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Original Article

Estimation of Atorvastatin Calcium and Fenofibrate in Human Plasma by UV Spectrophotometric Method

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ABSTRACT

An UV spectrophotometric method was developed for the estimation of atorvastatin calcium & fenofibrate in human plasma by using simultaneous equation method. Fenofibrate is a drug of the fibrate class. It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease. Atorvastatin calcium is a member of the drug class known as statins. It is used for lowering cholesterol. The drug obeyed Beer's law & showed good correlation near to 0.998. 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 1-5µg/ml for atorvastatin calcium & 2-10 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.

Keywords: Atorvastatin calcium, Fenofibrate, Spectrophotometry.

INTRODUCTION

Fenofibrate is a drug of the fibrate class and 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. Like other fibrates, it reduces both low density lipoprotein (LDL) and very low-density lipoprotein (VLDL) levels, as well as reducing triglycerides (TG) level. It also increases high density lipoprotein (HDL) levels. It is used alone or in combination with statins in the treatment of hypercholesterolemia and hypertriglyceridemia. Atorvastatin calcium is chemically 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-, calcium salt, (βR,δR)- (2:1) is a member of the drug class known

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as statins. It is used for lowering cholesterol. Atorvastatin calcium is a competitive inhibitor of hydroxymethylglutaryl-coenzyme-A (HMG-CoA) reductase, the rate-determining enzyme in cholesterol biosynthesis via the mevalonate pathway. HMG-CoA reductase catalyses the conversion of HMG-CoA to mevalonate. Decreased hepatic cholesterol levels increases hepatic uptake of cholesterol and reduces plasma cholesterol levels.

Literature survey revealed that very few methods have been reported for the analysis of Atorvastatin calcium and Fenofibrate combinational dosage forms which include UV spectroscopy, Reverse Phase High Performance Liquid Chromatography, Densitometric method, HPTLC methods. The present study illustrates development and validation of simple, economical, selective, accurate, precise spectrophotometric method for the determination of Atorvastatin calcium and Fenofibrate in human plasma.

MATERIALS AND METHODS

Apparatus: A UV – Visible double beam spectrophotometer (LAB-INDIA 3000) with 1 cm matched quartz, A Sartorius analytical balance, Centrifuge, Bath Sonicator.

Chemicals and Reagents: Methanol [AR Grade], Acetonitrile [AR Grade], Fenofibrate and Atorvastatin calcium.

EXPERIMENTAL WORK

Preparation of standard stock solution: 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. 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 100µg/ml. This stock solution is used for making dilutions for calibration curve.

Determination of λ_{max}: The standard solution of Atorvastatin calcium and Fenofibrate were separately scanned at different concentration in the range of 200-400 nm and the λ max was determined. The λ Max of Atorvastatin calcium and Fenofibrate was determined 246nm and 286nm.

Extraction of Plasma (Liquid-Liquid Extraction): An accurately weighed quantity of about 10mg of drug was taken in 50ml volumetric flask and 10ml of plasma was added and volume was made up to 50ml with methanol and kept aside for sometime and supernatant was collected and 10ml of methanol was added and again supernatant was collected and centrifuged at 3000rpm for 15 minutes. This solution was used for spectrophotometric analysis.

Preparation of Calibration curve:

For Standard drugs: 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 1-5µg/ml of Atorvastatin calcium and 2-10µg/ml of Fenofibrate. Solutions of different concentrations for each drug were scanned at their respective wavelengths and absorbances are recorded.

For Standard drugs with extracted plasma: The calibration curve was plotted by taking 1-5 µg/ml concentration of Atorvastatin calcium and 2-10 µg/ml for Fenofibrate and calibration curve was plotted against concentration and absorbance.

Validation study:

An integral part of analytical method development is validation. Method validation is the process to confirm that the analytical procedure employed for a specific test is suitable for its intended use. The newly developed Spectrophotometric method was validated as per International Conference on Harmonization (ICH) guidelines for parameters like accuracy, linearity, precision (Intraday and Inter day), and robustness.

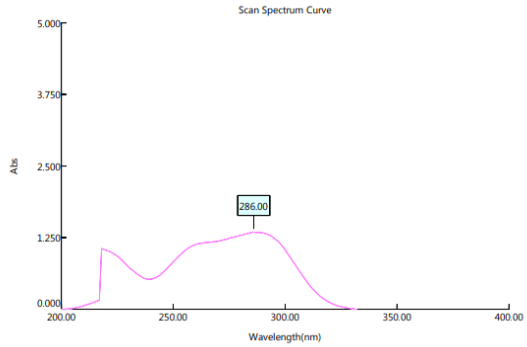
Precision: Precision study of sample was carried out by estimating corresponding responses 3 times on the same day and another day for the 100% target concentration.

Accuracy: The accuracy of the method is determined by known amount of Atorvastatin calcium and Fenofibrate at 50%, 100%, 150% is added to a pre-quantified sample solution.

Linearity: The linearity graphs for the proposed methods were obtained over the concentration range of 1-5µg/ml and 2-10µg/ml Atorvastatin calcium and Fenofibrate respectively.

Robustness: The robustness is evaluated by the analysis of Atorvastatin calcium and Fenofibrate under different experimental conditions such as making small changes in wavelength.

RESULTS



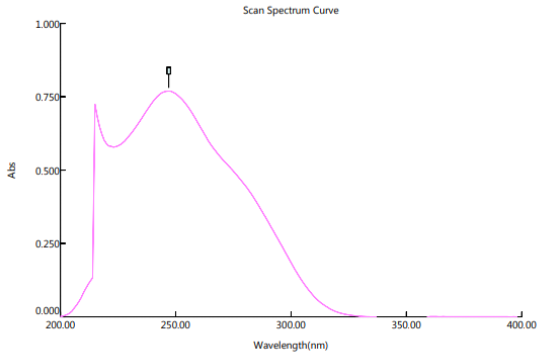


Figure 1: UV spectrum of Fenofibrate UV spectrum of Atorvastatin calcium

Table 1:Linearity data of Atorvastatin calcium standard

Concentration (µg/ml)	Absorbance
1	0.32
2	0.51
3	0.67
4	0.81
5	0.95

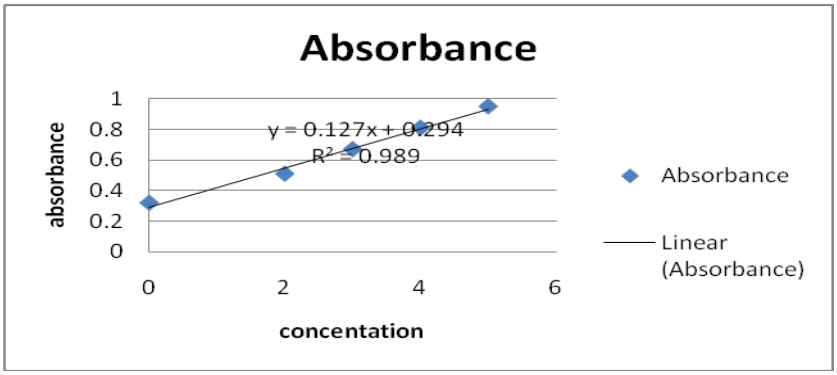


Figure 2: Calibration curve of Atorvastatin calcium

Table 2: Linearity data of Fenofibrate standard

Concentration (µg/ml)	Absorbance
2	0.48
4	0.78
6	1.15
8	1.50
10	1.90

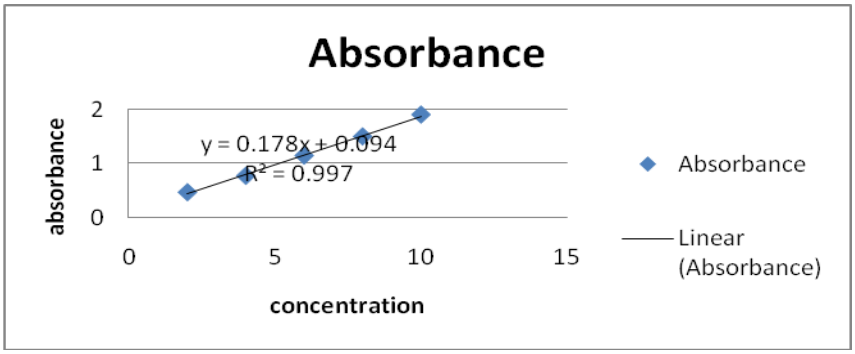


Figure 3: Calibration curve of Fenofibrate

Table 3: Linearity data of Atorvastatin calcium with plasma

Concentration (µg/ml)	Absorbance
1	0.091
2	0.185
3	0.262
4	0.361
5	0.462

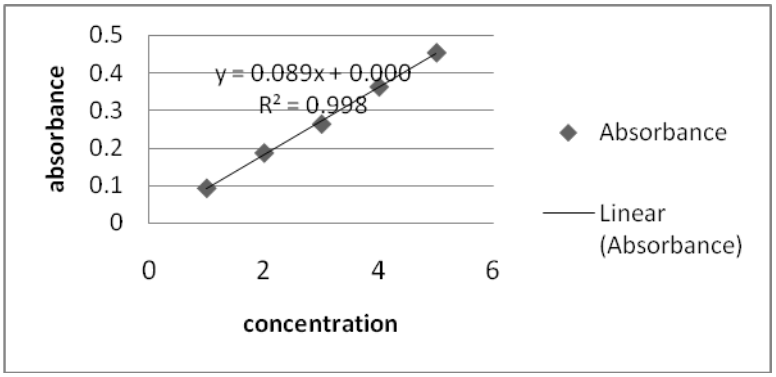


Figure 4: Calibration curve of Atorvastatin calcium with plasma

Table 4: Linearity data of Fenofibrate with plasma

Concentration (µg/ml)	Absorbance
2	0.112
4	0.149
6	0.248
8	0.319
10	0.372

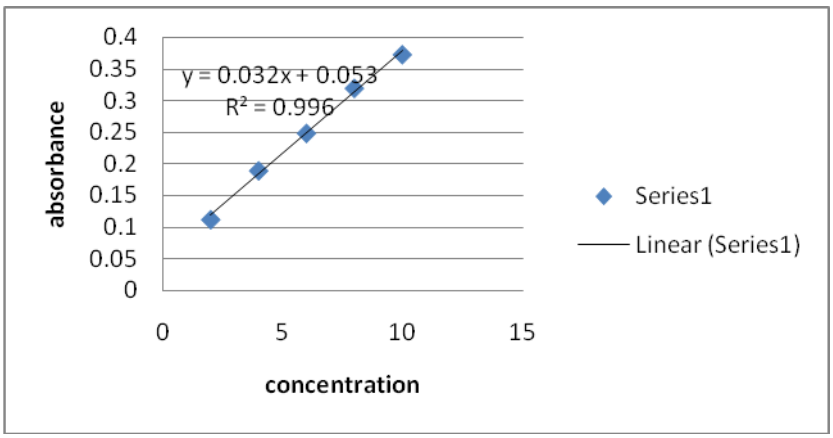


Figure 5: Calibration curve of Fenofibrate

Table 5: Accuracy of Atorvastatin Calcium

Concentration (µg/ml)	Absorbance	Amount recovered	% Recovery	Avg %recovery
50%	0.015	5.01	100.2	99.06
	0.016	4.90	98.00	
	0.015	4.95	99.00	
100%	0.034	9.95	99.5	100.1
	0.036	10.05	100.5	
	0.035	10.03	100.3	
150%	0.062	14.98	99.86	100.06
	0.063	15.01	100.0	
	0.062	15.03	100.2	

Table 6: Accuracy of Fenofibrate

Concentration(µg/ml)	Absorbance	Amount found	% Recovery	Avg %recovery
50%	0.045	5.03	100.6	100.98
	0.045	5.09	101.18	
	0.046	4.96	99.2	
100%	0.063	9.98	99.8	100.2
	0.064	10.03	100.3	
	0.064	10.01	100.1	
150%	0.095	15.07	100.4	99.26
	0.095	14.85	99.00	
	0.096	14.76	98.4	

Table 7: Robustness of Atorvastatin Calcium

Concentration (µg/ml)	244nm	246nm	248nm
2	0.047	0.034	0.025
2	0.044	0.037	0.029
2	0.049	0.043	0.030
2	0.046	0.039	0.032
2	0.045	0.038	0.030
2	0.047	0.047	0.031
Mean	0.046333	0.039667	0.0295
SD	0.001751	0.004633	0.002429
%RSD	0.03779	0.1167	0.08233

Table 8: Robustness of Fenofibrate

Concentration (µg/ml)	284nm	286nm	288nm
6	0.079	0.082	0.084
6	0.080	0.082	0.083
6	0.078	0.081	0.082
6	0.079	0.080	0.082
6	0.078	0.081	0.083
6	0.081	0.083	0.084
Mean	0.079167	0.0815	0083
SD	0.001169	0.001049	0.000894
%RSD	0.0146	0.0127	0.01

Table 9: Precision data of Atorvastatin calcium Intraday

Concentration (µg/ml)	Absorbance
3	0.058
3	0.056
3	0.057
3	0.056
3	0.057
3	0.058
Mean	0.057
SD	0.000894
%RSD	0.0156

Table 10: Precision data of Fenofibrate Intraday

Concentration (µg/ml)	Absorbance
6	0.116
6	0.117
6	0.116
6	0.115
6	0.115
6	0.118
Mean	0.116167
SD	0.001169
%RSD	1.006352

DISCUSSION

In this method, linearity was obtained in the concentration range of 1- 5µg/ml for Atorvastatin Calcium and 2-10µg/ml for Fenofibrate. The Correlation coefficient for Atorvastatin Calcium was found to be 0.99998 and 0.99793 at 246nm and 286nm, respectively. The slope and intercept was found to be -0.05977, 0.01938 and 0.00073, -0.00011 at 246nm and 286nm, respectively. The correlation coefficient for Fenofibrate was found to be 0.99978 and 0.99994 at 246nm and 286nm, respectively. The slope and intercept was found to be 0.02190, 0.04891 and - 0.00197, 0.00108 at 246nm and 286nm, respectively. The percentage recovery was found to be in the range of 98.41 – 99.74 % and 100.02-100.44% for Atorvastatin Calcium and Fenofibrate, respectively. The standard deviation and % RSD values were found to be less than 2% shows the high precision and accuracy of the method.

CONCLUSION

Based on the results obtained, it was found that the developed and validated UV- Spectrophotometric technique in human plasma is quite simple, accurate, economical, and rapid for routine analysis of atorvastatin calcium and fenofibrate. The recovery was found to be 99.74 % and 100.44% for Atorvastatin calcium and Fenofibrate respectively indicates reproducibility & accuracy of method.

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