 DOI: 10.18231/2393-9087.2016.0018

Method development and validation for simultaneous determination of Telmisartan and Ramipril by UV Spectrophotometry

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Abstract

A simple, validated, accurate and precise simultaneous UV Spectrophotometric method has been developed for the simultaneous estimation of Telmisartan (TEM) and Ramipril (RAM) in pharmaceutical dosage form. Telmisartan exhibits absorption maximum at 254.4nm and Ramipril shows absorption maximum at 209nm in methanol. The Beer's law obeyed the concentration range of 2-12µg/ml for both TEM and RAM. Mean recovery of 99.14% for TEM and 99.05% for RAM respectively signifies the accuracy of the method. The method was validated as per ICH guidelines. The method shows good linearity, accuracy, precision, limit of detection and limit of quantification. This method can be successfully employed for the routine simultaneous estimation of TEM and RAM in pharmaceutical dosage forms.

Keywords: Telmisartan, Ramipril, Estimation, Spectrophotometry, Dosage form.

Introduction

Telmisartan (Fig. 1) is non-peptide angiotensin II receptor antagonist, indicated for the treatment of hypertension, heart failure and myocardial infarction. Telmisartan is chemically 4'-[(1,4'-dimethyl-2'-propyl[2,6'-bi-1*H*-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid.(1) Telmisartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Its action is therefore independent of the pathways for angiotensin II synthesis. Blockade of the renin-angiotensin system with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I, is widely used in the treatment of hypertension.(2)

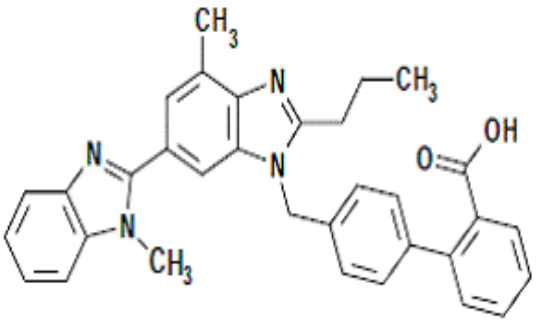

Fig. 1: Molecular structure of Telmisartan

Ramipril (Fig. 2) is an ACE inhibitor, indicated for the treatment of hypertension, heart failure, myocardial infarction and kidney problems.(3) Ramipril acts as a prodrug of the diacid Ramiprilat. It may be used alone or in combination with other antihypertensive agents. Angiotensin converting enzyme is a peptidyl dipeptidase that catalyzes the conversion of angiotensin I to the vasoconstrictor substance, angiotensin II.(4) Angiotensin II also stimulates aldosterone secretion by the adrenal cortex.It is chemically (2S, 3aS,6aS)-1[(S)-N-[(S)-1-Carboxy-3-phenylpropyl] alanyl]octahydrocyclopenta[b]pyrrole-2-carboxylicacid, 1-ethylester.(5)

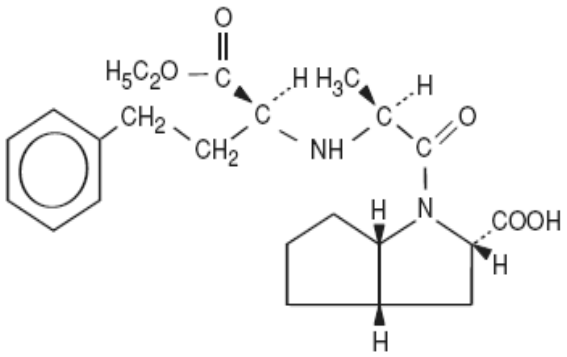

Fig. 2: Molecular structure of Ramipril

The combined dosage forms of these drugs are used in preventing cardiovascular events in high-risk patients with vascular disease or diabetes mellitus.

Literature survey revealed that there are many methods like UV-Spectrophotometric,(6,7) HPLC(8) and HPTLC(9) for individual determination of TEM and RAM but very few UV methods are reported for simultaneous estimation of TEM and RAM in their combined dosage form. An attempt was made to develop accurate, precise and economical method for estimation of these drugs in combined dosage form.

Materials and Methods

Chemicals & Reagents: The reference samples of Telmisartan (API) and Ramipril (API) were provided from Yarrow Chemicals, Mumbai, India. The

commercial formulations (tablets) (TAZLOC-R tablets containing 40mg of Telmisartan and 5mg of Ramipril) were procured from the local market. Methanol (AR grade) was purchased from E.Merck (India) Ltd., Mumbai, India and was used as solvent. Fresh purified distilled water was used throughout the experiment.

Instrument: Shimadzu UV1800 Double Beam UV-Visible Spectrophotometer was used for spectral studies. Shimadzu BL220H Digital Weighing Balance was used for weighing the materials.

Preparation of standard stock solution: Accurately weighed and transferred TEM and RAM 100mg of each drug in two separate 100ml volumetric flasks and dissolved in 100ml of methanol to get concentration of 1mg/ml. From the stock solution dilution was made with methanol to get working standard solution of 100µg/ml of both drugs.

Determination of λmax: The standard dilutions of 10µg/ml concentration were prepared for both TEM and RAM. Both the solutions were scanned in UV range (200-400nm) against solvent blank. The wavelength spectra of TEM and RAM in methanol are shown in Fig. 3, 4 respectively. The representative spectra revealed that TEM shows a well defined λmax at 254.4nm whereas RAM shows at 209nm. These two wavelengths were selected for development of simultaneous equation.

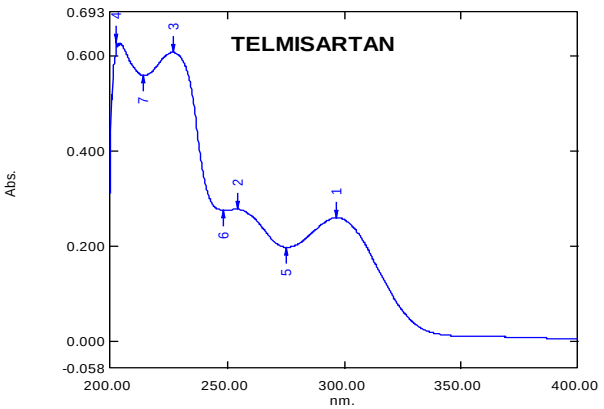

Fig. 3: UV Spectrum of Telmisartan

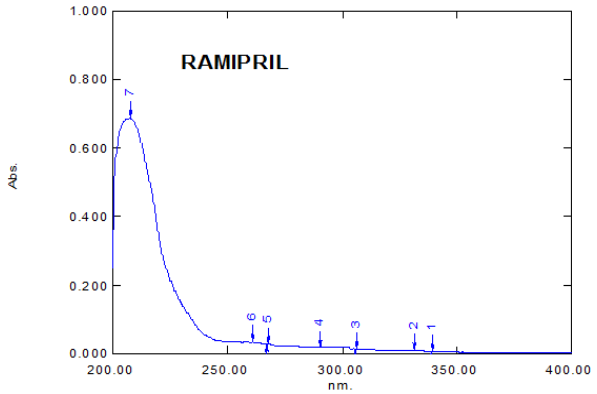

Fig. 4: UV Spectrum of Ramipril

Preparation of calibration curve: Working standard solutions were prepared for the TEM and RAM from the standard solution of 100µg/ml. Different aliquots were taken from standard stock solution and diluted with methanol separately to prepare 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml, 10µg/ml and 12µg/ml solutions respectively. Prepared working solutions of Telmisartan and Ramipril were scanned at 254.4nm and 209nm respectively. The respective absorbances were recorded and these absorbances were plotted against the concentrations to obtain the respective calibration curves (Fig. 5 & Fig. 6).

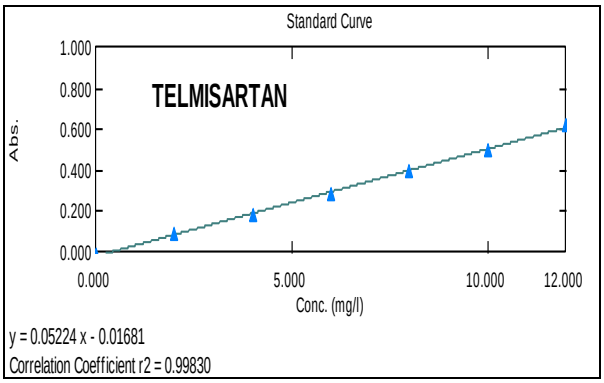

Fig. 5: Standard calibration curve for Telmisartan

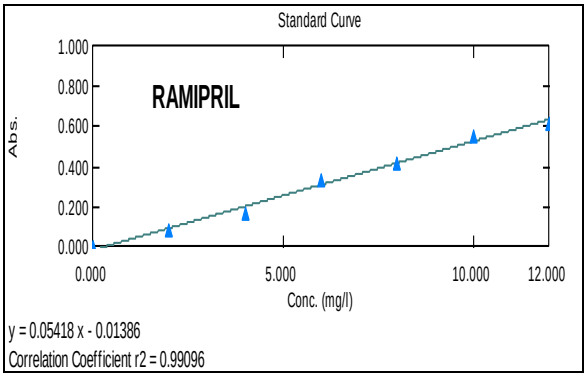

Fig. 6: Standard calibration curve for Ramipril

Sample preparation: Twenty tablets were weighed and finely powdered. Powder mixture equivalent to 40mg of Telmisartan and 5mg of Ramipril was accurately weighed and transferred into a 100ml clean dry volumetric flask containing 70ml of methanol. The solution was sonicated for 5min and the drug was dissolved completely. The volume was made up to the mark with a further quantity of the methanol to get a stock concentration of Telmisartan and Ramipril. The resulting solution was filtered by using whatmann filter paper. Pipette out 2.5ml of the above stock solution into a 10ml volumetric flask and the volume was made up to the mark with the methanol. Later pipette out 1ml of the above stock solution into a 10ml volumetric flask and the volume was made up to the mark with the methanol.

Results

Estimation of Telmisartan and Ramipril from bulk samples and their tablet dosage forms was achieved by simultaneous equation method by using UV Spectrophotometer. The wavelengths selected in methanol for estimation of Telmisartan were found to be 254.4nm and for Ramipril was found to be 209nm. The linearity was checked in different concentration and Beer's law was obeyed in the concentration range of 2-12µg/ml for both Telmisartan and Ramipril. The regression equation of the linearity curve between concentrations of Telmisartan and Ramipril over its absorbances were found to be y=0.05224x-0.01681 and y=0.05418x-0.01386 (Table 1) respectively with a correlation coefficient (r^2) of 0.9983 for Telmisartan and 0.9909 for Ramipril. Precision of the method was measured in terms of intra-day and inter-day variation (%RSD). The %RSD for intra-day precision and inter-day precision for Telmisartan were found to be 0.08% and 0.25% respectively. The %RSD for intra-day precision and inter-day precision for Ramipril were found to be 0.16% and 0.24% respectively (Table 2 & Table 3). This confirms that the method is sufficiently precise. Accuracy was determined for both drugs by spiking with 50, 100 and 150% of additional pure drug and the mean recovery of the Telmisartan and Ramipril were found to be 99.14% and 99.05% respectively (Table 4). The limit of detection (LOD) and limit of quantification (LOQ) for Telmisartan were found to be 0.10µg/ml and 0.30µg/ml respectively. The limit of detection (LOD) and limit of quantification (LOQ) for Ramipril were found to be 0.30µg/ml and 0.92µg/ml (Table 5) respectively. The percentage purity for the assay of Telmisartan and Ramipril were found to be 99.60% and 100.04% respectively (Table 6). The assay results showed that the proposed method was selective for simultaneous estimation of Telmisartan and Ramipril without interference from the excipients used in tablet dosage form.

Table 1: Linearity results of Telmisartan and Ramipril

S. No.	Concentration (µg/ml)	Telmisartan Absorbance	Ramipril Absorbance
1	0	0	0
2	2	0.089	0.087
3	4	0.184	0.166
4	6	0.284	0.338
5	8	0.397	0.421
6	10	0.504	0.548
7	12	0.697	0.619
Slope		0.05224	0.05418
Intercept		-0.01681	-0.01386
Regression Equation(y)		0.05224x-0.01681	0.05418x-0.01386
Correlation Coefficient		0.9983	0.9909

Table 2: Intra-day precision results of Telmisartan and Ramipril

S. No.	Time (Hours)	Telmisartan Absorbance	Ramipril Absorbance
1	0	0.502	0.548
2	3	0.501	0.546
3	6	0.501	0.548
4	9	0.503	0.547
5	12	0.502	0.546
6	15	0.503	0.545
Mean		0.502	0.546
SD		0.00044	0.00089
%RSD		0.08	0.16

Table 3: Inter-day precision results of Telmisartan and Ramipril

S. No.	Time (Days)	Telmisartan Absorbance	Ramipril Absorbance
1	1	0.504	0.548
2	2	0.503	0.546
3	3	0.502	0.549
4	4	0.502	0.544
5	5	0.5	0.546
6	6	0.505	0.547
Mean		0.502	0.546
SD		0.00013	0.0013
%RSD		0.25	0.24

Table 4: Recovery studies for Telmisartan and Ramipril

Level	Standard conc. (µg/ml)	Conc. added (µg/ml)	Conc. found (µg/ml)	% Recovery	% Mean recovery
Telmisartan					
80%	10	8	7.96	99.50	99.14
100%	10	10	9.86	98.60	
120%	10	12	11.92	99.33	
Ramipril					
80%	10	8	7.94	99.25	99.05
100%	10	10	9.90	99.00	

120%	10	12	11.87	98.91	

Table 5: LOD and LOQ of Telmisartan and Ramipril

Parameter	Telmisartan Measured value (µg/ml)	Ramipril Measured value (µg/ml)
Limit of detection	0.10	0.30
Limit of quantification	0.30	0.92

Table 6: Assay results of Telmisartan and Ramipril formulations

Formulation		Label claim	Amount found	%Assay
TAZLOC-R	Telmisartan	40mg	39.84mg	99.60%
	Ramipril	5mg	5.002mg	100.04%

Conclusion

The proposed UV Spectrophotometric method for simultaneous estimation of Telmisartan and Ramipril in bulk sample and in pharmaceutical formulations is simple, accurate and reproducible. The assay results, satisfying recoveries and low %RSD values indicated that the developed method can be used for the routine quality control analysis for simultaneous determination of Telmisartan and Ramipril in pharmaceutical formulations. The method was validated as per International Conference on Harmonization Guidelines and the results are within the limits. To conclude, the UV Spectrophotometric method is successfully used for analysis of bulk drugs and pharmaceutical formulations.

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