

## SIMULTANEOUS ESTIMATION OF TELMISARTAN AND AMLODIPINE BY UV SPECTROPHOTOMETRIC METHOD USING MULTI COMPONENT MODE OF ANALYSIS

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### ABSTRACT

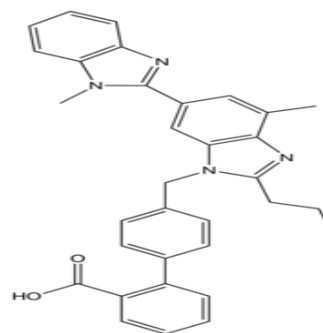
A simple, specific, precise and accurate spectrophotometric method has been developed for the simultaneous estimation of Telmisartan and Amlodipine by multi component mode of analysis. For this, simultaneous equation method is used. The method involved measurement of absorbance at two wavelengths, 296 nm and 363 nm of Telmisartan and Amlodipine respectively. Beer's law obeyed in concentration range of 2 - 22 µg/ mL and 1- 3 µg/ mL for Telmisartan and Amlodipine respectively and limit of detection and limit of quantification is found to be 0.413,0.3 µg/ mL at 296nm ,0.3786 µg/ mL at 363nm and 1.25,0.91 µg/ mL at 296nm ,1.1475 µg/ mL at 363nm respectively. The proposed method is recommended for routine analysis since it is rapid, simple, accurate and also sensitive and specific. The result of the assay of Telmisartan in Telma-AM tablet was found to be 95.60±0.447% and in Teldey-AM tablet was found to be 96.55±0.912%. The result of the assay for Amlodipine in Telma-AM was found to be 97.87±0.110% and in Teldey-AM was found to be 9102.16±1.620%.

**KEY WORDS:** Telmisartan, Amlodipine, Estimation, Formulation.

### INTRODUCTION

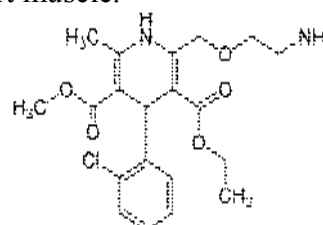
Telmisartan (TEM) 2-(4-{[4-methyl-6-(1-methyl-1*H*-1,3-benzodiazol-2-yl)-2-propyl-1*H*-1,3-benzodiazol-1-yl] methyl}phenyl)benzoic acid<sup>1</sup> is an Angiotensin Receptor Blocker (ARB) that shows high affinity for the angiotensin II type 1 (AT<sub>1</sub>) receptors, has a long duration of action, and has the longest half-life of any ARB. Telmisartan is a recently introduced angiotensin II receptor antagonist, for the treatment of essential hypertension<sup>2,3</sup>.

In addition to blocking the Renin-Angiotensin System (RAS), Telmisartan acts as a selective modulator of Peroxisome proliferator-activated receptor gamma (PPAR-γ), a central regulator of insulin and glucose metabolism. It is believed that Telmisartan's dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease (CVD)<sup>4</sup>. Telmisartan has binding affinity 3000 times with AT-2 receptor than AT-1 receptor. Telmisartan is also having maximum half life in sartans - 24 Hrs. Literature survey revealed that estimation of Telmisartan is performed by RP-HPLC<sup>5</sup>.



### Telmisartan

Amlodipine (AMO), chemically, 2-[(2- aminoethoxy methyl]-4-(2-chlorophenyl)-1, 4-dihydro- 6-methyl-3, 5-pyridinedicarboxylic acid 3-ethyl, 5-methyl ester, is a long-acting calcium channel blocker (dihydropyridine class) used as an anti-hypertensive and in the treatment of angina. Like other calcium channel blockers, Amlodipine acts by relaxing the smooth muscle in the arterial wall, decreasing peripheral resistance and hence reducing blood pressure; in angina it increases blood flow to the heart muscle.



### **Amlodipine**

Amlodipine is in the form of the Besylate salt, Amlodipine is not official in any Pharmacopoeia. Various analytical methods have been reported for the assay of Amlodipine Besylate<sup>6</sup> in pure form as well as in pharmaceutical formulations. They include high performance liquid chromatography<sup>7-12</sup>, reversed phase high performance liquid chromatography<sup>13-16</sup>, high performance thin layer chromatography<sup>17-20</sup>, gas chromatography<sup>21</sup>, gas chromatography-mass<sup>28</sup> spectrometry<sup>22</sup>, liquid chromatography with tandem mass spectrometry<sup>23</sup> and fluorimetry<sup>24</sup>, derivative spectroscopy<sup>25, 26</sup>, simultaneous multi-component mode of analysis and difference spectrophotometry<sup>27</sup>.

### **MATERIALS AND METHODS**

#### **Apparatus**

Spectral runs were made on a Shimadzu UV-Visible spectrophotometer, model- 1601 (Japan).

#### **Materials**

Telmisartan reference standard was kindly donated by Lupin pharmaceuticals suppliers, Amlodipine reference standard was kindly donated by mankind suppliers, Telday-AM was donated by Torrent suppliers and Telma-AM was donated by Glenmark. Methanol which is of analytical grade was brought from Merck pharmaceuticals.

#### **Selection of common solvent**

Methanol of analytical reagent grade was selected as common solvent for developing spectral characteristics of drug. The selection was made after assessing the solubility of both the drugs in different solvents.

#### **Preparation of stock solutions**

##### **Telmisartan**

99.3mg of Telmisartan was weighed and transferred in two 100ml volumetric flask dissolved in methanol and diluted with 50%v/v aqueous methanol and volume made up to mark. The final solution contained 993 µg/ mL of Telmisartan.

##### **Amlodipine**

35.67mg of Amlodipine Besylate (eq.25.62 mg Amlodipine ) was weighed and transferred in 100ml volumetric flask dissolved in methanol and diluted with 50%v/v aqueous methanol and volume made up to mark. The final solution contained 256.2µg/ml of Amlodipine.

#### **Preparation of standard solutions**

##### **Telmisartan**

10ml of the stock solution was diluted to 100ml and further 5ml to 50ml with the 50%v/v aqueous methanol .this gave the solution of 9.93 µg/ml of Telmisartan. This was considered as 100% test concentration.

### **Amlodipine**

5ml of stock solution was diluted to 100ml and further 5ml to 50ml with the 50%v/v aqueous methanol. This gave the solution of 1.28 µg/ ml of Amlodipine. This was considered as 100% test concentration.

#### **Preparation of synthetic mixture of Telmisartan and Amlodipine**

The synthetic mixture of Telmisartan and Amlodipine was prepared in ratio of 8:1.The decision of this ratio of drugs in the synthetic mixture was based upon the dosage strength of combination, which is available in the market. 10ml of stock solution of Telmisartan and 5ml of stock solution of Amlodipine was diluted to 100ml and further 5ml to 50ml.This gave the solution of 9.93 µg/ml of Telmisartan and 1.28 µg/ml of Amlodipine. This concentration was considered as 100% test concentration.

#### **Determining of wavelength of maximum absorbance**

Standard Telmisartan and Amlodipine solution were taken and absorbance of final solution was scanned in the range 200-400 nm against 50%v/v aqueous methanol as blank. Fig 1 shows the spectra of Telmisartan and Amlodipine respectively. Fig 1 shows the overlay spectra of maximum absorbance at 239nm and 363 nm for Amlodipine and for Telmisartan maximum was found to be 296nm.

#### **Preparation of calibration curve for Telmisartan and Amlodipine**

##### **Calibration curve for Telmisartan**

Standard stock solution of Telmisartan 10ml to 100ml and further (1 to 11 ml) were pipetted in to a series of 50ml volumetric flask. The volumes in volumetric flask were made up to mark with 50% aqueous methanol and mixed the content so to obtain a final concentration in range of 2 to 22 µg/ml. The volume was made up with 50%aqueous methanol and mixed the content.

##### **Calibration curve for Amlodipine**

Standard stock solution of Amlodipine 5ml to 100ml and further (1 to 9 ml) were pipetted in to a series of 50ml volumetric flask. The volumes in volumetric flask were made up to mark with 50% aqueous methanol and mixed the content so to obtain a final concentration in range of 1 to 3 µg/ml. the volume was made up with 50% aqueous methanol and mixed the content.

#### **Estimation of Telmisartan and Amlodipine in tablet dosage forms**

Twenty tablets were taken and accurately weighed (for TELMA-AM 0.4346 gm and for TELDEY –AM 0.4386 gm )the tablets were crushed to a fine powder .the powder sample equalent to 40 mg of Telmisartan and equalent 5mg of Amlodipine was transferred to a separate 50ml volumetric flask and about 10ml of

methanol was sonicated to dissolve. The volume was made up to the mark with 50%v/v aqueous methanol for both. This solution was filtered through whattman filter paper. 4ml of this solution was diluted to 50ml with 50%v/v aqueous methanol and further 4ml to 25ml. the solution were analyzed by multicomponent mode of analysis as given under section. The samples were analyzed in triplicate 50%v/v aqueous methanol was used as blank. The data are shown in table 1 and 2.

## RESULTS AND DISCUSSION

The developed method is recommended for routine analysis method for estimation of Telmisartan and Amlodipine in pharmaceutical dosage form by UV spectrophotometer, using multicomponent mode analysis. Overlain spectra of TEM and AMO. Overlainspectra of Telmisartan (TEM) and Amlodipine Besylate (AMO) in methanol which has been shown in the absorbance of the solution was measured at 296nm and 363nm against 50%v/v aqueous methanol as blank. The calibration data and calibration curve are shown in table 1. The correlation coefficient for Amlodipine was found to be 0.9981 at 296nm and 0.9996 at 363nm. The regression equation for Amlodipine Besylate was found to  $y=0.0016x+0.0001$  at 296nm, and  $y=0.0183x+0.0021$  at 363nm presented in Fig. 1 and Fig. 2 respectively. The absorbance of the solution was measured at 296nm and 363nm against 50%v/v aqueous methanol as blank. Telmisartan shows no absorbance on 363nm. The calibration data and calibration curve are shown in table 1 and figure 2. The correlation coefficient for Telmisartan was found to be 0.9993 at 296nm. the regression equation for Telmisartan was found to be  $y=0.0528+0.0048$  at 296nm. Regression analysis of the calibration curve for Amlodipine showed a linear relationship between the intensity of absorbance and the concentration, with correlation coefficients higher than 0.9996 at 363nm in all the curves assayed was presented in Fig. 4. Since it is rapid, simple, accurate and also sensitive and specific the result of assay for Telmisartan in Telma-AM tablet was found to be  $95.60 \pm 0.447\%$  and in Teldey-AM tablet was found to be  $96.55 \pm 0.912\%$ . the result of assay for Amlodipine in Telma-AM was found to be  $97.87 \pm 0.110\%$  and in Teldey-AM was found to be  $9102.16 \pm 1.620\%$ .

## CONCLUSION

The obtained results from the multi-component mode analysis method for simultaneous estimation of Telmisartan and Amlodipine indicate that the method is simple, accurate and precise hence can be used for routine analysis of commercially available drugs.

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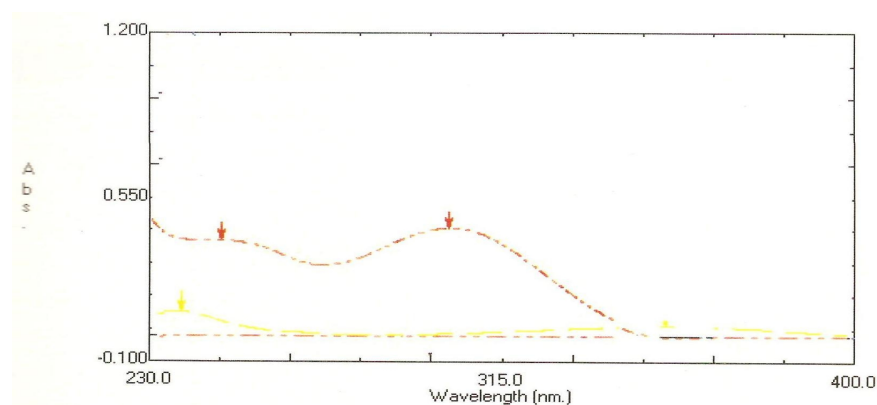
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**Table 1:** Optical characteristics and the validation parameters

Parameters	Telmisartan	Amlodipine
Wave length	296	296,363
Beer's law limit (µg/ml)	2-22	1-3
Range	70 to 130%	70 to 130%
Accuracy *	97.83%	97.74%
Precision RSD** Repeatability(n=6)		
Intra-day(n=3)	0.850	1.429
Inter-day(days=3)	1.075	1.055
	0.493	0.534

**Table 2:** Regression, detection and quantization parameters at the selected wavelength

Regression equation	Amlodipine at 296nm	Amlodipine at 363nm	Telmisartan at 296nm
Slope	0.0016	0.0183	0.0528
intercept	0.0002	0.0021	0.0048
LOD	0.4125	0.3786	0.3000
LOQ	1.2500	1.1470	0.9090



**Figure 1:** Overlain spectra of TEM and AMO. Overlain spectra of Telmisartan (TEM) and Amlodipine Besylate (AMO) in methanol.

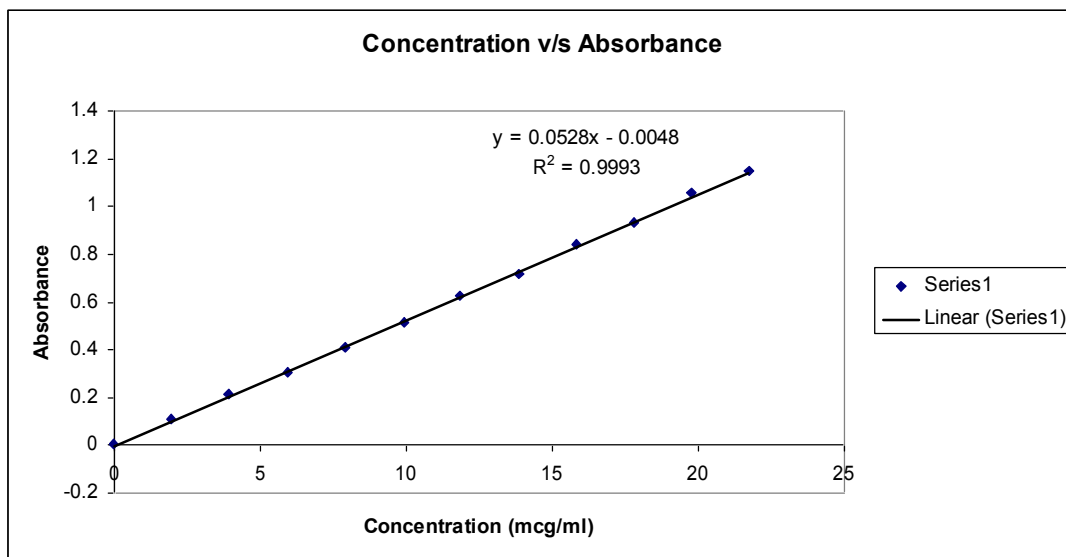


Figure 2: Regression analysis of the calibration curve for Telmisartan showed a linear relationship between the intensity of absorbance and the concentration, with correlation coefficients higher than 0.9993 in all the curves assayed.

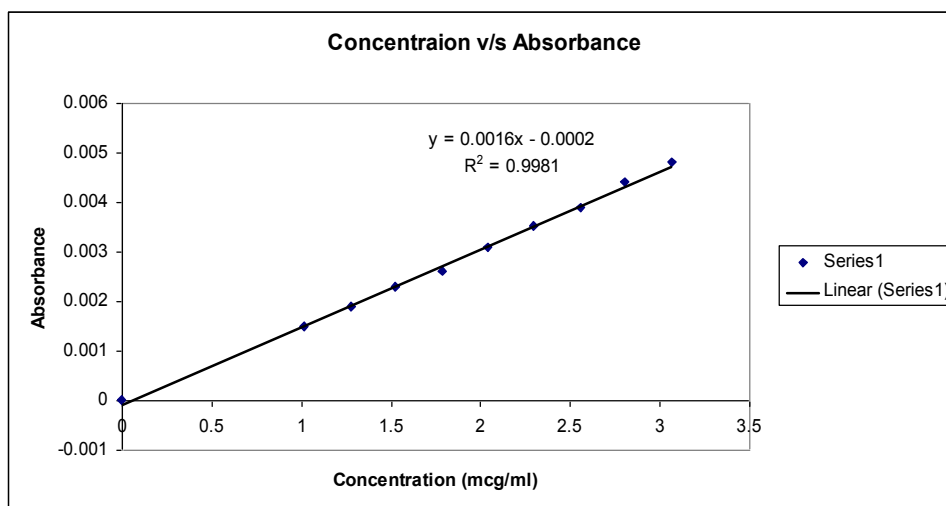
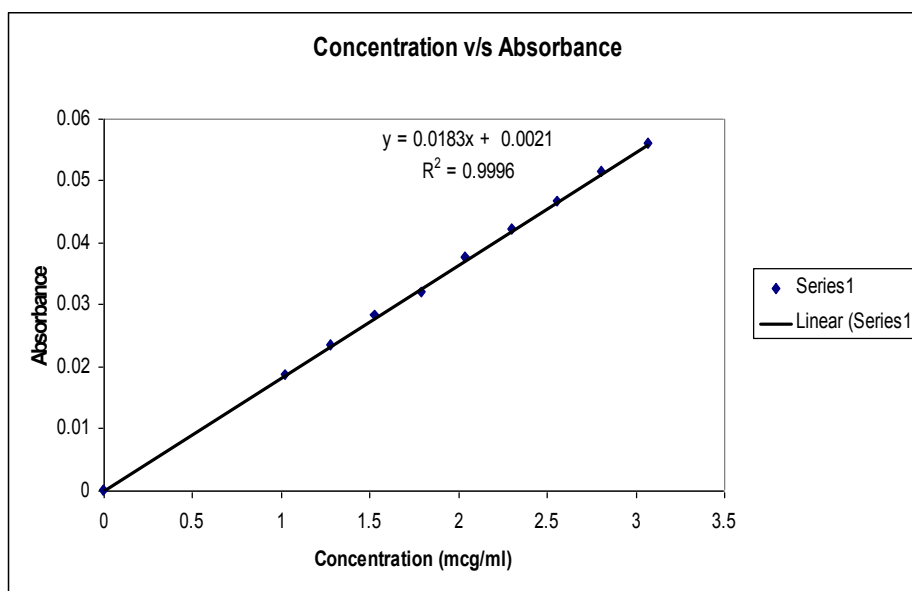


Figure 3: Regression analysis of the calibration curve for Amlodipine showed a linear relationship between the intensity of absorbance and the concentration, with correlation coefficients higher than 0.9981 at 296nm in all the curves assayed



**Figure 4:** Regression analysis of the calibration curve for Amlodipine showed a linear relationship between the intensity of absorbance and the concentration, with correlation coefficients higher than 0.9996 at 363nm in all the curves assayed

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