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Simultaneous Spectrophotometric Estimation of Fluvastatin and Fenofibrate in Bulk Drug and Dosage Form by using Simultaneous Equation Method

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Abstract
Fluvastatin - fenofibrate combination used in the treatment of hypercholesterolemia and hyper-triglyceridemia. 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 Fluvastatin – Fenofibrate from tablet formulation. The drug obeyed the Beer's law and showed good correlation. Absorption maxima of Fluvastatin and Fenofibrate in methanol were found to be at 304 nm and 288 nm respectively. Beer's law was obeyed in concentration range 8-24 µg/ml for Fluvastatin 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, and robust.

Key words: Fluvastatin, Fenofibrate, UV spectrophotometry

INTRODUCTION

Fluvastatin, new member of a class of cholesterol-lowering[1] drugs commonly referred to as "statins", was approved for the treatment of dyslipidemia [1–3].Fluvastatin(FST) is chemically (3*R*,5*S*,6*E*) -7-[3-(4-fluorophenyl)-1-(propan-2-yl)-1*H*-indol-2-yl] -3,5-dihydroxyhept-6-enoic acid. FST is used to reduce the amounts of LDL cholesterol, total cholesterol, triglycerides and apo lipoprotein[2] B in the blood.

Fenofibrate which is chemically propan-2-yl 2-{4-[(4-chlorophenyl) carbonyl] phenoxy}-2-methyl propanoate. It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease[3]. Like other fibrates[4], it reduces both low-density lipoprotein[5] (LDL) and very low density lipoprotein (VLDL) levels, as well as increasing high-density lipoprotein (HDL) levels and reducing triglycerides[6] level. It also appears to have a beneficial effect on the insulin resistance featured by the metabolic syndrome[7-8].

Only very few HPLC methods have been reported in the literature for the estimation of FEN & FST present in biological fluids[9]. There are no reported methods for the determination of FEN & FST by UV spectrophotometry in pharmaceutical dosage[10] forms. Hence the author has made an attempt to develop a UV spectrophotometry method for the determination of FEN & FST in pharmaceutical formulations[11].

EXPERIMENTAL DETAILS

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 sulphuric acid rinsed with 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. Fluvastatin and Fenofibrate pure drug was obtained as a gift sample from SPARC (sun pharma advance research center). Tablets Fluvastatin 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 Fluvastatin was weighed in to 200ml of clean and dry volumetric flask and 140ml methanol was added and sonicated for 10 minutes and volume made up to 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.

Preparation of mixed standard solution:
Accurately 20 mg of Fluvastatin 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)

Preparation of tablet formulation for assay:
Twenty Fluvastatin – Fenofibrate tablets (150mg Fluvastatin and 200 mg Fenofibrate) were weighed and powdered. A portion equivalent to 80mg 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 up to 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 absorbance's were recorded at the respective wavelengths.

Determination of λmax:
The standard solutions of 100 µg/ml of Fluvastatin and Fenofibrate were individually scanned in the range of 200-400nm and the λmax 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 up to the mark with methanol to get concentrations of 8-24 µg/ml (n= 5) of Fluvastatin and 2-16 µg/ml (n=8) of Fenofibrate. Solutions of different concentrations for each drug were scanned at there respective wavelengths and absorbance's are recorded. The calculations done by simultaneous equation method.

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 Fluvastatin and Fenofibrate were plotted at 304 nm and 288 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 µg/ml for Fluvastatin and 2 to 16 µg/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 Fluvastatin 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 Fluvastatin and Fenofibrate in the spectrophotometric method.

Table 1: Results of analysis of UV method

Parameters	***Fluvastatine***	***Fenofibrate***
Detection Wavelength	304nm	288nm
Beer's Law Limit	8-24 µg/ml	2-16 µg/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

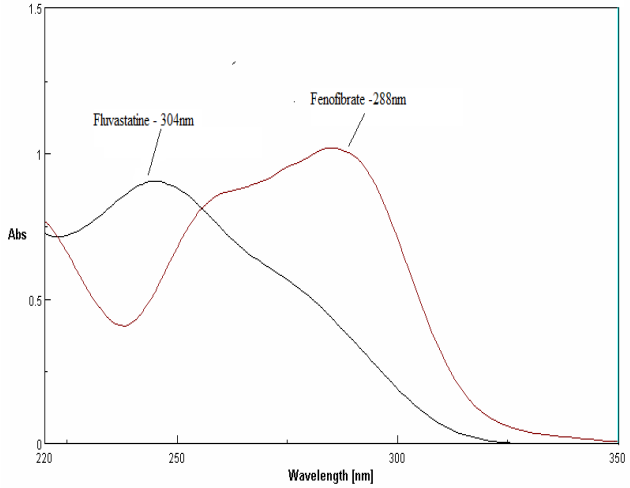
Table 2: Results of analysis of Tablet formulation

Formulation	***Drug***	***Label Claim (mg)***	***% Label Claim *(Mean ± S.D.)***	***Coefficient of Variance***
Tablet	Fluvastatine	150 mg	99.79 ± 1.78	0.801
	Fenofibrate	200mg	98.67 ± 1.021	0.943

Table 3: Results of recovery studies

Formulation	***Drug***	***Label Claim(mg)***	***%Recovery estimated * (Mean ± S.D.)***	***Coefficient of variance***
Tablet	Fluvastatine	150 mg	99.63 ± 0.742	0.744
	Fenofibrate	200mg	98.12 ± 0.738	0.743

Figure 1: UV overlain spectra for of Fluvastatine and Fenofibrate



CONCLUSION

The Spectrophotometry provides versatile technique 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 none interfering spectrophotometric method for estimation Fluvastatin 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.

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