents of the capsules were accurately weighed. An amount equivalent to one capsule (containing 2.5mg of RAM and 80mg of VAL) was weighed and dissolved in about 50ml in methanolic HCl. stirred for 30min and final volume was made up to 100ml with the same. The solution was filtered through Whatman filter paper no.41, and first few drops were rejected. 15.5ml of standard stock solution of RAM (100µg/ml) was added to 1ml of the filtered solution in a 50ml volumetric flask, to make the solution of equal concentration for both the drugs, final volume was made upto the mark with methanolic HCl.

The above solutions were analyzed for the content of RAM and VAL using the methods described above.

Table 1: Results of marketed formulation analysis and recovery studies of RAM and VAL in tablets

Drug	Label Claim	Absorbance corrected for interference method			Derivative spectroscopy method		
	(mg/tablet)	% of Label Claim ± S.D*	%RSD*	%Mean Recovery*	% of Label Claim ± S.D*	%RSD*	%Mean Recovery*
RAM	5	99.77±0.596	0.598	100.09	99.62±0.531	0.533	100.30
VAL	80	99.87±0.431	0.431	100.33	99.88±0.497	0.498	100.28

* Denotes average of six determinations.

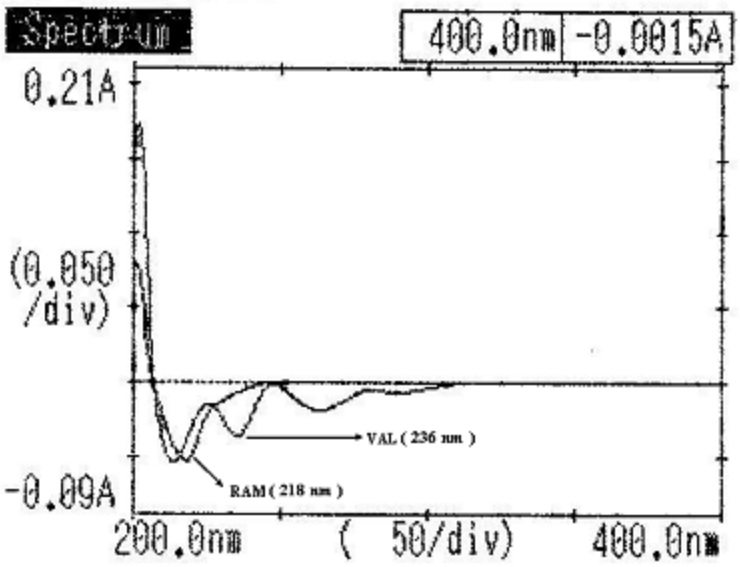

Fig. 2: Overlain first order derivative spectra of Ramipril (RAM) and Valsartan (VAL)

RESULTS AND DISCUSSION

The methods were employed for the analysis of formulations containing the two drugs. The developed methods were validated for repeatability, intermediate precision (inter-day and intra-day precision studies). The accuracy of the proposed methods was determined by performing recovery studies at 80%, 100% and 120% of the test concentration as per ICH guidelines. The mean % content and mean % recoveries by absorbance corrected for interference and area under curve methods are given in Table 1. The %RSD for Intra-day precision was 0.138% for RAM and 0.129% for VAL and for Inter-day precision was 0.590% for RAM and 0.414% for VAL respectively which is less than 2% indicating high degree of precision.

CONCLUSION

The standard deviation, %RSD and standard error calculated for both the methods are low, indicating high degree of precision of the methods. The %RSD is also less than 2% as required by ICH guidelines. The results of the recovery studies performed at three levels (80, 100 and 120 % of the test concentration as per ICH guidelines) shows the high degree of accuracy of the proposed methods. Hence the developed methods are simple, rapid, precise, accurate and can be employed for the routine estimation of Ramipril and Valsartan in both bulk and tablet dosage form.

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