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Research Article

DEVELOPMENT AND VALIDATION OF UV-SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF TELMISARTAN AND ATORVASTATIN CALCIUM IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

An UV spectrophotometric method using simultaneous equation was developed for the simultaneous determination of Telmisartan and Atorvastatin calcium in a binary mixture. In the proposed method, the signals were measured at 296.0 nm and 247.0 nm corresponding to absorbance maxima of Telmisartan and Atorvastatin Calcium in methanol respectively. Linearity range was observed in the concentration range of 5-30 µg/ml for both the drugs. Concentration of each drug was obtained by using the absorptivity values calculated for both drugs at two wavelengths, 296.0 nm and 247.0 nm and solving the simultaneous equation. Developed method was applied to laboratory mixture and its pharmaceutical formulation. The method was validated statistically and recovery study was performed to confirm the accuracy of the method. The method was found to be rapid, simple, accurate and precise.

Key words: Atorvastatin, Simultaneous equation, Spectrophotometry, Telmisartan.

INTRODUCTION

Telmisartan (TEL), 4'-[(1,4'-dimethyl-2'-propyl[2,6'-bi-1H benzimidazol]-1'-yl) methyl]-[1,1'-biphenyl]-2-carboxylic acid[1] is highly selective, non-peptide angiotensin II type 1 (AT1)-

receptor antagonist, that lowers blood pressure through blockade of the renin–angiotensin–aldosterone system (RAAS) and widely used in treatment of hypertension[2]. Literature survey reveals, few spectroscopic methods have been reported for determination of TEL as single drug or in combination with other drugs[3-4]. HPLC and HPTLC methods have also been reported for estimation of TEL in pharmaceutical dosage forms[5-7]. Atorvastatin (ATV), [*R*-(*R**,*R**)]-2-(4-fluorophenyl)-β, dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenyl amino) carbonyl]- 1*H*-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate[8] is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate-limiting step in cholesterol biosynthesis. Atorvastatin is indicated to reduce the risk of myocardial infarction, stroke and reduce the risk for revascularization procedures and angina[9]. Literature survey reveals, few spectroscopic methods have been reported for determination of ATV as single drug or in combination with other drugs[10-12]. Also some HPLC and HPTLC methods have been reported for estimation of ATV in pharmaceutical dosage forms[13-15].

Extensive literature survey reveals, none of the method is available that is based on estimation of Telmisartan and Atorvastatin Calcium by simultaneous equation method. Aim of present work was to develop simple, precise, accurate and economical spectrophotometric methods for simultaneous determination of binary drug formulation. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines[16].

MATERIALS

Spectrophotometric analysis was carried out on double beam spectrophotometer (Systronic 2201) with a fixed slit width (3 nm) using a pair of 1 cm matched quartz cells. The software system of the instrument was used for obtaining the spectra. Drug solutions were sonicated on ultrasonicator (Innertech). Pure drug samples of TEL and ATV were kindly gifted by Dr. Reddy's Laboratory, Mumbai. Methanol was procured from Merck Chemical Corporation, Mumbai.

Commercial pharmaceutical preparation (Telsartan- ATR, Dr. Reddy's Lab, Hyderabad) was procured from commercial source. All the reagents used were of analytical grade.

METHOD

1. Study of overlain spectra and selection of wavelength

TEL and ATV, 50 mg each, were accurately weighed and dissolved separately in 50 ml methanol. From the above solutions 5 ml were diluted separately to 50 ml with methanol to produce 100 µg/ml each of TEL and ATV. Suitable aliquots of these stock solutions of TEL and ATV were diluted with methanol to obtain 5-30 µg/ml of TEL and ATV separately. Absorbances of the above dilutions were determined [Table 1]. Calibration curves were plotted as concentration vs. absorbance [Figure 1-2]. From the overlain spectra [Figure 3] two wave lengths, 296.0 nm and 247.0 nm were selected and absorptivity values E (1%, 1cm) of both the drugs at both wavelengths were determined for formation of simultaneous equation.

$C_1 = (A_2ay_1 – A_1ay_2) / (ax_2ay_1 - ax_1ay_2)$ ---------- (1)

$C_2 = (A_1ax_2 – A_2ax_1) / (ax_2ay_1 - ax_1ay_2)$ ---------- (2)

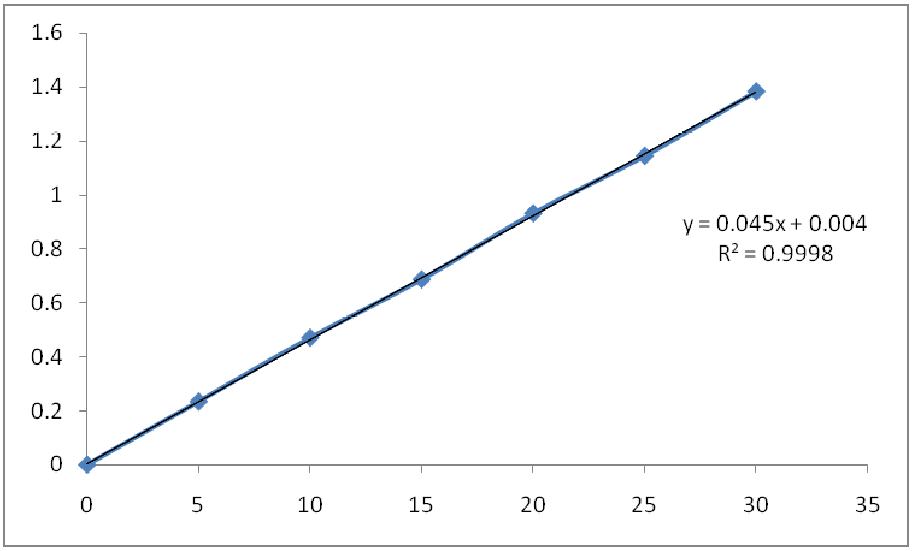

Fig 1. Showing Calibration Curve of TEL

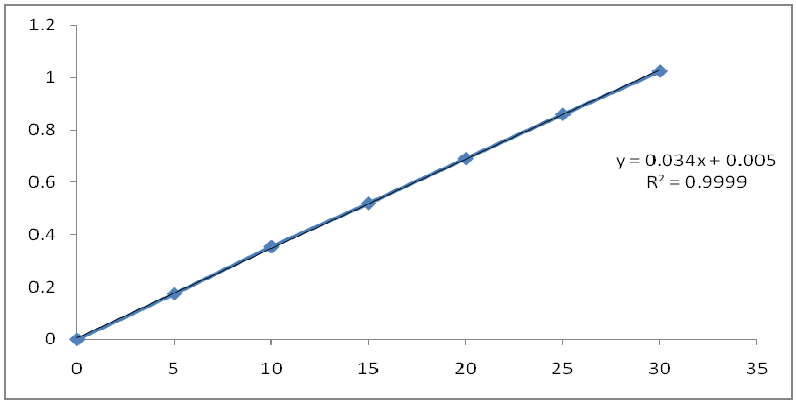

Fig 2. Showing Calibration Curve of ATV

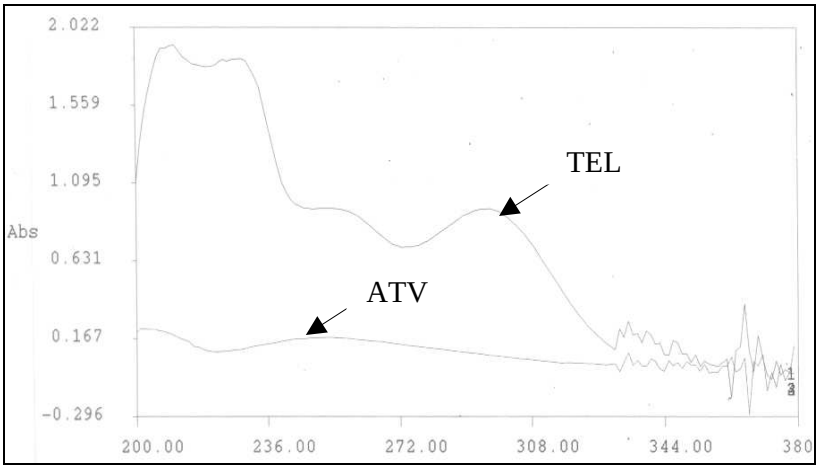

Fig 3. Showing Overlain Spectra of TEL and ATV

Table 1. Linearity Study of TEL and ATV

Sr. No.	Conc. of TEL [µg/ml]	Absorbance mean ± S.D. [n=5]	% R.S.D.	Conc. of ATV [µg/ml]	Absorbance mean ± S.D. [n=5]	% R.S.D.
1	5	0.2342 ± 0.00319	1.3638	5	0.1734 ± 0.00261	1.5040
2	10	0.4702 ± 0.00259	0.5504	10	0.3532 ± 0.00217	0.6138
3	15	0.6862 ± 0.00259	0.3771	15	0.5192 ± 0.00164	0.3164
4	20	0.9308 ± 0.00130	0.1401	20	0.6902 ± 0.00130	0.1889
5	25	1.1436 ± 0.00351	0.3067	25	0.8588 ± 0.00249	0.2899
6	30	1.3820 ± 0.00791	0.5721	30	1.0232 ± 0.00377	0.3683

2. Analysis of laboratory mixture

Accurately weighed 40 mg of TEL and 10 mg of ATV were transferred to 100 ml volumetric flask, dissolved in methanol and volume was adjusted up to the mark with same solvent. Appropriate aliquot 0.5 ml was transferred to 10 ml volumetric flask and volume was adjusted up to the mark with same solvent to get concentration 20 µg/ml of TEL and 5 µg/ml of ATV. The absorbances of solutions were recorded at 247.0 nm and 296.0 nm against blank. Concentration of each drug was obtained by solving the simultaneous equation [Table 2].

Table 2. Results of Analysis of Laboratory Mixture (TEL: ATV, 20: 5)

Amount taken TEL [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
20	20.05	100.26
20	20.01	100.01
20	20.03	100.15
20	19.96	99.88
20	20.05	100.26
Mean ± S.D.	20.02 ± 0.03742	100.11 ± 0.1654
% R.S.D.	0.1869	0.1652
Amount taken ATV [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
5	4.96	99.08
5	4.95	99.02
5	4.95	99.05
5	5.00	100.06
5	4.96	99.08
Mean ± S.D.	4.96 ± 0.0207	99.23 ± 0.4490
% R.S.D.	0.4173	0.4525

3. Application of proposed method for analysis of tablet formulation

Twenty tablets **'Telsartan ATR'** (containing 40 mg of TEL and 10 mg of ATV**)** were weighed and ground to fine powder. A quantity of sample equivalent to 40 mg of Telmisartan and

10 mg of Atorvastatin was transferred into 100 ml volumetric flask containing methanol, sonicated for 10 min; the volume was made up to the mark and filtered through Whatmann filter paper (no. 41). An appropriate volume of this solution was transferred to 10 ml volumetric flask, dissolved and volume was adjusted to mark. The absorbances of the solutions were measured at 247.0 nm and 296.0 nm against blank. Concentration of each drug was obtained by solving the simultaneous equation [Table 3].

Table 3. Application of Proposed Method for Analysis of Tablet Formulation

Amount taken TEL [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
20	19.96	99.88
20	19.92	99.60
20	20.02	100.10
20	20.03	100.15
20	20.07	100.36
Mean ± S.D.	20.00 ± 0.05958	100.02 ± 0.2893
% R.S.D.	0.2979	0.2892
Amount taken ATV [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
5	5.00	100.06
5	4.96	99.15
5	4.91	98.14
5	4.95	99.05
5	4.96	99.12
Mean ± S.D.	4.96 ± 0.03209	99.10 ± 0.6798
% R.S.D.	0.6470	0.6860

4. Validation of proposed method

The method was validated in terms of accuracy, precision and ruggedness.

4.1 Accuracy: To assess the accuracy of proposed method, recovery experiment was performed. To the preanalyzed sample solution of TEL and ATV, a known amount of standard drug solution was added that is 2 µg/ml and absorbance were recorded. The % recovery was then calculated [Table 4].

Table 4. Results of Recovery Studies

Drug	Initial amount [µg/ml]	Amount added [µg/ml] [n=3]	% Drug recovered	% R.S.D.
	20	0	100.10	0.1953
	20	2	100.84	0.6556
TEL	20	2	100.85	0.6498
	20	2	101.09	1.0852
	5	0	99.40	0.5782
	5	2	101.98	0.1614
ATV	5	2	102.01	0.2094
	5	2	101.99	0.1558

4.2 Precision

Precision of the method was assessed by repeatability; determined by analyzing 20 µg/ml of TEL and 5 µg/ml ATV of drug solutions for five times; results were recorded [Table 5]. Method precision was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing TEL and ATV in the concentration range of 10, 15 and 20 µg/ml for three times in the same day. Inter-day precision was determined by analyzing the same concentration of solutions daily for three days, results were recorded [Table 6].

Table 5. Results of Intra-day and Inter-day Precision

Drug	Concentration [µg/ml]	Intra-day amount found [µg/ml] [n=3]	% R.S.D.	Inter-day amount found [µg/ml] [n=3]	% R.S.D.
	10	9.85 ± 0.0208	0.2114	09.92 ± 0.0361	0.3639
TEL	15	15.24 ± 0.0404	0.2652	15.08 ± 0.0306	0.2029
	20	20.00 ± 0.0346	0.1732	19.95 ± 0.0116	0.0581
	10	10.11 ± 0.0452	0.4471	10.03 ± 0.0231	0.2303
ATV	15	14.79 ± 0.0117	0.0791	14.84 ± 0.1212	0.8167
	20	19.99 ± 0.0173	0.0865	20.06 ± 0.0551	0.2748

Table 6. Results of Repeatability Studies

Drug	Amount taken [µg/ml]	Amount found [µg/ml] [n=5]	% R.S.D.
TEL	20	20.04 ± 0.0460	0.2295
ATV	5	4.95 ± 0.0286	0.5778

4.3 Ruggedness

Ruggedness of the method was determined by analysis of aliquots from homogeneous slot by two analyst using same operational and environmental conditions [Table 7].

Table 7. Results of Ruggedness Studies

Drug	Amount taken [µg/ml]	Analyst I [n=3]	% R.S.D.	Analyst II [n=3]	% R.S.D.
TEL	20	100.31 ± 0.2488	0.2480	100.17 ± 0.2532	0.2528
ATV	5	98.80 ± 0.4727	0.4784	100.17 ± 0.5546	0.5537

RESULTS AND DISCUSSION

In this simultaneous equation method, the overlain spectra of drugs showed the λ_{max} of 296.0 nm and 247.0 nm for TEL and ATV respectively. Both the drugs obeyed linearity range 5-30 µg/ml and correlation coefficient (r^2) were found to be <1 in both cases. The absorptivity values were calculated and along with absorbances, these values were submitted in equation (1) and (2) to obtain concentration of drugs. The percentage purity of drugs in binary mixture was found to be 100.11 ± 0.1654 % for TEL and 99.23 ± 0.4490 % for ATV. The percentage purity of drugs in combined dosage form was found to be 100.02 ± 0.2893 % for TEL and 99.10 ± 0.6798 % for ATV. The accuracy of the method was determined by performing recovery study by standard addition method. The % recoveries were found near to 100 for both drugs. The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The

method was found to be precise as % RSD for intra-day and inter-day precision were found to be <2. The method was found to be rugged as the percentage purity of the drugs determined by two different analysts were 100.31 ± 0.2488 for TEL, 98.80 ± 0.4727 for ATV and 100.17 ± 0.2532 for TEL, 100.17 ± 0.5546 for ATV.

CONCLUSION

The proposed method for simultaneous determination of TEL and ATV is a suitable technique for reliable analysis of the commercial formulation containing combination of these drugs and may be successfully applied in control laboratories for their determination in combined dosage form. The results of validation showed that the proposed method is simple, linear, accurate and precise and it can be employed in routine assay of TEL and ATV in combined dosage form.

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