

# SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF ATORVASTATIN AND FENOFIBRATE IN BULK DRUG AND DOSAGE FORM BY USING SIMULTANEOUS EQUATION METHOD

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**Abstract:** Atorvastatin– fenofibrate combination used in the treatment of hypercholesterolemia and hypertriglyceridemia. Various methods for analysis of the same are available but are time consuming and expensive. Here we have developed a new, precise and simple UV spectrophotometric method for estimation of atorvastatin – fenofibrate from tablet formulation. The drug obeyed the Beer's law and showed good correlation. Absorption maxima of atorvastatin and fenofibrate in methanol were found to be at 245nm and 285nm respectively. Beer's law was obeyed in concentration range 8-24 µg/ml for atorvastatin and 2-16 µg/ml for fenofibrate. The results of analysis were validated by recovery studies. The recovery was more than 98%. The method was found to be simple, accurate, precise, economical and robust.

**Keywords:** Atorvastatin, Fenofibrate, Recovery, UV spectrophotometry.

## Introduction and Experimental

Atorvastatin calcium chemically [R-(R, R\*)]-2-(4-fluorophenyl)-β, δ-dihydroxy-5(1-methylethyl)-3-phenyl-4-[phenylamino] carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate, is a synthetic HMG –CoA reductase inhibitor [1]. It has been demonstrated to be efficacious in reducing both cholesterol and triglycerides [2]. The typical dose of Atorvastatin calcium is 10-80 mg per day and it reduces 40-60% LDL [3]. Literature survey revealed that various analytical methods such as HPLC [4, 5], GC-MS [6], LC-MS [7], HPLC-Electrospray tandem mass spectrometry [8] and HPTLC [9] have been reported for estimation of Atorvastatin calcium from its formulations and biological fluids.

Fenofibrate is a drug of the fibrate class. Fenofibrate chemically propan-2-yl 2-{4-[(4-chlorophenyl)-carbonyl]phenoxy}-2-methylpropanoate. It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease. Like other fibrates, it reduces both low-density lipoprotein (LDL) and very low

density lipoprotein (VLDL) levels, as well as increasing high-density lipoprotein (HDL) levels and reducing triglycerides level. It also appears to have a beneficial effect on the insulin resistance featured by the metabolic syndrome. [10] It is used alone or in conjunction with statins in the treatment of hypercholesterolemia and hypertriglyceridemia.

## Apparatus:

Spectral runs were made on a Shimadzu UV-Visible spectrophotometer, model- 1700 (Japan) was employed with spectral bandwidth of 1 nm and wavelength accuracy of ± 0.3 nm with automatic wavelength corrections with a pair of 10 mm quartz cells. Glasswares 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.

**Reagents and Solution:**

All the reagents used in this assay were of analytical grade and the reagent solutions were prepared using preanalysed double distilled water. Atorvastatin and fenofibrate pure drug was obtained as a gift sample from Emcure, Pune. Tablets of atorvastatin and fenofibrate were purchased from local market for analysis. Methanol was used as a solvent for the assay.

**Preparation of Stock solution:**

Accurately 20mg of atorvastatin was weighed in to 200ml of clean and dry volumetric flask and 140ml methanol was added and sonicated for 10 minutes and volume made upto 200ml with methanol.

Accurately about 32mg of fenofibrate was weighed into 200ml clean and dry volumetric flask, 100ml of methanol was added, sonicated for 10 minutes and made volume with methanol.

All solutions were freshly prepared prior to analysis. This stock solution is used for making dilutions for calibration curve.

**Determination of  $\lambda_{\max}$ :**

The standard solutions of 100  $\mu\text{g/ml}$  of atorvastatin calcium and fenofibrate were individually scanned in the range of 200-400nm and the  $\lambda_{\max}$  was determined. The overlain spectrum of both the drugs is also run.

**Preparation of Calibration Curve:**

For each drug appropriate aliquots were pipetted out from standard solution into the series of 10 ml volumetric flask and the volume was made upto the mark with methanol to get concentrations of 8-24  $\mu\text{g/ml}$  ( $n=5$ ) of atorvastatin and 2-16  $\mu\text{g/ml}$  ( $n=8$ ) of fenofibrate. Solutions of different concentrations for each drug were scanned at there respective wavelengths and absorbances are recorded. The calculations done by simultaneous equation method.

**Preparation of mixed standard solution:**

Accurately 20 mg of atorvastatin was weighed into 200 ml clean and dry volumetric flask and 140 ml of methanol is added. It is sonicated for 10 minutes and volume made upto mark with methanol. (Solution A)

Accurately 32 mg of fenofibrate was weighed into 200 ml clean and dry volumetric flask then 10ml of solution A was added using pipette and 100 ml of methanol is added. It is sonicated for 10 minutes and volume made upto mark with methanol. (Mixed Standard)

All solutions were freshly prepared prior to analysis.

**Preparation of tablet formulation for assay:**

Twenty atorvastatin – fenofibrate tablets (10mg atorvastatin and 160 mg fenofibrate) were weighed and powdered. A portion equivalent to 80 mg of fenofibrate was weighed into 100 ml clean and dry volumetric flask, added about 70 ml of methanol and sonicated for 20 minutes and volume made upto the mark with methanol. Mixed well and filtered through Whatman filter paper No. 41. First few ml filtrate discarded and then 10ml of filtrate pipetted out and diluted to 50 ml with mobile phase. Then the absorbances were recorded at the respective wavelengths.

**Recovery Studies:**

Recovery study is carried out by spiking known amount of pure drug into the preanalysed formulations and the proposed method is followed. And the solutions were subjected to analysis.

**Results and Discussion**

The representative calibration curves of atorvastatin and fenofibrate were plotted at 245 nm and 285 nm respectively. The calculation of concentration levels was done by simultaneous equation method. A strict linear relationship was obtained for both the drugs in the concentration range of 8 to 24  $\mu\text{g/ml}$  for atorvastatin and 2 to 16  $\mu\text{g/ml}$  for fenofibrate. The results of analysis by standard addition method showed excellent recovery for both the drugs in the range of 98.16% to 102.63% for atorvastatin and 98.02% to 101.75% for fenofibrate. The results of tablet formulation analysis clearly indicated that none of the excipients interfered in the estimation of the atorvastatin and fenofibrate in the spectrophotometric method.

**Conclusion**

The Spectrophotometry provides versatile techniques for resolving complex spectra and makes it possible to analyse drug in multicomponent pharmaceutical formulation in presence of various interferences. The present work describes simple, economical and non interfering spectrophotometric method for estimation of atorvastatin and fenofibrate using simultaneous equation method. The method was found to be economic, simple, precise, accurate and reproducible during analysis of drug formulations containing the two drugs.

Table 1: Results of analysis of UV method

Parameters	Atorvastatin	Fenofibrate
Detection Wavelength	245nm	285nm
Beer's Law Limit	8-24 $\mu\text{g/ml}$	2-16 $\mu\text{g/ml}$
Accuracy	99.99%	98.79%
Precision	100.10%	99.40%
% Coefficient of Variance	0.671	0.947
Regression Equation Data		
Slope	0.0456	0.0691
Intercept	0.0031	0.0068
Correlation Coefficient	0.9991	0.9996

Table 2: Results of analysis of Tablet formulation

Formulation	Drug	Label Claim (mg)	% Label Claim * (Mean $\pm$ S.D.)	Coefficient of Variance
Tablet	Atorvastatin	10 mg	99.79 $\pm$ 1.78	0.801
	Fenofibrate	160mg	98.67 $\pm$ 1.021	0.943

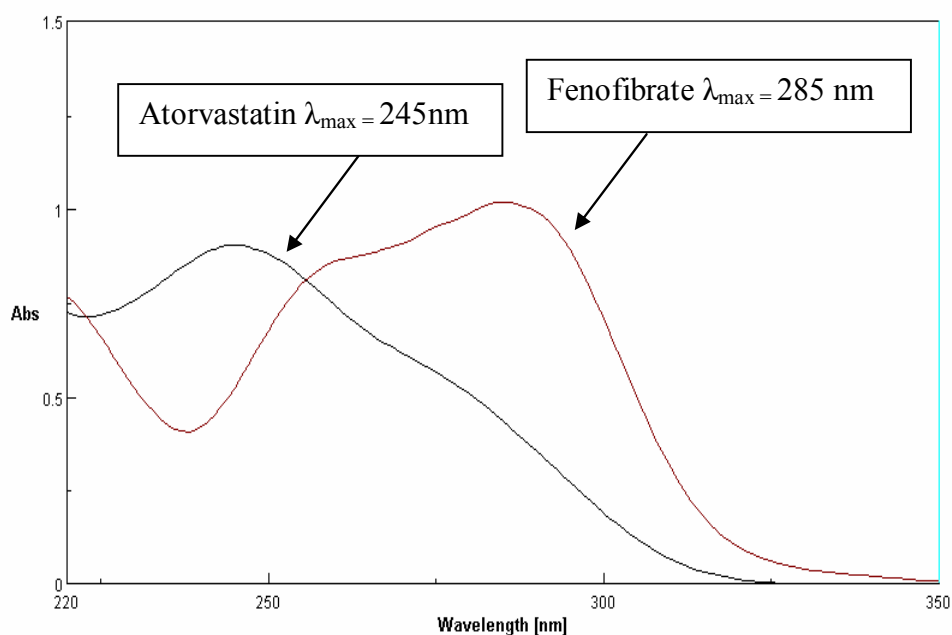
S.D.- Standard Deviation, \*Average of six determinations.

Table 3: Results of recovery studies

Formulation	Drug	Label Claim (mg)	% Recovery estimated* (Mean $\pm$ S.D.)	Coefficient of Variance
Tablet	Atorvastatin	10 mg	99.63 $\pm$ 0.742	0.744
	Fenofibrate	160mg	98.12 $\pm$ 0.738	0.743

S.D. - Standard Deviation, \*Average of six determinations

Figure 1: UV overlain spectra for of Atorvastatin and Fenofibrate



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### References

1. Moffat A.C., Osselton M.D. and Widdop B., Clarke's Analysis of Drugs and Poisons in Pharmaceuticals, body fluids and Postmortem material, 3<sup>rd</sup> Edition., Part 2, The Pharmaceutical Press, Great Britain, 2004, 654.
2. Poswar E.L., Radulovic L.L., Cilla D.D., Whitfield L.R. and Sedman A.J., Tolerance and pharmacokinetics of single-dose atorvastatin, a potent inhibitor of HMG-CoA reductase, in healthy subjects, J. Clin. Pharmacol., 1996, 36, 728.
3. Page, Curtis, Sutter, Walkar and Hoffmann, Integrated Pharmacology 2nd, Mosby International Ltd., 2002, 303
4. Altuntas T.G. and Erk N., Liquid chromatographic determination of Atorvastatin in bulk drugs, tablets and human plasma, J. Liq. Chro., 2004, 27 (1), 83.
5. Gowari S.D., Raju M. S. M., Sumanth K.S. and Latha P. V. M., Estimation of Atorvastatin by high performance liquid chromatography in pure and pharmaceutical dosage form, Asian J. Chem, 2005, 17(4), 2571.
6. McKenney J.M., McCormik L.S., Weis S., Koren M., Kotonek S., and Black D.M., A Randomized Trial of the Effects of Atorvastatin and Niacin in Patients with Combined Hyperlipidemia or Isolated Hypertriglyceridemia, Amer. J. Med., 1998, 104, 137.
7. Black A.E., Sinz M.W., Hayees R.N. and Woolf T.F., metabolism and excretion studies in mouse after single and multiple oral doses of the 3 – hydroxyl-3-methylglutaryl- CoA reductase inhibitor atorvastatin, Drug Metab. Dispos., 1998, 26, 755.
8. Bullen W.W., Miller R.A., Hayes R.N., Development and validation of a high performance liquid chromatography tandem mass spectrometry assay for atorvastatin, orthohydroxy Atorvastatin and para- hydroxy Atorvastatin in human, dog and rat plasma, Amer. Soc. Mass Spectrom., 1999, 10, 55.
9. Yadav S.S., Mhaske D.V., Kakad A.B., Patil B.D., Kadam S.S. and Dhaneshwar S.R., A simple and sensitive HPTLC method for the determination of content uniformity of Atorvastatin calcium tablets, Indian J. Pharm. Sci., 2005, 67(2), 182.
10. Wysocki J., Belowski D., Kalina M., Kochanski L., Okopien B. and Kalina Z., Effects of micronized fenofibrate on insulin resistance in patients with metabolic syndrome, Int. J. Clin. Pharmacol. Ther., 2004, 42 (4), 212–217.

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