

Simultaneous spectrophotometric estimation of Atorvastatin calcium and fenofibrate in tablet dosage form

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ABSTRACT

Two analytical methods have been developed for simultaneous quantification of atorvastatin calcium and fenofibrate from combined pharmaceutical dosage form using spectrophotometer. Excellent simplicity, accuracy, precision and economy were achieved. The 'method I' is based upon 'Q-absorbance' whereas the 'method II' is based upon multicomponent mode of analysis of instrument. In methanol, atorvastatin calcium showed maximum absorbance at 245 nm and fenofibrate at 287 nm. Iso-absorptive point for both drugs was found to be 258 nm. Linearity lies in the concentration range 2 - 20 µg/ml for both drugs at their respective wavelength. The methods were validated statistically and by recovery studies.

Key words: Atorvastatin calcium, Fenofibrate, Spectrophotometry, Q-absorbance analysis, Multicomponent mode of analysis

INTRODUCTION

Atorvastatin calcium(ATV), (âR,âR)-2-(4-fluorophenyl)-â,â-dihydroxy-5-(1-methylethyl)-3-phenyl-4- [(phenylamino)carbonyl]-1H- pyrrole-1-heptanoic acid calcium is a competitive inhibitor of HMG-CoA reductase¹. Fenofibrate (FNB), chemically is 1-methylethyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate². In literature, few Spectrophotometric³, HPLC^{4,5}, HPTLC⁶ methods have been reported for estimation of ATV and FNB alone and in combination with other drugs.

This paper describes two simple, rapid and economical Spectrophotometric methods for the simultaneous determination of both drugs in combined dosage form using 'Q-absorbance method' and 'multicomponent mode of analysis'. Both the methods were compared with reported derivative spectrophotometric method⁷.

EXPERIMENTAL

Preparation of standard stock solution and selection of wavelength

The standard stock solutions 100 µg/ml for ATV and FNB were prepared separately in methanol. From these stock solutions, appropriate dilutions were made in double reverse osmosis (R.O.) water and scanned on Spectrophotometer (Shimadzu - 2450 with UV probe 2.21 software) in the UV range 400 - 200 nm. ATV and FNB showed absorbance maxima at 245 nm and 287 nm, respectively. Linearity was observed in the concentration range 2- 20 µg/ml for both the drugs at their respective wavelengths.

Method I: Q-absorbance method

From the overlain spectra of ATV and FNB; two wavelengths 258 nm (iso-absorptive point) for both drugs and 287 nm (λ_{max} FNB) were selected.

The E (1%, 1cm) of both drugs at 258 nm and 287 nm wavelengths were determined; results are presented in table I. The concentration of two drugs in the sample solutions can be calculated by using equations;

$$C_{ATV} = Q_M - Q_Y / Q_X - Q_Y \times A_1 / a_{X1} \quad \dots(1)$$

$$\dots(2)$$

Where, A_1 and A_2 are the absorbances of the sample solution at selected wavelength i.e. 258 nm and 287 nm, respectively. $Q_M = A_2 / A_1$, $Q_Y = aY_2 / aY_1$, $Q_X = aX_2 / aX_1$

Multicomponent mode of analysis

From the standard stock solutions, six mixed standard solutions of ATV and FNB in the ratio 20:0, 0:20, 4:4, 8:8, 12:12, 16:16 ($\mu\text{g/ml}$) were prepared. All the mixed standard solutions were scanned on Spectrophotometer (Shimadzu -1700) over the range 400 - 200 nm, in the multicomponent mode using two sampling wavelength 245 (λ_{max} of ATV) and 287nm (λ_{max} of FNB). The spectral data from these scans were used to determine the concentration of two drugs in tablet sample solutions.

Preparation and analysis of tablet formulations

Twenty tablets were accurately weighed; average weight determined and ground to fine powder. An accurately weighed quantity of powder equivalent to 10 mg Atorvastatin and 160 mg of fenofibrate was transferred into 100 ml volumetric flask containing 40 ml methanol. To it 150 mg atorvastatin calcium bulk powder was added and shaken manually for 15 min, volume was adjusted to mark with same solvent and filtered through Whatmann filter paper no. 41. After appropriate dilutions, absorbance of the sample solution in 'method I' were recorded at 258 nm and 287 nm; the amount of ATV and FNB was determined using equation I and II.

While in 'method II', the above mentioned solutions were scanned in multicomponent mode of instrument over the range 400 - 200 nm and concentrations of both the drugs were determined by analysis of spectral data of the sample solutions with reference to mixed standards. Also, the same sample solutions were analysed by reported derivative spectrophotometric method. The results

are summarized in table 2.

$$C_{FNB} = Q_M - Q_X / Q_Y - Q_X \times A_2 / a_{Y1}$$

Table 1: E (1%, 1cm) values for ATV and FNB

Wavelength	258 nm		287 nm	
	ATV	FNB	ATV	FNB
*Mean \pm SD	ax1= 448.16 \pm 0.811	ay1=447.91 \pm 0.676	ax2=239.12 \pm 0.68	ay2=554.75 \pm 1.668

*mean of six estimations

Table 2: Analysis of tablet formulation

Drugs	Method I (*Amount found \pm SD)	Method II (*Amount found \pm SD)	Reported method (*Amount found \pm SD)
ATV	99.87 \pm 0.418	100.51 \pm 0.0609	98.49 \pm 0.406
FNB	100.064 \pm 0.728	99.81 \pm 0.04105	98.64 \pm 0.341

*mean of five estimations

RESULTS AND DISCUSSION

In methanol, ATV showed maximum absorbance at 245 nm and FNB at 287 nm. The iso-absorptive point for both the drugs was found to be 258 nm. Linearity was observed in the range 2 - 20 µg/ml ($r^2 = 0.9998$) for ATV and 2 - 20 µg/ml ($r^2 = 0.9999$) for FNB at their respective wavelengths. Amount of drugs estimated by the proposed methods was in good agreement with label claimed. The results of drug estimated by the proposed methods were compared with reported

derivative spectrophotometric method and found to be satisfactory. The proposed methods were validated for accuracy, precision and ruggedness as per USP⁸. Accuracy of the methods was assessed by recovery studies and carried out by adding standard drug solutions (2 µg/ml) to preanalysed sample solutions. Precision of the methods were studied as intra-day, inter-day and repeatability. Results of validation parameters demonstrates that the methods are accurate, precise and reproducible (relative standard deviation < 2%). The results did not show any statistical

Table 3: Results of recovery, precision and ruggedness data

Parameters	Method I		Method II	
	ATV	FNB	ATV	FNB
% Recovery	99.86	100.57	100.91	100.41
%RSD	0.40	0.812	0.515	0.626
Precision [%RSD]				
Intra-day (n = 3)	0.435 - 0.630	0.315 - 0.477	0.521 -1.059	0.109 -1.022
Inter-day (n = 3)	0.299 - 0.690	0.454 - 0.722	0.0630 - 1.344	0.188 - 0.657
Repeatability (n = 5)	0.858	0.794	0.839	1.433
Ruggedness [%RSD]				
Analyst I (n = 3)	0.277	0.188	0.921	0.197
Analyst II (n = 3)	0.212	0.187	0.832	0.209

difference between operators suggesting that method developed were rugged. The results from accuracy, precision and ruggedness are shown in table 3. Both these methods are simple, rapid, and accurate and can be used for routine analysis of ATV and FNB in tablet formulations.

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