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Development and Validation of Spectrophotometric Method for Simultaneous Estimation of Atorvastatin Calcium and Telmisartan in Combined Dosage Form

Vaishali Gadekar*[1]; Nimita Manocha[1]; Archana Tiwari[1]; PK Dubey[1]

[1]Swami Vivekanand College of Pharmacy, Indore, M.P., India

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ABSTRACT: A simple, reproducible, economical, accurate, and precise UV spectrophotometric method for simultaneous estimation of Atorvastatin Calcium (ATC) and Telmisartan (TEL) in tablet dosage form has been developed. The absorption maxima at 246 nm and 273 nm were used for the estimation of Atorvastatin Calcium and Telmisartan respectively. A calibration curve was plotted over a degree range of 2-20 µg/ml for Atorvastatin Calcium and 1-6 µg/ml for Telmisartan respectively. Recovary was found at 90.14%for ATR and TEL 99.05 % using proposed UV spectrophotometric Telmisartan. The method was validated according to International Conference on Harmonization (ICH) guidelines with respect to linearity, recovery, precision, LOD, and LOQ. The validation study statistically significant as all the statistical parameters are within the acceptance range (%RSD < 2%). The developed method is simple, inexpensive, and accurate

KEYWORDS: UV spectroscopy, Simultaneous Estimation method, Atrovastatin, Telmisartan

INTRODUCTION

Atorvastatin is a dihydroxy monocarboxylic acid that is a member of the drug class known as statins, used primarily for lowering blood cholesterol and for preventing cardiovascular diseases. It has a role as an environmental contaminant and a xenobiotic. It is an aromatic amide, a member of monofluorobenzenes, a statin (synthetic), a dihydroxy monocarboxylic acid and a member of pyrroles. It derives from a heptanoic acid. It is a conjugate acid of an atorvastatin (1))

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Telmisartan is a member of the class of benzimidazoles used widely in the treatmentof hypertension. It has a role as an antihypertensive agent, an angiotensin receptor antagonist, (peptidyl-dipeptidase A) inhibitor, a xenobiotic and an environmental contaminant. It is a member of biphenyls, a member of benzimidazoles and a carboxybiphenyl.(2)

MATERIAL AND METHOD:

Chemical and reagents

Atrovastatin and Telmisartan standard materials obtainedas gift from cipla pharma.indore. tablets (Telista plus) make Verdant life science . Containing Atrovastatin (10 mg) and telmisartan (40 mg) were purchased from locak market.

Instrumentation

A double beam UV Spectrophotometer using Shimadzu UV-1800 (Shimadzu Corp. Japan). With spectral width of 2 nm quartz cell (1.0cm path) was employed to measure absorbance of solutions. On the basis of solubility study Ethanol was selected as the solvent for dissolving Atrovastatin and Telmisartan .(3)

Preparation of standard stock solution

A. Prepration of standard stock solutions Accurately weighed (10 mg) each of standard Atorvastatin Calcium (10 mg) and Telmisartan (10 mg) were transferred to two separate 100 mL calibrated volumetric flasks (100 mL) dissolved in Ethanol which were further diluted with the Ethanol to obtain standard solutions of Atorvastatin Calcium and Telmisartan (100 µg/mL)(4)

B. Selection of working wavelength

Working standard stock solutions of both the drugs were diluted to obtain final concentration of Atorvastatin Calcium (10 µg/mL) and Telmisartan (10 µg/mL). Solutions were scanned in the wavelength range of 200 - 400 nm. wavelength range of 210 -236, 237-246 nm were selected for the analysis(4)

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C. Preparation of calibration curve of Atorvastatin Calcium and Telmisartan

A. calibration curve was plotted over a degree range of 2-20 µg/ml for Atorvastatin Calcium and 1-6 µg/ml for Telmisartan. Accurately measured standard stock solution of Atorvastatin Calcium (2, 4, 8, 12, 16 & 20 ml) and standard stock solution of Telmisartan (1, 2, 3, 4, 5 & 6 ml) were transferred to a separate series of 10 ml of volumetric flasks and diluted to the mark with Ethanol. The absorbance of each solution was measured at the wavelengths 246 nm and 273 nm.Calibration curves were constructed for Atorvastatin Calcium and Telmisartan by plotting absorbance versus concentrations at both wavelengths. (5)

Simultaneous estimation of atorvastatin calcium and telmisartan by simultaneous equation method

Standard Stock solutions of ATR and TEL in the concentration range 1-10 µg/mL and 220µg/ml were made in the water and absorbance of these solutions was measured at 246nm and 273nm. Calibration curves were plotted to confirm the Beer‟s law and the absorptivity values calculated at the respective wavelengths for both the drugs. Two simultaneous equations as below were formed using these absorptivity values

A (1%, 1 cm)

λ1 A1= ax1bCx+ay1bCy ……..... (1)

λ2A2= ax2bCx+ay2 bCy……. (2)

For measurements in 1 cm cells b=1 Rearrange eq. (2) Cy= A2- ax2Cx/ ay2

Substituting for Cy in eq (1) and rearranging

Cx = A2ay1-A1 ay2/ax2 ay1-ax1 ay2…….. (3)

Cy = A1ax2-A2 ax1/ax2 ay1-ax1 ay2……... (4)

Where Cx and Cy are the concentration of ATR and TEL, respectively, A1 and A2 are absorbance at 246 nm and 273 nm respectively, ax1 and ax2 are absorptivities of ATR at 246 nm and 273 nm respectively; ay1 and ay2 are absorptivities TEL of at 246 nm and 273 nm

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respectively. By solving the two simultaneous equations, the concentrations of ATR and TEL in sample solutions were obtained.(6)

Analysis of tablets formulation

Twenty tablets of (Telistaplus 40 tablet) each contained 10mg of ATC and 40 mg Accurately weighed. their average weight determined .they was crushed to fine powder The powder equivalent to 10mg ofamount of drug combination(10 mg ATC+ 40 mg TEL) was weighed and dissolved in 10 mg Of ethanol with the aid of ultrasonication for 5 min. The solution was filtered through Whatman Filter paperno.41 to get sample stock solution . 0.1 ml of this solution was further diluted with 10 ml distilled water to get required concentration in the liner range the absorbance was measured at the selected wavelength for the drug the absorbance of the solution was measured at 246 nm and 273 nm.(7)

Validation of proposed method

The method was validated according to ICH guidelines for validation of analytical procedures in order to determine linearity, sensitivity, accuracy and precision for each analyte

Linearity

The linearity of the method is its ability to elicit test results that are directly proportional to the concentration of the analyte in samples. The calibration curve was taken in the range of 1-6 µg/ml for Telmisartan and 2-20 µg/mL for Atorvastatin Calcium at the respective λmax (8)

Accuracy

10 mg of Atorvastatin Calcium, standard drugs of Atorvastatin calcium and Telmisartan were added at 80%, 100% and 120% levels. This was extracted diluted and reanalyzed as per the formulation procedure. Absorbance was noted at respective wavelength.(8)

Precision

The intraday and interday precisions of the proposed spectrophotometric methods were determined by estimating t he corresponding response 3 times on the same day and on 3 different days over a period of 1 week for 3 different concentrations of TEL (1, 2, 3 µg/mL) and ATR (2, 4, 8 µg/mL) and the results are reported in terms relative standard deviation (RSD)52. The

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developed method was found to be precise as the %RSD value for intermediate precision studies(9)

Limit of Detection

It is the lowest amount of analyst in a sample that can be detected but not necessarily quantitated under the stated experimental conditions. Limit of detection can be calculated using following equation as per ICH guidelines(10)

$LOD = 3.3 \times N/S$

Where, N = Standard deviation of the response and S = Slope of the corresponding calibration curve

Limit of quantification

It is the lowest concentration of analyte in a sample that can be determined with the acceptable precision and accuracy under stated experimental conditions. Limit of quantification can be calculated using following equation as per ICH guideline(10)

$LOQ = 10 \times N/S$

Where, N = Standard deviation of the response and S = Slope of the corresponding calibration curve. Slope of the corresponding calibration curve.

RESULTS AND DISCUSSION

In the present study, we have to develop UV-vis spectrophotometric method for the simultaneous estimation of Atrovastatin and Telmisartan in combined dosage form. The developed method was validated as per the ICH guidelines. Linearity was evaluated by analysis of working standard solution of Atorvastatin Calcium and Telmisartan at six different concentrations. TEL found to be linear within conc. range of 1-6 µg/ml with regression coefficient of 0.998 and ATR was found to be linear within conc. range of 2-20 µg/ml with regression coefficient of 0.999 the results of regression The Absorptivity were found approximately same for all the concentrations hence both drugs obeyed Beer Lambert's law in indicated concentration range. The high value of correlation coefficient (R2) also indicates good linearity for both the drugs. The absorbances

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were measured at the selected wavelengths and absorptivities for both drugs were determined at both wavelengths

Table 1: Absorptivity Values Of ATR and TEL at 246.0 nm and 273.0 nm

Concentration (Mcg/ml)		**Absorptivity (246.0nm)**		**Absorptivity (273.0nm)**	
ATR	**TEL**	**ATR**	**TEL**	**ATR**	**TEL**
2	1	0.44	0.79	0.051	0.116
4	2	0.043	0.089	0.046	0.115
8	3	0.036	0.108	0.034	0.112
12	4	0.034	0.115	0.03	0.11
16	5	0.033	0.126	0.025	0.112
20	6	0.032	0.133	0.022	0.11
Mean		0.103	0.226	0.034	0.096
SD		Ax1=0.023	Ay1=0.055	Ax2=0.002	Ay2=0.032

Table 2: Analysis of drug formulation

Sr. No	**Concentration of Drug taken (equipment weight) mg/ml**		**Absorbance**	
			At Lambda Max	**At Lambda Max**
			1(246nm)	**2 (273nm)**
	TEL	ATC	A1	A2
1	40	10	0.079	0.11
2	40	10	0.11	0.112
3	40	10	0.115	0.116

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4	40	10	0.117	0.118
5	40	10	0.12	0.12
Mean			0.115	0.116

PRECISION

The repeatability is expressed as percentage relative standard deviations (% RSD) for the ATR at the concentration of 2, 4 and 8 µg/ml and their average % RSD value were0.350, 0.168 and 0.286 while for the TEL the concentration of 1,2 and 3 µg/ml and their average % RSD value were 0.387, 0.170 and 0.282.

TABLE 3: Result of intraday precision studies

S.no	Parameters	% Amt. found (Atorvastatin Calcium)			% Amt. found (Telmisartan)		
		2 µg/ml	4 µg/ml	8µg/ml	1µg/ml	2 µg/ml	3 µg/ml
1.	Morning	99.89	99.65	99.48	99.93	99.56	99.35
2.	Afternoon	99.69	99.69	100.05	99.66	99.97	99.98
3.	Evening	99.21	99.21	99.72	99.28	99.22	99.78
4.	Mean	99.59	99.79	99.75	99.48	99.84	99.76
5.	S.D.	0.349	0.168	0.286	0.385	0.170	0.282
6.	% R.S.D.	0.350	0.168	0.286	0.387	0.170	0.282

Accuracy: The accuracy was assessed by the standard addition method of three replicate determinations of three different solutions containing 8, 10 and 12 µg/ml of TEL and ATR. The average % recoveries for three different concentrations were found to be 90.14% for ATR and

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TEL 99.05 % using proposed UV spectrophotometric method. The higher values indicate that the proposed method is accurate for the determination of ATR and TEL in pharmaceutical dosage form

Table 4 Recovery (Accuracy) analysis for Atorvastatin Calcium and Telmisartan

S.no	Recovery Level	Standard Conc. µg/ml	Conc. added µg/ml	Conc. Found	%Recovery	% Mean Recovery
Atorvastatin Calcium						
1.	80 %	10	8	7.96	99.50	
2.	100%	10	10	9.86	98.60	99.14
3.	120%	10	12	11.92	99.33	
Telmisartan						
1.	80 %	10	8	7.94	99.25	
2.	100%	10	10	9.90	99.00	99.05
3	120 %	10	12	11.87	98.90	

LOD and LOQ: The limit of detection and limit of quantification were found to be 0.31µg/ml and 0.1023µg/ml for Atorvastatin Calcium and 0.2805µg/ml and 0.85µg/ml for Telmisartan respectively by proposed UV spectrophotometric method. Results of LOD and LOQ are summarized in Table 5 limit of detection (LOD) and limit of quantification (LOQ) of Atorvastatin Calcium and Telmisartan.

S.no	Parameters	Method(Simultaneous estimation method)	
		Atorvastatin Calcium	Telmisartan
1.	LOD(µg/ml)	0.1023	0.2805
2.	LOQ(µg/ml)	0.31	0.85

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CONCLUSION: The validation procedure followed were as per the ICH guidelines study. The linearity was achieved with Ethanol solvent, Linearity, Accuracy and precision were satisfactory and the limit of detection (LOD), limit of quantitation achieved was also satisfactory. Hence we conclude that the simple, rapid, less-time consuming, cost effective and precise method was developed and validated by UV-spectroscopy with the simultaneous estimation of Atorvastatin Calcium & Telmisartan.

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