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UV Spectrophotometric estimation of Amlodipine besylate and Telmisartan in Bulk drug and Dosage form by Multiwavelength Analysis

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Abstract: A simple, accurate and reproducible spectrophotometric method has been developed for the simultaneous estimation of amlodipine besylate (AML) and telmisartan (TEL) in combined tablet dosage forms. The tablet is determined by the multi-wavelength technique, at the wavelengths of 360 nm and 298 nm over the concentration ranges of 15-75 mcg ml^{-1} and 1-10 mcg ml^{-1} with mean recovery more than 98% for both drug amlodipine besilate and telmisartan respectively. The results of the analysis were validated statistically and recovery studies were carried out as per ICH guidelines. Thus the proposed method can be successfully applied for simultaneous determination of amlodipine besilate and telmisartan in routine analysis work.
Keywords: Amlodipine besylate and Telmisartan, spectrophotometric, simultaneous, multi-wavelength.

INTRODUCTION:

Amlodipine besylate (AML) is a calcium channel blocker; chemically it is [3-ethyl-5-methyl (4RS)-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-methyl-1-dihydropyridine-3,5-di-carboxylatebenzene sulfonate].[1-5] Telmisartan (TEL), is an angiotensin receptor blocker, chemically it is 4'-[(1,4'- dimethyl – 2'-propyl [2,6' –bi-1H- benzimidazol] - 1'-yl) methyl] [1,1'- biphenyl] - 2- carboxylic acid.[2-4] Literature survey reveals that, there are several spectroscopic,[6-9] HPLC[10-16] and HPTLC[17-19] methods for the estimation of both amlodipine besylate and telmisartan individually as well as in combination with other drugs. A combination of Telmisartan and Amlodipine besylate reported to show substantial and sustained 24- hour blood pressure (BP) reduction and is well-tolerated in a range of patients with hypertension and at risk of cardiovascular (CV) events. Both drugs are available in combined tablet dosage form for the treatment of hypertension. There are few *UV* and HPLC methods are reported for the simultaneous analysis of AML and TEL in their combined dosage form. So a need was felt, to develop new methods to analyze the drugs simultaneously. A successful attempt has been made to estimate two drugs simultaneously by *UV* spectrophotometric analysis. The present work demonstrates simple, rapid, accurate, reproducible and economical method for the simultaneous determination of AML and TEL in tablet formulations by multi-wavelength method.

EXPERIMENTAL

INSTRUMENTATION:

The developed new method was carried out on JASCO spectrophotometer, model no. V-530 with 1 cm matched quartz cells was used for experiments. The absorption spectra of reference and test solution were carried out in a 1 cm quartz cell over the range of 200-400 nm. A Shimadzu electronic analytical balance (AUX-220) was used for weighing the sample. An ultrasonic cleaner was used for sonicating the tablet sample solution.

REAGENTS AND CHEMICALS:

Analytical pure samples of Amlodipine besylate and Telmisartan (Unichem labs ltd. India), were used in the study. Methanol was used as a solvent which was procured from Finar Chemicals Ltd. Ahmadabad, India. The pharmaceutical dosage form used in this study was

Telpres-AM (Glenmark Generics Ltd., Uttarkhand, India) labelled to contain 5 mg AML and 40 mg of TEL per tablet.

EXPERIMENTAL CONDITION:

According to the solubility characteristics of drug, methanol was selected as solvent for analysis. From the scanning of both the drug by *UV* spectra, wavelengths were selected for estimation of AML at 360nm and for TEL at 298nm.

WORKING STANDARD SOLUTION:

Tablets of TEL and AML combination are available in 1:16 and 1:8 ratios. Working standards was prepared in the ratio of 1: 8 from standard stock solution of 100 µg/ml.

PREPARATION OF STANDARD STOCK SOLUTION:

Standard stock solutions (100 mcg ml^{-1}) of AML and TEL were prepared by dissolving separately 10 mg of drug each in 100 ml methanol. The working standard solutions of these drugs were obtained by dilution of the respective stock solution with methanol.

PREPARATION OF SAMPLE STOCK SOLUTIONS:

Twenty tablets were weighed and crushed to fine powder. An accurately weighed powder sample equivalent to 5 mg of Amlodipine besylate and 40 mg of telmisartan was transferred into a 100 ml volumetric flask and dissolved in 50 ml of methanol. After the immediate dissolution, the volume was made up to the mark with the same solvent to get a stock solution containing 50 µg/ml of amlodipine besylate and 400 µg/ml telmisartan, The solution was sonicated for about 30 mins and was then filtered through Whatmann filter paper No.41. The solution was suitably diluted with methanol to obtain sample solutions containing AML and TEL in the concentrations ratio of 1:8 mcg ml-1 respectively as in the tablet formulation.

WAVELENGTH SELECTION:

The standard solution of amlodipine besylate and telmisartan were separately scanned at different concentration in the range of 200-400 nm and the λ max was determined. The overlain spectrum of both the drugs was also run.

LINEARITY:

AML and TEL exhibited linearity with absorbencies in the range of 15-75 mcg ml^{-1} and 1-10 mcg ml^{-1} at their respective selected wavelengths. i.e. 360nm and 298nm respectively.

Table-1: Result of UV analysis

Parameters	Amlodipine besylate	Telmisartan
Detection Wavelength	360nm	298nm
Beers Law Limit	15-75µg/ml	1-10µg/ml
Molar absorptivity	0.6485×104 L/mol.cm	4.04×104 L/mol.cm
Regression Equation	y = mx + c	y = mx + c
Slope	0.11	0.077
Intercept	0.007	0.004
Correlation Coefficient	0.999	0.999

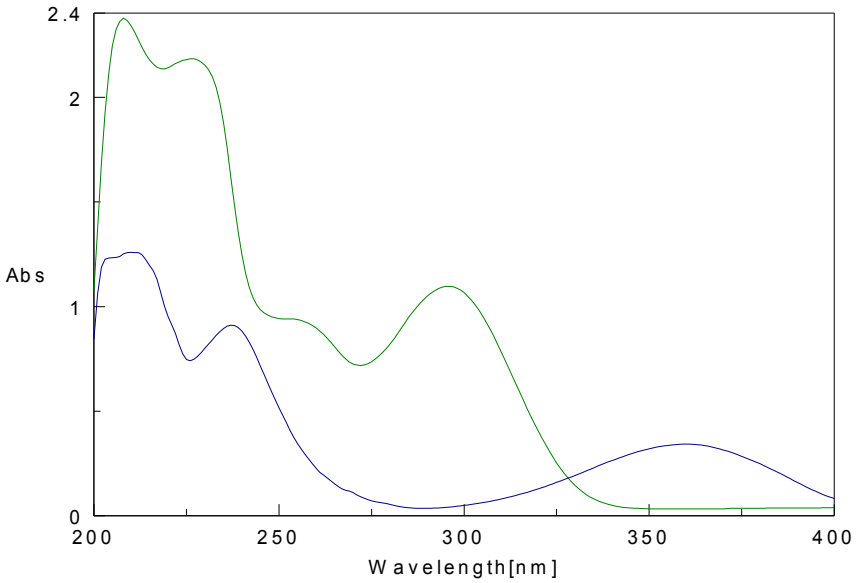

Figure 1: UV overlain spectra for Amlodipine besylate and Telmisartan

METHOD VALIDATION:

Accuracy was determined by recovery study. The recovery experiment was carried out by spiking the already analyzed sample of the tablets with their different known concentration of standard AML and TEL. Precision for assay were determined by repeatability, inter day, intraday precision for both drugs (each in three replicate).

RECOVERY:

To evaluate the accuracy, precision and reproducibility of the method, known amount of pure drug was added to the preanalyzed sample of tablet powder and the mixture was analyzed for the drug content using the proposed method. The percentage recovery was found to be within range. The recovery experiments indicated the absence of interference from the commonly encountered pharmaceutical additives and excipients. Result of recovery study has been shown in Table 3.

Table-2: Result of UV analysis for tablet formulation

Formulation	Drug	Label Claim (mg)	% Label Claim*, Mean ± S.D.	% R.S.D.
Tablet	Amlodipine besylate	5mg	99.72±0.000462	0.6377
	Telmisartan	40mg	99.67±0.003776	0.2085

S.D. - Standard Deviation, R.S.D. - Relative Standard Deviation, *Average of six determinations.

Table-3: Result of recovery study

Drug	Level of Recovery (in %)	Amount present (in µg / ml)	Amount found (in µg / ml)	% Recovery	%RSD
Amlodipine besylate	80%	4	3.9315	99.23%	0.1545
	100%	5	4.9325	99.32%	0.1751
	120%	6	6.0160	100.15%	0.1917
Telmisartan	80%	32	32.2049	100.28%	0.0566
	100%	40	39.5096	99.38%	0.1370
	120%	48	47.65	99.61%	0.0171

Table no.4- Precision study of Amlodipine besylate

Conc. (µg/ml)	Intra-day Absorbance			Inter-day Absorbance		
	Mean absorbance	± SD	%RSD	Mean Absorbance	± SD	%RSD
4	0.03133	0.00057	1.81934	0.0317	0.0005773	1.8212
5	0.04333	0.0005774	1.3316	0.0433	0.0005774	1.333
6	0.0553	0.0005774	1.044	0.053	0.001000	1.886

Table no.5- Precision study of Telmisartan

Conc. (µg/ml)	Intra-day Absorbance			Inter-day Absorbance		
	Mean absorbance	± SD	%RSD	Mean Absorbance	± SD	%RSD
32	1.59367	0.001155	0.7247	1.59133	0.002082	0.13084
40	1.9663	0.0005774	0.02936	1.9667	0.002887	0.1467
48	2.28633	0.002082	0.09106	2.28733	0.002082	0.09102

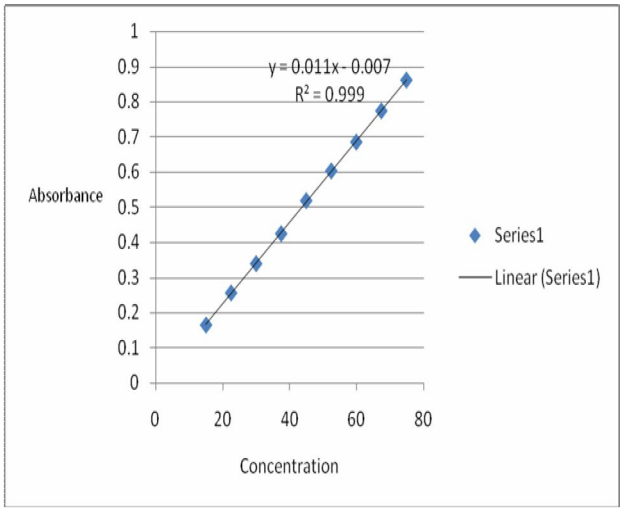

Figure 2: Calibration curve for Amlodipine besylate

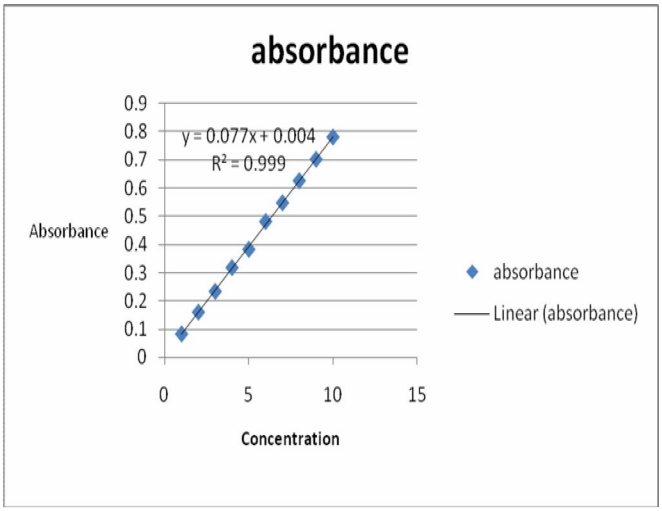

Figure 3: Calibration curve for Telmisartan

RESULTS AND DISCUSSION:

The proposed new method for determination of amlodipine besylate and telmisartan showed molar absorptivity. Linear regression of absorbance on concentration gave the equation y = 0.11+ 0.019 (for amlodipine besylate) and y =0.077x + 0.004 (for telmisartan) with a correlation coefficient (r) 0.999 (for amlodipine besylate) and 0.999 (for telmisartan). Result of UV analysis has been shown in Table 1.

The standard deviation and RSD calculated for the method is low, indicating high degree of precision. The RSD is also less than 2% as required by ICH guidelines and shown in table 2. The % recovery was between 98- 102% indicating high degree of accuracy and specificity of the proposed method. The results of the recovery study are shown in table 3. The developed spectrophotometric method was validated for simultaneous estimation of AML and TEL using linearity, range, accuracy and precision. The RSD for all parameters was found to be less than two, which indicates the validity of method and assay results obtained by this method are in fair agreement.

CONCLUSIONS:

The developed method is simple, rapid, precise, accurate and can be employed for the routine estimation of AML and TEL in both bulk and tablet dosage form.

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