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SIMULTANEOUS DETERMINATION OF ATORVASTATIN CALCIUM AND TELMISARTAN IN TABLET DOSAGE FORM BY SPECTROPHOTOMETRY

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ABSTRACT: Three accurate, precise, sensitive and economical procedures for simultaneous estimation of Atorvastatin Calcium and Telmisartan in tablet dosage form have been developed. The methods employed were absorbance correction method (I), first order derivative spectroscopic method (II) and duel wavelength method (III). The first method employs wavelength 328 nm for direct estimation of Telmisartan where Atorvastatin Calcium shows nil absorbance. Estimation of Atorvastatin Calcium is carried out after correction for absorbance of Telmisartan at 241 nm. The second method is based on first order derivative spectroscopy. Wavelengths 297 nm and 241.8 nm were selected for the estimation of the Atorvastatin Calcium and Telmisartan, respectively. In the third method, Atorvastatin Calcium was determined by plotting the difference in absorbance at 258 and 291 nm (difference is zero for Telmisartan) against the concentration of Atorvastatin Calcium. Similarly for the determination of Telmisartan, the difference in absorbance at 225 and 252 nm (difference is zero for atorvastatin calcium) was plotted against the concentration of Telmisartan. Both the drugs obey Beer's law in the concentration range 5-30 μg/ml. The results of analysis have been validated statistically and by recovery studies.
KEY WORDS: Atorvastatin Calcium, Telmisartan, Absorbance correction Method, First order derivative spectroscopic method, Duel wavelength method.

INTRODUCTION

Atorvastatin calcium (ATV), (βR,dR)-2-(4-fluorophenyl)-β,d-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-lH-pyrrole-1-heptanoic acid, calcium salt, is a synthetic cholesterol-lowering agent[1]. Literature survey reveals spectroscopic method for determination of ATV in combination with amlodipine besylate[2]. HPTLC methods have been reported for estimation of ATV in biological sample as a single drug[3] and in pharmaceutical sample in combination with ezetimibe[4].

Telmisartan (TEL) is described chemically as 4[(1, 4-dimethyl-2-propyl (2, 6-bi-1H-benzimidazol]-1-yl) methyl] [1, 1-biphenyl]-2-carboxylic acid[5]. TEL is useful in the treatment of mild to moderate hypertension[6]. Few spectrophotometric methods have been reported for estimation of TEL in pharmaceutical dosage form as a single drug or in combination with other drugs[6-7]. HPTLC methods are also reported for the determination of TEL in formulation[8,9].

Extensive literature survey reveals that no spectrophotometric method is available for simultaneous determination of Atorvastatin Calcium and Telmisartan in combined tablet dosage form. 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.[10]

EXPERIMENTAL

INSTRUMENTATION:

The instrument used in the present study was JASCO double beam UV/Visible spectrophotometer (Model UV-550) with slit width fixed at 2 nm. All weighing was done on electronic balance (Model Shimadzu AY -120).

REAGENTS AND CHEMICALS:

Analytically pure sample of ATV was kindly supplied by Hetero Drugs Ltd. (HP, India) and that of TEL was supplied by Glenmark Pharmaceuticals Ltd. (Nasik, India) used as such without further purification. The pharmaceutical dosage form used in this study was Tele Act ST 20 film coated tablets (Hetero Drugs Ltd. HP, India) labeled to contain Telmisartan 20 mg and Atorvastatin Calcium equivalent to Atorvastatin 10 mg per tablet.

THEORY

ABSORBANCE CORRECTION METHOD (METHOD I):

In this method two wavelengths in the zero order spectra (Fig. 1) were selected such that one of the drugs shows practically nil absorbance at the detection wavelength of the other drug. While other wavelength selected where both the drugs have considerable absorbance. At detection wavelength 328 nm (λ_1), ATV has practically nil absorbance so used for direct determination of TEL. The other wavelength selected was 241 nm (λ_2, λmax of ATV) where ATV was estimated after correction for absorbance of TEL at this wavelength. The equations obtained for the determination of drugs concentration are

$C_{TEL} = A_{328} / 10.67$ .... (1)
$C_{ATV} = A_{241} - (58.41 \times C_{TEL}) / 31.13$ ....(2)

FIRST ORDER DERIVATIVE SPECTROSCOPIC METHOD (METHOD II):

This method is based on first order derivative spectroscopy to overcome spectral interference from other drug. First order derivative spectra of both the drugs were recorded (Fig. 2). It was observed that TEL showed $dA/d\lambda$ zero at 297 nm in contrast to ATV that has considerable $dA/d\lambda$ at this wavelength. Further, ATV has zero $dA/d\lambda$ at 241.8 nm while at this wavelength TEL has significant $dA/d\lambda$. Therefore these two wavelengths were employed for the estimation of TEL and ATV without any interference. The calibration curves were plotted at these two wavelengths of concentrations against $dA/d\lambda$ within the above mentioned range. The equations of line obtained to determine concentration of TEL and ATV are as follows:

$C_{TEL} = (dA/d\lambda_{241.8} + 0.0007) / 0.0034$ .... (3)
$C_{ATV} = (dA/d\lambda_{297} - 0.0002) / 0.0006$ .... (4)

DUEL WAVELENGTH METHOD (III):

In this method difference in absorbance at two selected wavelengths is calculated. The difference in absorbance at 258 and 291 nm was found to be zero for TEL. Hence these two wavelengths were selected for the determination of ATV. Similarly, 225 and 252 nm were selected for the determination of TEL, where the difference in absorbance was found to be zero for ATV. Zero order spectra was recorded for solutions of different concentration of ATV and TEL between 200-400 nm. The difference in absorbances at 258 and 291 nm were

plotted against the concentration of ATV and that 225 and 252 nm were plotted against the concentration of TEL to construct two separate calibration curves for ATV and TEL. The equations of line obtained to determine concentrations of TEL and ATV are as follows:

$C_{ATV} = (A_{258-291} - 0.0043) / 0.0121$ ......(5)
$C_{TEL} = (A_{225-252} - 0.0809) / 0.0337$ .....(6)

PREPARATION OF STANDARD STOCK SOLUTIONS:

Standard stock solutions were prepared by dissolving separately 10 mg of each drug in 20 ml of methanol to get concentration of 0.5 mg/ml. 0.1 ml of the stock solution was further diluted to 10 ml with distilled water to get a working standard solution of concentration 5 μg/ml of both TEL and ATV. All the dilutions were scanned in the wavelength range of 200-400 nm

PREPARATION OF SAMPLE STOCK SOLUTION:

Contents of twenty tablets were weighed accurately and powdered. Powder equivalent to 10 mg of ATV was weighed and dissolved in 10 ml of methanol with the aid of ultrasonication for 5 min. The solution was filtered through Whatman filter paper no. 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 linear range. This solution was scanned in wavelength range 200-400 nm. Six replicate analysis was carried out on powdered homogenous sample.

RESULTS AND DISCUSSION

Under the experimental conditions described calibration curve, assay of tablets and recovery studies were performed. Both the drugs obey Beer's law within the concentration range of 5-30 μg/ml. The proposed method was also evaluated by the assay (n = 6) of commercially available tablets containing TEL and ATV. The results of assay are presented in Table 1. The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to preanalyzed sample solution at three different concentration levels within the range of linearity for both the drugs. Results of recovery studies are shown in Table 2. The accuracy and reproducibility is evident from the data as results are close to 100 % and low standard deviation. The proposed methods are simple, economical, rapid, precise and accurate. Hence these can be used for routine analysis of TEL and ATV in tablet formulation.

CONCLUSION

The validated spectrophotometric methods employed here proved to be simple, economical, rapid, precise and accurate. Thus these can be used for routine simultaneous determination of TEL and ATV in tablet dosage form instead of processing and analyzing each drug separately.

Table 1: Results of commercial formulation analysis

Method	Label Claim (mg/TAB)	% Label Claim estimated* (Mean ± S.D)	% R. S. D.
I	ATV-10	100.03 ± 0.750	0.750
	TEL-20	98.80 ± 0.700	0.708
II	ATV-10	99.40 ± 1.002	1.008
	TEL-20	99.40 ± 1.212	1.219
III	ATV-10	100.16 ± 1.644	1.641
	TEL-20	99.83 ± 0.404	0.408

*Mean of six determinations, R.S.D. is relative standard deviation

Table 2: Recovery studies of TEL and ATV

Drug	Conc. of drug added		% Recovery * (Mean ± S.D)		
	μg /ml	% Level	Method I	Method II	Method III
ATV	5	50	99.55 ± 0.660	99.00 ± 1.380	99.11 ± 1.145
	10	100	99.50 ± 0.480	99.64 ± 1.001	99.99 ± 1.522
	15	150	99.41 ± 0.367	99.98 ± 0.897	100.60 ± 1.366
TEL	5	50	101.09 ±1.144	100.38 ± 0.644	99.57 ± 0.755
	10	100	101.27 ± 0.886	99.74 ± 0.932	98.78 ± 0.549
	15	150	100.42 ± 0.698	100.54 ± 0.659	100.30 ± 0.643

*Avg. of three determinations

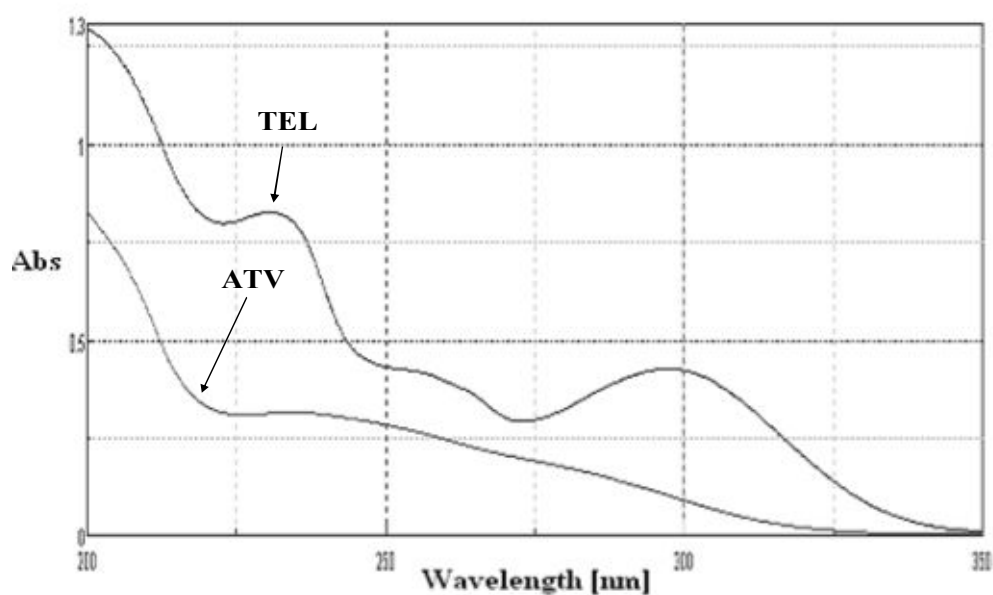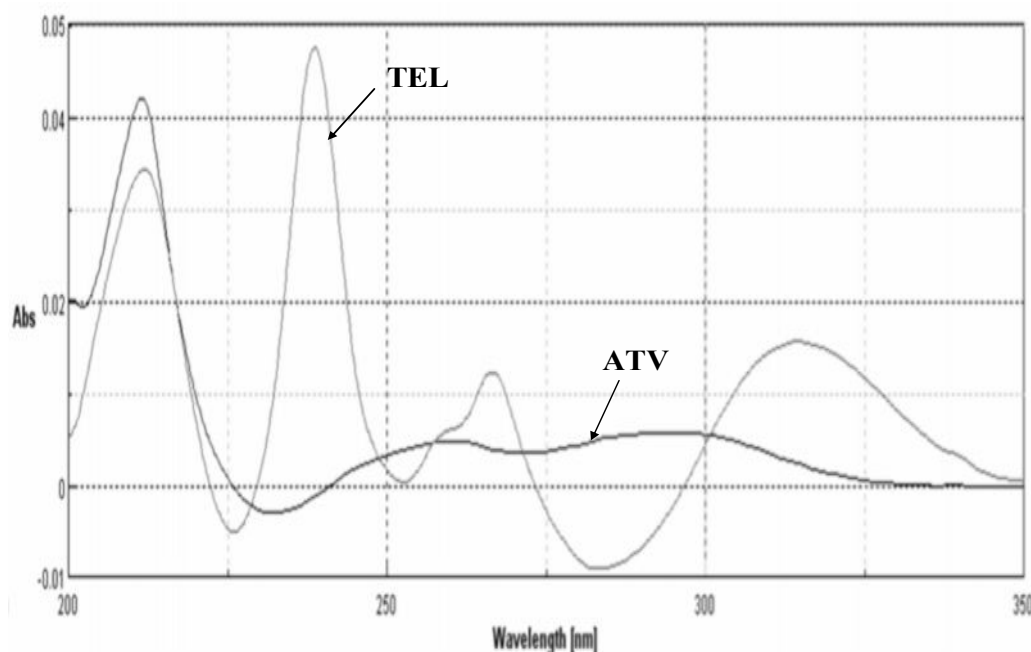**Fig. 1:. Zero order overlain spectra of TEL (10 μg/ml) and ATV (10 μg/ml)**

Fig. 2: First order derivative overlain spectra of TEL (10 µg/ml) and ATV (10 µg/ml)

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