



# JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

## UV-Spectrophotometric Determination for Simultaneous Estimation of Amlodipine Besylate and Telmisartan in Combination

K. P. Hirpara \*, Dave V. M., Dr. S. D. Faldu, Dr. B. D. Patel

Smt. R.D.Gardi B.Pharmacy College, Nyara, Rajkot, India

### ABSTRACT:

Two simple spectrophotometric methods have been developed for simultaneous determination of Amlodipine besylate and Telmisartan in tablet formulation. Method 1 is Absorbance correction method, which is based on determination of Amlodipine besylate at 362 nm using its absorptivity value and Telmisartan at 292 nm. Method 2 is based on Absorbance ratio in which wavelengths selected were 326 nm, an isoabsorptive point and 292 nm as  $\lambda_{max}$  of Telmisartan. Linearity was observed in the concentration range of 0.5-20, 0.5-15.5  $\mu\text{g/ml}$  for AMLB and 3-24, 3-24  $\mu\text{g/ml}$  for TELM by method A and B respectively. The methods can be routinely adopted for quality control of these drugs in tablet. Recovery study was performed to confirm the accuracy of the methods. The methods were validated as per ICH guidelines.

**KEY WORDS:** Amlodipine Besylate, Telmisartan, UV-Spectrophotometric determination, validation

### Article history:

Received 25 Apr 2012

Accepted 14 May, 2012

Available online 13 Jun 2012

### INTRODUCTION:

Amlodipine (as besylate, mesylate or maleate), chemically (Fig 1.) is 3-Ethyl-5-methyl ( $\pm$ ) -2- [(2-aminoethoxy) methyl]-4- (2-chlorophenyl) -1, 4-dihydro-6-methyl-3, 5-pyridinedicarboxylate benzenesulfonat<sup>1</sup>. Amlodipine is a dihydropyridine derivative with calcium antagonist activity<sup>2</sup>. It is used in the management of hypertension, chronic stable angina pectoris and Prinzmetal variant angina<sup>1</sup>. Amlodipine acts by inhibiting the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle and also acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure<sup>3</sup>.

Telmisartan is a new angiotensin II receptor antagonist. It is chemically 4'-[(1, 4'-dimethyl-2'-propyl [2, 6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1, 1'-biphenyl]-2-carboxylic acid<sup>3</sup>. The molecular structure of Telmisartan is shown in Figure 2.

Literature survey reveals few analytical methods for the determination of Amlodipine alone and in combination with other drugs in pharmaceutical preparations and biological fluids, viz. spectrophotometry<sup>4-10</sup> HPLC<sup>11-45</sup> and HPTLC<sup>15</sup>.

Also there are some analytical methods reported for determination of Telmisartan alone and in combination<sup>16-20</sup>.

However, there is no evidence in literature for simultaneous determination of Amlodipine Besylate and Telmisartan. Hence present work describes two spectrophotometric methods for estimation these two drugs simultaneously from tablet dosage form.

### For Correspondence:

Ms. Hirpara Kinjal P.

Smt. R.D.Gardi B.Pharmacy College, Nyara,  
Rajkot, India

Email: kinjalpatel131@gmail.com

(www.jpsbr.org)

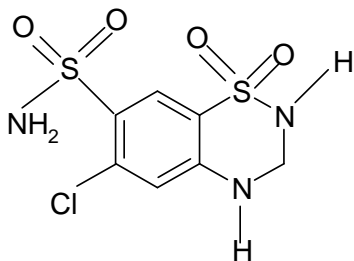


Figure 1 Amlodipine Besylate

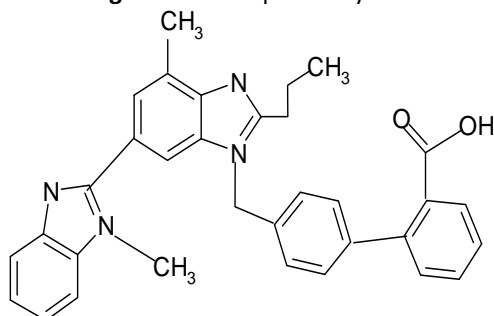


Figure 2 Telmisartan

**EXPERIMENTAL**

**Materials**

Amlodipine Besylate reference standard was kindly donated by Intas Pharmaceuticals; Telmisartan reference standard was kindly donated by Torrent pharmaceuticals. The pharmaceutical formulation that is SARTAL-AM (INTAS PHARMACEUTICALS LTD.) was procured from the local market.

Hydrochloric acid: 8.5ml of concentrated hydrochloric acid Chemdias Corporation, Mumbai, India, (Sp. gr. 1.18) was diluted to 1000 ml with water, and used in spectrophotometric studies.

**Instrumentation**

Spectral and absorbance measurements were made on Helios alpha (Thermo Scientific) model - UVA 1002 E. Digital precision Balance (A series) Contech Model CA34 was used for weighing the samples.

**Method**

**PREPARATION OF STANDARD STOCK SOLUTIONS OF AMLB AND TELM:**

The stock standard solutions containing 1 mg/ml of amlodipine and Telmisartan were prepared by dissolving 100 mg of amlodipine and Telmisartan respectively in sufficient quantity of 0.1 N HCl and diluting up to the mark in a 100 ml volumetric flask with 0.1 N HCl.

**ABSORPTION CORRECTION METHOD (METHOD 1)**

Stock solutions of AMLB and TELM were diluted further with 0.1N HCl to get working concentrations (10µg/ml) of

amlodipine and telmisartan for the spectrophotometric study. The diluted solutions were scanned over the wavelength range of 200-400 nm. From the overlain spectra (Figure-3), wavelengths 362 λmax of AMLB and 292 nm the λmax of TELM were selected for quantitation by proposed method. For studying Beer’s law, two series of different concentrations in range of 0.5-20 µg/ml for amlodipine and 3-24 µg/ml Telmisartan were prepared from stock solutions. The calibration curves were constructed at 292 and 362 nm respectively. The absorptivities (A1%, 1 cm) of both the drugs at both the selected wavelengths were determined. The quantitative determination of AMLB is carried out by using A (1%, 1cm) value at a 362 nm where TELM, interfering substance does not have any absorption and quantitation of TELM is carried out by subtracting absorption due to AMLB, interfering drug in the overlapping region of spectrum, on the basis of its absorption ratio at two wavelengths.

**ABSORPTION RATIO METHOD (METHOD 2)**

The quantitation of AMLB and TELM by proposed method was done using the selected wavelengths, 292 nm was taken as λmax for TELM and 326 nm, an isoabsorptive point for estimation of AMLB, respectively. Series of different concentrations in range of 0.5-15.5 µg/ml for AMLB and 3-24 µg/ml TELM were prepared from stock solutions. The calibration curves were constructed and regression analysis (Table I), was carried out at 292 and 326 nm. The absorptivities (A1%, 1 cm) of both the drugs at both the wavelengths were determined. By using the following equations, one can easily find out the concentration of the individual drug in admixture at the two wavelengths.

For estimation of AMLB:

$$C_x = \frac{Q_M - Q_Y}{Q_X - Q_Y} \times \frac{A_1}{a_{x1}} \dots\dots\dots (1)$$

And for estimation of TELM:

$$C_y = \frac{Q_M - Q_X}{Q_Y - Q_X} \times \frac{A_1}{a_{y1}} \dots\dots\dots (2)$$

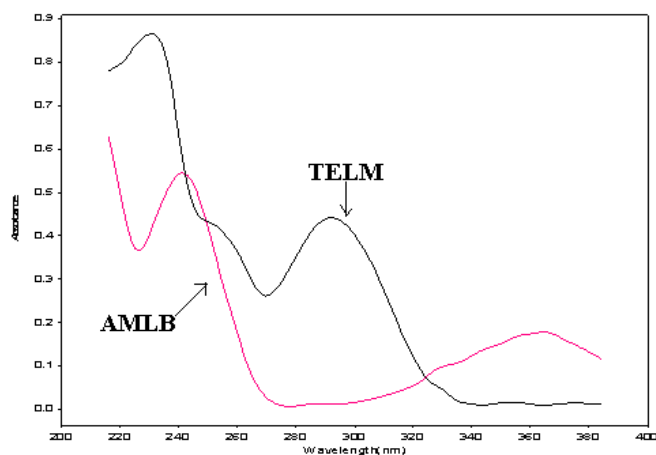
Where,  
 C<sub>x</sub> and C<sub>y</sub> are concentrations of AMLB and TELM respectively (g/1000 ml in final solution),  
 Q<sub>x</sub>= the ratio of absorptivity of AMLB at 292 and 326 nm.  
 Q<sub>y</sub>= the ratio of absorptivity of TELM at 292 and 326 nm.  
 Q<sub>M</sub>= the ratio of absorbance of mixture at 292 and 326 nm  
 A = the absorbance of mixture at isoabsorptive point.  
 a<sub>x1</sub> = the absorptivity value of AMLB at isoabsorptive point  
 a<sub>y1</sub>=the absorptivity value of TELM at isoabsorptive point.

**Table I:** Regression Analysis of the Calibration Curves

Method	Drug	Wavelength (nm)	Concentration (µg/ml)	Intercept	slope	R <sup>2</sup>
1.	AMLB	362	0.5-20	0.0127	0.0998	0.9995
		292	0.5-20	0.0057	0.0031	0.9997
	TELM	362	3-24	-	-	-
		292	3-24	0.0183	0.0327	0.9991
2.	AMLB	326	0.5-15.5	0.0057	0.0386	0.9985
		292	0.5-15.5	0.0055	0.0033	0.9990
	TELM	292	3-24	0.0155	0.0329	0.9991
		326	3-24	0.0042	0.0048	0.9998

Method 1= Absorbance Correction Method and Method 2= Absorbance Ratio Method

**Figure 3** Overlain spectra of Amlodipine Besylate and Telmisartan



**Table II:** Assay Results of Amlodipine Besylate and Telmisartan in Marketed Formulation

Tablet	Method 1			
	mg/tablet		Assay (% of label claim*)	
SARTEL-AM	AMLB	TELM	AMLB	TELM
	5	40	100.28 ± 0.52	99.52 ± 0.69
Tablet	Method 2			
	mg/tablet		Assay (% of label claim*)	
SARTEL-AM	AMLB	TELM	AMLB	TELM
	5	40	99.86 ± 0.82	100.94 ± 0.71

\*Average of three experiments

**ASSAY**

An amount equivalent to two tablets (5 mg of amlodipine and 40 mg of Telmisartan) was taken into a 100 ml

volumetric flask and shaken for about 10 min with 5 ml of 0.1 N HCl, diluted up to the mark with 0.1 N HCl. The contents of the flask were filtered using a Whatman No. 40 filter paper. Aliquot portion of the filtrate was further diluted with 0.1 N HCl to achieve a concentration of 5 µg/ml of amlodipine and 40 µg/ml Telmisartan respectively (On labeled claim basis). The above solution was analyzed for the content of AMLB and TELM using the methods described above.

**RESULTS AND DISCUSSION**

For absorption correction method, the overlain spectra of both the drugs showed the λ<sub>max</sub> of 292 nm for TELM and 362 nm for AMLB where TELM does not show a significant absorption. Hence these wavelengths were selected for estimation of AMLB and TELM. Absorbances were determined at both the wavelengths. AMLB and TELM obeyed linearity in the concentration range of 0.5-20 µg/ml and 3-24 µg/ml respectively. The absorptivity was then calculated and along with absorbance. The content of AMLB was determined at 362 nm using its absorptivity value and TELM at 292 nm after subtraction of absorbance due to AMLB deduced using absorptivity value at 292 nm. In absorption ratio method, two

wavelengths are selected from overlain spectra out of which one is isoabsorptive point and another is λ<sub>max</sub> of one of the drugs. The spectra of AMLB and TELM when overlaid indicated that the isoabsorptive point was at 326 nm at which estimation of AMLB was done and estimation of TELM was done at its λ<sub>max</sub>, 292 nm. The absorptivity was then calculated and along with absorbance, these values were submitted in the equations 1 and 2 to obtain concentration of drugs. Both the methods were successfully used to estimate the amounts AMLB and TELM in marketed tablet formulation containing amlodipine 5 mg and telmisartan 40 mg. The results obtained were comparable with the corresponding labeled amounts (Table II). The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The accuracy of the method was determined by performing recovery studies by standard addition method in which preanalyzed samples were taken and standard drug was added at three different levels. By observing the validation parameters (Table III), accuracy, intra-day and inter-day precision expressed as %RSD, reproducibility (% RSD), specificity, linearity (correlation coefficient) and range, both the methods were found to be specific, accurate, precise, repeatable, and reproducible. Hence, both methods can be employed for routine analysis of tablets for assay.

**Table III:** Summary of Validation Parameters

Parameters	Method 1		Method 2	
	AMLB	TELM	AMLB	TELM
Linearity Range ( $\mu\text{g/ml}$ )	0.5-20	3-24	0.5-15.5	3-24
Correlation coefficient ( $R^2$ )	At 362 nm 0.9995	At 362 nm -	At 326 nm 0.9985	At 326 nm 0.9998
	At 292 nm 0.9997	At 292 nm 0.9991	At 292 nm 0.9990	At 292 nm 0.9991
Precision (% C.V.)				
1. Repeatability (n=3)	0.312 $\pm$ 0.03	0.10 $\pm$ 0.049	0.390 $\pm$ 0.002	0.181 $\pm$ 0.003
2. Intraday (n=3)	0.571 $\pm$ 0.21	0.273 $\pm$ 0.52	0.503 $\pm$ 0.42	0.335 $\pm$ 0.23
3. Interday (3 days)	0.851 $\pm$ 0.22	0.521 $\pm$ 0.30	0.901 $\pm$ 0.82	0.50 $\pm$ 0.54
Ruggedness	0.0203 $\pm$ 0.00503	0.017 $\pm$ 0.00102	0.0089 $\pm$ 0.002	0.0179 $\pm$ 0.00102
Accuracy(% Recovery)	98.75-100.55	99.54-100.33		
Limit of Detection ( $\mu\text{g/ml}$ )	0.0542	0.178	0.0939	0.264
Limit of Quantitation ( $\mu\text{g/ml}$ )	0.178	0.541	0.238	0.801
Reproducibility	Reproducible		Reproducible	
Specificity	Specific		Specific	

Method 1= Absorbance Correction Method and Method 2= Absorbance Ratio Method  
% C.V. = Coefficient of Variation

## CONCLUSION

Both the methods for the determination of Amlodipine Besylate and Telmisartan have been developed and validated. The methods rely on the use of simple and cheap chemicals and techniques and provide sensitivity comparable to that achieved by sophisticated and expensive technique like HPLC,

HPTLC. Thus these can be used as alternatives for rapid and routine determination of bulk sample and tablets.

## ACKNOWLEDGEMENTS

The authors are thankful to INTAS PHARMACEUTICAL and Torrent Pharmaceuticals, Ahmedabad, India for providing gift sample of Amlodipine Besylate and Telmisartan for research. The authors are highly thankful to Smt R. D. Gardi College of Pharmacy, Gujarat Technological University, Rajkot, India for providing all the facilities to carry out the work.

## REFERANCES

7. Oneil MJ, Smith A, Heckelman PE, Budawari S, The Merck Index- an Encyclopedia of Chemicals, Drugs and Biologicals, 13rd ed.: Merck and Co Inc., White House Station, New jersey; 2001.
8. Martindale, Sweetman SC, The complete drug reference. 32<sup>nd</sup> ed.: Pharmaceutical Press; 1999
9. Amlodipine Besylate Monograph [online]. April 2009; Available from URL:<http://www.AmlodipineBesylateMonographDrugs.com.mht>
10. Pournima S. Patil, Pramodini D. Kulkarni, Mallappa S. Burkul, Harinath N. More, Sachin A. Pishawikar. Simultaneous estimation of Amlodipine besylate and

Olmesartan medoxomil by First Order Derivative Spectroscopy from Tablet. International Journal of pharmtech Research, 3(2):668-675, 2011.

1. Devi ramesh, S. Ramakrishna. New spectrophotometric methods for simultaneous determination of amlodipine besylate and atorvastatin calcium in tablet dosage forms. International Journal of Pharmacy and Pharmaceutical Sciences, 2(4):215-219, 2010.
2. Pratap Y. Pawar, Rupali S. Joshi, Vijay Sandhan, Santosh Wagh and Kunal Jangale. Simultaneous spectrophotometric estimation of Amlodipine Besylate and Benazepril HCl in pure and pharmaceutical dosage form. Der Pharmacia Lettre, 3(3):397-403, 2010.
3. Vijaya Vichare, Vrushali Tambe, Vrushali Kashikar and Dhole S.N. Spectrophotometric simultaneous determination of Amlodipine Besylate and Hydrochlorothiazide in combined tablet dosage form by simultaneous equation, absorption ratio and first order derivative spectroscopy methods. International journal of chemistry research, 2(1):7-10, 2011.
4. Priyanka R Patil, Sachin U Rakesh, PN Dhabale, and KB Burade. Simultaneous UV Spectrophotometric Method for Estimation of Losartan Potassium and Amlodipine Besylate in Tablet Dosage Form. Asian J. Research Chem. 2(1):183-187, 2010.
5. AV Kasture, Madhuri Ramteke. Simultaneous UV-spectrophotometric method for the estimation of Atenolol and Amlodipine Besylate in combined dosage form. IJPS, 68 (3):394-396, 2006.
6. Chandan Kumar Giri. Simultaneous estimation of Nebivolol Hydrochloride and Amlodipine Besylate in combined tablet dosage form by Q-analysis method. IJPRD, 2(5):1-8, 2010.

11. S. B. Wankhede et al. Spectrophotometric and HPLC Methods for Simultaneous Estimation of Amlodipine Besilate, Losartan Potassium and Hydrochlorothiazide in Tablets. *IJPS*, 72(1):136–140, 2010.
12. Kardile D.P. et al. Simultaneous estimation of amlodipine besylate and olmesartan medoxomil drug formulations by HPLC and UV-spectrophotometric methods. *J. Pharm. Sci. & Res.*, 2(9):499-514, 2010.
13. Murlidhar S. Shingare et al. Stability indicating RP-HPLC method for simultaneous determination of Amlodipine and Benazepril Hydrochloride from their combination drug product. *Journal of Pharmaceutical and Biomedical Analysis*, 3(9):147–155, 2005.
14. SS Chitlange. Stability Indicating RP- HPLC Method for Simultaneous Estimation of Valsartan and Amlodipine in Capsule Formulation. *Asian J. Research Chem.*, 1(1): 15-18, 2010.
15. B.K.Chakravardhy et al. Detection and determination of total Amlodipine by High-Performance thin-layer Chrometography: a useful technique for pharmacokinetic study. *Journal of Chromatography B*, 2(3):315-320, 1995.
16. Iango K, Shiji Kumar P. S. Simultaneous Estimation of Telmisartan and Hydrochlorthiazide in Pharmaceutical Dosage Form. *Journal Homepage*, 2(1):12-15, 2011.
17. Szczeklik A, Sanak M. Spectrophotometric Determination of Telmisartan with Congo red Dye. *Indian Journal Pharmaceutical Sciences*, 7(1):97-105, 2005.
18. David MA, Eric GH. Simultaneous analysis of Telmisartan and HCTZ by HPTLC method, *Indian Journal Pharmaceutical Sciences*, 1(2):234-240, 2003.
19. F. Coceani, I. Bishai, J. Lees. RP HPLC estimation for simultaneous estimation of Telmisartan and Hydrochlorothiazide in tablet dosage form, *Indian Journal of Pharmaceutical Sciences*, 7(2):589-592, 2003.
20. Smith JW, Johnson JE, Cluff LE. RP-HPLC estimation of Ramipril and Telmisartan in tablets. *J of Young Pharmacist*, 35(8):269-285, 2001.

