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# Simultaneous Estimation of Ramipril and Telmisartan in Tablet Dosage Form by Spectrophotometry

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**Abstract**

Two simple, accurate, sensitive and specific methods are described for the simultaneous determination of Ramipril and Telmisartan in binary mixture. The method based on UV-spectrophotometric determination of two drugs, Method A is by using multicomponant method. It involves absorbance measurement at 205.0 nm($\lambda_{max}$ of Ramipril) and 291.0 nm ($\lambda_{max}$ of Telmisartan) in 0.2M $H_2SO_4$;. Beer's law is obeyed in the concentration range of 5-40 µg $mL^{-1}$ for Ramipril and 2-20 µg $mL^{-1}$ for Telmisartan. Method B is graphical absorbance method which is based on measurement of absorbance of Ramipril and Telmisartan at 222.0nm (iso-absorptive point of Ramipril and Telmisartan) and 291.0 nm ($\lambda_{max}$ of Telmisartan) Both these methods have been successively applied to pharmaceutical formulation and were validated according to ICH guidelines.

***Keywords:***

Ramipril, Telmisartan, Multicomponant Method, Graphical Absorbance Method

## 1. Introduction

Ramipril's chemical name is (2S, 3aS, 6aS) -1[(S)-N-[(S) -1-Carboxy-3-phenyl-propyl]alanyl] octahydrocyclopenta[b] pyrrole-2-carboxylic acid, 1-ethyl ester. Ramipril is an angiotensin converting enzyme (ACE) inhibitor. An inactive prodrug, Ramipril is converted to ramiprilat in the liver and is used to treat hypertension and heart failure, to reduce proteinuria and renal disease in patients with nephropathies, and to prevent stroke, myocardial infarction, and cardiac death in high-risk patients. Ramiprilat, the active metabolite, competes with angiotensin I for binding at the angiotensin-converting enzyme, blocking the conversion of angiotensin I to angiotensin II [1]. As angiotensin II is a vasoconstrictor and a negative-feedback mediator for renin activity, lower concentrations result in a decrease in blood pressure and an increase in plasma rennin. Ramiprilat may also act on kininase II, an enzyme identical to angiotensin-converting enzyme that degrades the vasodilator bradykinin [2]. The chemical structure of Ramipril is shown in Fig 1. The typical dose of Ramipril is 5 mg per day. Literature survey reveled that various analytical methods for quantitative determination of Ramipril in pharmaceutical formulations have been reported in literature like LC-MS (Liquid chromatography-mass spectrophotometry) [3], Atomic-absorption spectrometry [4], Capillary electrophoresis [5], HPLC (High-performance liquid chromatography) [6,7],

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Spectrophotometry and atomic-absorption spectrometry [8], Spectrophotometry [9], RP-HPLC (Reverse phase-high performance liquid chromatography) [10].

Telmisartan chemically 4- [[4-methyl-6- (1-methyl-2-benzimidazolyl)-2-propyl- 1-benzimidazolyl] methyl]–2–-biphenyl carboxylic acid, which is Angiotensin II receptor antagonist Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity and circulating angiotensin II levels do not overcome the effect of Telmisartan on blood pressure. Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE,) kininase II. Angiotensin II is the principal presser agent of the renin-angiotensin system, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation and renal reabsorption of sodium [11]. The dose of Telmisartan is 40 mg daily]. The structure of Telmisartan is shown in Fig 2. There are very few methods reported for estimation of Telmisartan in pharmaceutical dosage form, which includes a validated RP –HPLC [12], spectrophotometric method [13].

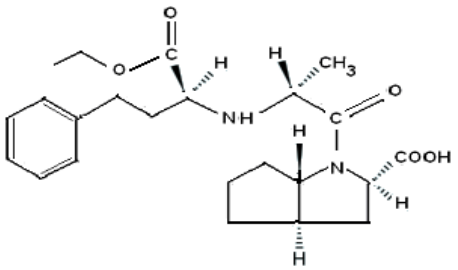


**Fig1** Structure of Ramipril

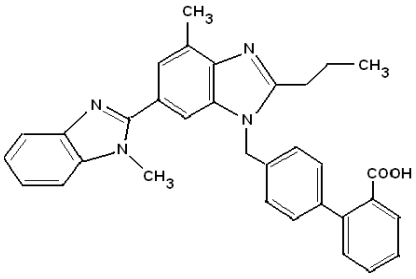


**Fig 2** Structure of Telmisartan

Both these drugs are not official in Indian Pharmacopoeia, British Pharmacopoeia, United States and European Pharmacopoeia.

At present no UV spectrophotometric methods are reported for the simultaneous estimation of Ramipril and Telmisartan in combined dosage formulation.

Therefore, it was thought worthwhile to develop simple, precise, accurate UV spectrophotometric methods for simultaneous determination of Ramipril and Telmisartan in tablets.

## 2. Experimental

### 2.1. Materials

Pharmaceutical grade Ramipril (batch no. AC 1030E03) and Telmisartan (AT120805) were kindly supplied as a gift sample by Blue Cross Laboratories Ltd., Nashik, (M.S.) India, used without further purification and certified to contain 99.53 % (w/w) and 99.66% (w/w), respectively on dried basis. All chemicals are of AR grade and were purchased from Qualigens fine Chemicals, Mumbai, India

### 2.2. UV- spectrophotometry

#### 2.2.1. Multicomponant method

UV-Vis spectrophotometer V-630 (Jasco, Japan) with spectral bandwidth of 1 nm and 10 mm matched quartz cells was used. Standard stock solutions of 100 $\mu g.mL^{-1}$ were prepared by dissolving 10 mg of each in 100 mL of 0.2 mol $L^{-1}$ $H_2SO_4$. From these stock solutions,

working standard solutions having concentration15 µg.mL-1 each were prepared by appropriate dilutions. They were scanned in the wavelength range of 400−200 nm and the overlain spectrum of five different conc.of 2.5:5, 5:10, 7.5:15, 10:20, 12.5:25 was obtained (Fig 3). Two wavelengths 205.0 nm (λmax of Ramipril) and 291.0 nm (λmax of Telmisartan) were selected for the estimation of both drugs by multicomponant mode analysis. The calibration curves were found to be linear in the concentration range of 5−40 µg.mL$^{-1}$, for Ramipril and 2-20 µg.mL$^{-1}$ for Telmisartan.The absorptivity coefficients of each drug at both wavelengths were determined. The concentration of two drugs in the mixture were calculated [14,15], (Table 1).

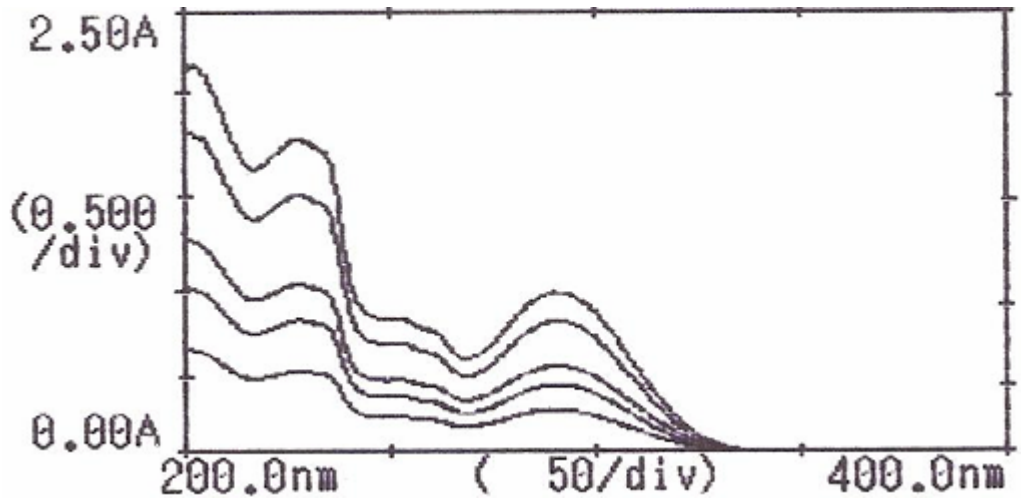


**Fig 3.** Overlain Spectrum of Ramipril And Telmisartan of different conc. in binary mixtures in 0.2 mol L$^{-1}$ $H_2SO_4$. taken on UV – Vis spectrophotometer Jasco V-630

**Table 1.** Absorptivity Values at 205.0 nm (λmax of Ramipril) and 291.0 nm (λmax of Telmisartan)

| | Absorptivity at 205.0 nm | | Absorptivity at 291.0 nm | |
|---|---|---|---|---|
| | Ramipril | Telmisartan | Ramipril | Telmisartan |
| *Mean | ax1= 327.12 | ay1= 394.97 | ax2= 352.08 | ay2= 288.96 |
| ± S.D. | 1.05 | 0.38 | 0.61 | 0.54 |

* Absorptivity values are the mean of six determinations. S.D. is standard deviation.
ax1 and ax2 absorptivities of Ramipril at 205. nm and 291.0 nm, respectively;
ay1 and ay2 absorptivities of Telmisartan at 205.0 nm and 291.0 nm, respectively.

### 2.2.2. Graphical Absorbance Method

From the overlain spectra of RAM and TEL shows that both the drugs are having same absorbance at 218.0 nm. For estimation of tablet content, the two wavelengths 218.0 nm Isobestic point for RAM and TEL and other 291.0nm $\lambda_{max}$ of TEL, were selected by solving the equation.[14,15].

For RAM

$$C_1 = \frac{Q_m - Q_y}{Q_x - Q_y} x \frac{A_1}{ax_1}$$

For TEL

$$C_2 = \frac{Q_m - Q_x}{Q_y - Q_x} x \frac{A_2}{ay_1}$$

Where C1 = Conc. of RAM
C2 = Conc. of TEL
$A_1$ and $A_2$ =Absorbances of mixture at 218.0 nm and 291.0nm respectively.
$ax_1$ and $ay_1$= Absorptivity of RAM and TEL at 218.0 nm and 291.0nm respectively
$Q_m = A_2/A_1$, $Q_y = ay_2/ay_1$, $Qx = ax_2/ax_1$

### 2.4. Assay Of Tablet Formulation By Method A and B

To determine the content of Ramipril and Telmisartan simultaneously in marketed tablets (Telma-R-Biocon Ltd, Telista-AM-Glenmark Pharmaceuticals, label claim: 5 mg Ramipril and 40 mg Telmisartan, film coated) by method A; twenty tablets were weighed accurately; their average weight determined and were finely powdered. The weight equivalent to average weight one tablet was dissolved 0.2 mol $L^{-1}$ $H_2SO_4$ by stirring for 30 min. The excipients were separated by filtration through Whatmann filter paper grade I. After filtration, an appropriate amount of solvent was added and diluted up to mark with 0.2 mol $L^{-1}$ $H_2SO_4$ to get the concentration of 5 $\mu g.mL^{-1}$ of Ramipril and 40 $\mu g.mL^{-1}$ of Telmisartan respectively.

In method A, five different conc.of range 2.5:5, 5:10, 7.5:15, 10:20, 12.5:25 $\mu g.mL^{-1}$ were prepared. The solution was scanned over the wavelength range of 400-200 nm. Absorbances of sample solutions were recorded at 205.0 nm and 291.0 nm and the concentration of two drugs in the sample were determined by subjecting to multicomponant mode of instrument by analysis of spectral data of the sample solution with reference to the mixed standards.

For method B, same solution was subjected to analysis and Absorbances of sample solutions were recorded at 205.0 nm and 291.0 nm and the concentration of two drugs in the sample were determined by using Equation 1. The amount of Ramipril and Telmisartan were determined by the above methods. The results are reported in Table 2.

**Table 2.** Analysis data of tablet formulation

| | Multicomponant method | | Graphical Absorbance method | |
|---|---|---|---|---|
| Formulation | **Telma-R | | **Telista-AM | |
| Parameter | Ramipril | Telmisartan | Ramipril | Telmisartan |
| Label Claim | 5 | 40 | 5 | 40 |
| *Drug content | 100.06 | 99.89 | 101.11 | 101.43 |
| ± S. D. | 0.2621 | 0.2080 | 0.6368 | 0.5321 |
| % R.S.D. | 0.3614 | 0.4083 | 0.5285 | 0.4268 |

* Value for Drug content (%) are the mean of six estimations; S.D. is standard deviation and R.S.D. is relative standard deviation
**Telma-R-Biocon ltd.,**Telista-AM-Glenmark Pharmaceuticals

### 2.5. Recovery studies

To check the accuracy of the developed methods and to study the interference of formulation additives, analytical recovery experiments were carried out by standard addition

method, at 80, 100 and 120 % level. From the total amount of drug found, the percentage recovery was calculated. The results are reported in Table 3 and Table 4.

**Table 3.** Recovery studies

| Drug | Multicomponant method | | | Graphical Absorbance Method | | |
|---|---|---|---|---|---|---|
| Ramipril | Excess drug | *Recovery | %RSD | Excess drug | *Recovery | %RSD |
| | 80 | 99.83 | 0.2753 | 80 | 99.37 | 0.7405 |
| | 100 | 99.72 | 0.1026 | 100 | 100.11 | 0.0119 |
| | 120 | 99.07 | 0.0254 | 120 | 100.58 | 0.8547 |
| Telmisartan | 80 | 100.69 | 0.2953 | 80 | 100.32 | 0.1238 |
| | 100 | 100.43 | 0.1236 | 100 | 99.33 | 0.0357 |
| | 120 | 99.52 | 0.1265 | 120 | 98.80 | 1.0540 |

* Recovery is mean of three estimations.

**Table 4.** Parameters UV – spectrophotometry (Summary of repeatability, precision and ruggedness)

| Parameter | | Multicomponant Method | | Graphical Absorbance Method | |
|---|---|---|---|---|---|
| | | Ramipril | Telmisartan | Ramipril | Telmisartan |
| Repeatability | | 0.26 | 0.09 | 0.72 | 0.37 |
| Precision | Intra-day | 0.57 | 0.13 | 0.29 | 0.43 |
| | Inter-day | 0.67 | 0.24 | 0.56 | 0.25 |
| Ruggedness | Analyst 1 | 0.58 | 0.54 | 0.36 | 0.77 |
| | Analyst 2 | 0.22 | 0.59 | 0.30 | 0.44 |

## 3. Results and Discussion

Both, UV spectrophotometric methods were found to be simple, accurate, economic and rapid for routine simultaneous estimation of Ramipril and Telmisartan, in tablet dosage forms. For UV spectrophotometric method, linearity was obtained in concentration range of 5 – 40 µg .mL$^{-1}$, for Ramipril and 2-20 µg .mL$^{-1}$, for Telmisartan; with regression 0.9998 and 0.9999, intercept – 0.0677and – 0.0043 and slope 0.0457 and 0.0391 for Ramipril and Telmisartan, respectively.Recovery was in the range of 99 – 101 %; the value of standard deviation and % R.S.D. were found to be < 2 %; shows the high precision of the method.

## Acknowledgement

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