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Spectrophotometric method for Simultaneous estimation of Atorvastatin Calcium & Fenofibrate in tablet Dosage Form

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Abstract

A UV spectrophotometric method was developed for the estimation of atorvastatin calcium & fenofibrate in tablet dosage form by using simultaneous equation method. The drug obeyed Beer's law & showed good correlation near to 0.999. Absorption maxima of atorvastatin calcium & fenofibrate were found to be at 246 and 286 nm respectively. Beer's law was obeyed in concentration rang of 1-10 µg/ml for atorvastatin calcium & 2-20 µg/ml for fenofibrate. The method has been validated for linearity, accuracy & precision. The recovery was more than 99%. The developed method was found to be accurate, simple, precise, economical, and selective for simultaneous estimation of atorvastatin calcium & fenofibrate in tablet dosage form.

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***Key words*:**
Simultaneous determination, atorvastatin calcium, fenofibrate, development and validation.

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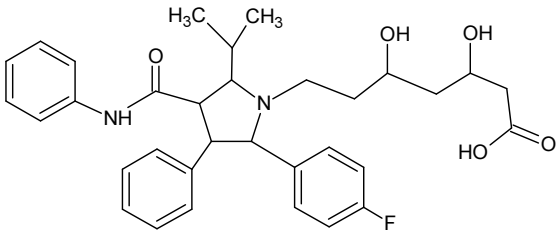
INTRODUCTION

Atorvastatin calcium (β R, δ R)-2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-(phenyl amino) carbonyl)-1 H-pyrrole-1-hepatonic acid as the calcium salt belongs to the group of statins[1]. All the statins, including atorvastatin reduce the production of cholesterol in the liver by the competitive inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase the rate limiting enzyme in the biosynthesis of cholesterol[2]. Fenofibrate is 2-[4-(4-chlorobenzoyl) phenoxy]-2-methyl-propanoic

acid, 1-methylethyl ester[3]. It is indicated for the treatment of hypercholesterolemia and mixed dyslipidemia[2]. Tablet containing 10 mg of atorvastatin calcium and 160 mg of fenofibrate is available. (Atorlip-F) The literature survey revealed some HPLC methods[4-12] & spectrophotometric[13-15]. methods for determination of atorvastatin calcium and fenofibrate individually and in combination with other drugs. The present work describes the development of simple, precise, and accurate UV spectrometric method for simultaneous estimation of atorvastatin calcium and fenofibrate in tablet by using Simultaneous equation.

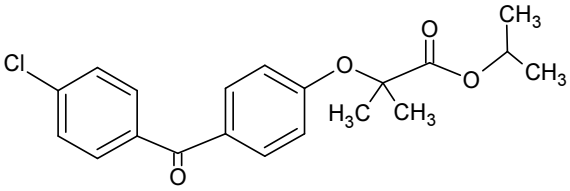
STRUCTURES:

Atorvastatin calcium:



$.Ca^{2} .3H_2O$

Fenofibrate:



MATERIALS AND METHODS:

Materials:

Spectral runs were made on a Shimadzu UV-Visible spectrophotometer, model- 1700 (Japan) was employed with spectral bandwidth of 0.5 nm and wavelength accuracy of ± 0.3 nm with automatic wavelength corrections with a pair of 10 mm quartz cells. Glassware used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven.

The drug sample, atorvastatin calcium and fenofibrate were obtained as gift samples from the Emcure Pharmaceuticals Ltd, Pune. The pharmaceutical preparation that is Atorolip-F manufactured by Cipla Ltd. was used. Methanol is used as a solvent. All the solutions were protected for light and were analyzed on the day of preparations.

Selection of common solvent:

Methanol of analytical reagent grade was selected as common solvent for developing spectral characteristics of drug. The selection was made after assessing the solubility of both the drugs in different solvents.

Standard stock solution of atorvastatin calcium:

An accurately weighed quantity of about 10 mg of atorvastatin calcium was taken in 100 ml volumetric flask dissolved in sufficient quantity of methanol then sonicated for 15 min and diluted to 100 ml with the same solvent so as to get the concentration of 100 µg/ml.

Standard stock solution of fenofibrate

An accurately weighed quantity of about 10 mg of fenofibrate was taken in 100 ml volumetric flask dissolved in sufficient quantity of methanol then sonicated for 15 min and diluted up to 100 ml with the same solvent so as to get the concentration of 100 µg/ml.

Preparation of mix standard Stock Solution:

From the standard stock solutions, the standard solutions were further diluted to contain a mixture of 2 µg/ml of atorvastatin calcium and 32 µg/ml of fenofibrate. Estimation of atorvastatin calcium and fenofibrate is done by simultaneous equation method.

Preparation of stock solution of tablet formulation:

Twenty tablets of Atorlip-F containing 10 mg of atorvastatin calcium and 160 mg of fenofibrate were weighed and finely powdered separately. Powder equivalent to 10 mg of atorvastatin calcium and 160 mg of fenofibrate was weighed and transferred to a volumetric flask in methanol, and then final volume

of the solution was made up to 100 ml with methanol to get a stock solution containing 100 µg/ml of atorvastatin calcium and 1600 µg/ml fenofibrate, and further dilutions were made to get a concentration of 1µgm/ml of atorvastatin calcium and 16 µg/ml of fenofibrate. The contents were mixed thoroughly and filtered through a 0.45 µ membrane filter.

Simultaneous Equation Method:-

Two wavelengths selected for the method are 246 nm and 286 nm that are absorption maxima of atorvastatin calcium and fenofibrate in methanol respectively. The stock solutions of both the drugs were further diluted with methanol to get a series of standard solutions of 1-10 µg/mL concentrations of atorvastatin calcium and 2-20 µg/mL concentrations of fenofibrate. The absorbance was measured at the selected wavelengths and concentrations in the sample were obtained by using following equations.

$$Cx = \frac{A1\ ay2 - A2\ a\ y1}{ax1ay2 - ax2ay1} \quad \ldots\ldots\ldots \text{Eq. (i)}$$

$$Cy = \frac{A1\ ax2 - A2\ ax1}{ay1ax2 - ay2ax1} \quad \ldots\ldots\ldots \text{Eq. (ii)}$$

Where, A1 and A2 are absorbance of mixture at 246 nm and 286 nm respectively, ax1 and ax2 are absorptivity of atorvastatin calcium at λ_1 and λ_2 respectively and ay1 and ay2 are absorptivity of fenofibrate at λ_1 and λ_2 respectively. Cx and Cy are concentrations atorvastatin calcium & fenofibrate of respectively.

Application of Proposed Method for Determination of atorvastatin calcium & fenofibrate in Tablets:

Marketed tablet formulation containing atorvastatin calcium 10 mg and fenofibrate 160 mg was analyzed. From 20 tablets, an amount equivalent to 10 mg of atorvastatin calcium and 160 mg of fenofibrate was weighed and dissolved in sufficient quantity of methanol to get the concentration of 100 µg/ml of atorvastatin calcium & 1600 µg/ml of fenofibrate. Then the solution was filtered through Whatman filter paper no. 41. Appropriate aliquots of atorvastatin calcium and fenofibrate within the Beer's law limit were taken. The absorbance of resulting solutions was measured at 246 nm and 286 nm. The concentration of atorvastatin calcium and fenofibrate present in the sample solution was calculated by using the equation generated from calibration curve of respective drugs.

Method validation:

The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for the analyte.

Accuracy:

To ascertain the accuracy of the proposed methods, recovery studies were carried at three different levels (80%, 100% and 120%). Percent recovery for atorvastatin calcium and fenofibrate was found in the range of 99.92 -98.99%.

Linearity:

The linearity of measurement was evaluated by analyzing series of different concentration of the standard solution of atorvastatin calcium and fenofibrate. For simultaneous equation method the Beer- Lambert's concentration range was found to be 1-10 µg/ml for atorvastatin calcium and 2-20 µg/ml for fenofibrate.

RESULT AND DISCUSSION:

Table 1: Linear regression analysis of calibration curves with their respective absorptivity values.

Parameter	Atorvastatin calcium	Fenofibrate
Detection of wavelength	246 nm	286 nm
Beer's law limit (µg/ml)	1-16	2-20
Correlation coefficient(r)	0.9996	0.9989
Molar absorptivity (lit/mol/cm)	47237.94	18757.32
Sandell's sensitivity(mcg/Sq.cm/0.001)	0.025604	0.019235
Slope	0.039056	0.0524
Intercept	- 0.001	+ 0.012
LOD	0.0376	0.4183
LOQ	0.1139	1.227

Table 2: Results of analysis of tablet samples.

Name of Drug	Label claim	Amount Found	% label claim	S.D.*	R.S.D.*	%Recovery*
Atorvastatin calcium	10	10.02	99.98	0.09263129	0.09263129	99.96
Fenofibrate	160	158.88	99.18	0.22771815	0.22771815	99.18

* indicates mean of six determinations.

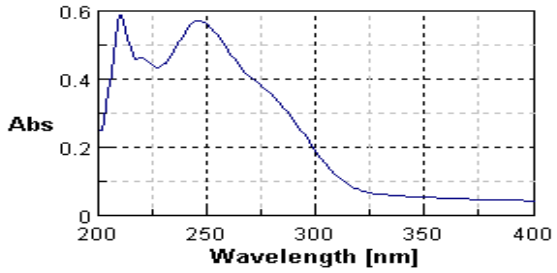


Fig. 1: Absorption spectra of Atorvastatin calcium at 246 nm

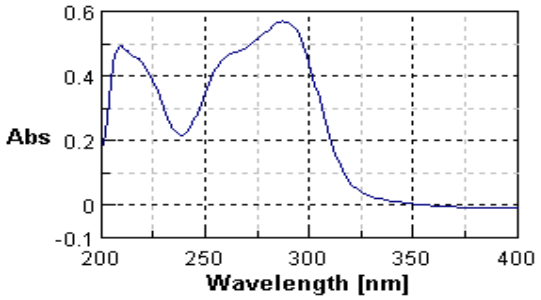


Fig. 2: Absorption spectra of Fenofibrate at 286 nm

- The values of standard deviation are satisfactorily low and recovery was close to 100% indicating reproducibility and accuracy of this method. Recovery studies were satisfactory and showed that there is no interference of excipients.

Method Validation

- Linearity: Linearity of atorvastatin and fenofibrate was observed in the range of 1-10 µg/ml and 2-20 µg/ml at both wavelengths 246 nm and 286 nm for one method. The calibration curve yielded coefficient of correlation (r) near to 0.999.
- Assay results: A tablet dosage form of atorvastatin calcium and fenofibrate in combination was analyzed by simultaneous equation, the percentage in dosage form were determined and found to be 99.92% & 98.99% respectively. Assay results obtained are within limit.
- Accuracy and precision: The low values of S.D and %COV interval indicate that method is precise. % recovery by using simultaneous equation method was found to be within limit indicate the non interference from the formulation excipients and confirm the accuracy and precision of the method.

CONCLUSION:

All above results indicate that, the simultaneous equation method employed here are very simple, accurate, economical, and rapid for routine analysis of atorvastatin calcium and fenofibrate. The recovery was found to be 99.98 % and 99.33% for atorvastatin calcium and fenofibrate respectively indicates reproducibility & accuracy of method.

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