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SIMPLE UV SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF FLUVASTATIN

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Abstract:

Objective: To determine the Statin (Fluvastatin) in pure form simple and cost effective spectrophotometric method was developed.

Methods: The UV spectrum of Fluvastatin in DMF showed absorption maximum at 304 nm and obeys Beer's law in the concentration range 5-30 µg/ml. The absorbance was found to be increases concentration with increasing linearity which is calculated by correlation coefficient value of 0.998. This method was validated for the accuracy, linearity, precision, ruggedness and robustness.

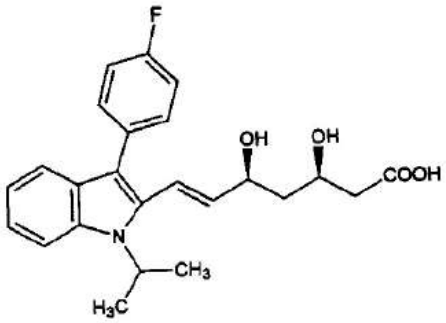
Results: The method has demonstrated excellent linearity over the range of 5-30 µg/ml with regression equation y = 0.022x + 0.053 and regression coefficient r^2 = 0.998. Furthermore, the method was found to be highly sensitive with LOD (1.501µg/ml) and LOQ (4.550µg/ml)

Conclusion: On the basis of the results, this method was successfully applied for the assay of Fluvastatin in different pharmaceutical dosage forms.

Keywords: Fluvastatin, Spectrophotometry, Dimethyl formamide, validation.

INTRODUCTION

Lipid and lipoproteins abnormalities are regarded as highly risk factor for influence of cholesterol, raised cholesterol increases the risk of heart diseases and stroke. Presence of abnormal levels of lipids in the blood causes disease like hyperlipidemia or hyperlipoproteinemia. Fluvastatin has been shown to reduced the cholesterol and prevent the coronary events in patients with heart disease. Fluvastatin reduces total cholesterol, LDL cholesterol hence, it is used as a treatment in homozygous and heterozygous familial hypercholesteremia also it is used in non-familial and mixed dyslipidemia. Other than this fluvastatin also lowers the high levels of VLDL cholesterol and triglyceride. Fluvastatin calcium a synthetics lipid lowering agent shows its therapeutic effects by competitive inhibition of 3-hydroxy -3methyl glutrtyl CoA.[1,2,3] More than a few analytical methods have been reported for the estimation of Fluvastatin such as only some chromatographic method[4,5] , spectrophotometric method[6,7], capillary electrophoresis (CE)[8,9,10] is one of the method and electrochemical as differential pulse voltammetry (DPV)[11] .



Structure of Fluvastatin

The chemical name of Fluvastatin is (3S, 5R, 6E)-7-[3-(4-flurophenyl)-1-(propan-2-yl)-1H-indol-2-yl]-3, 5-dihydroxyhept-6-enoic acid. It has molecular formula $C_{24}H_{26}FNO_4$ and molecular weight 411.46 gm/ml. Fluvastatin is brown crystalline powder and has melting point 194-197^0 C. The dry substance is soluble in dimethyl formamide.

MATERIAL AND METHOD

Fluvastatin was taken as a gift sample from DRL (Hyderabad, India). DMF (Dimethyl Formamide) was used as analytical grade.

Instruments

A UV visible double beam spectrometer [systronic 2201] and shimadzu 1800-UV spectrophotometer with 1 cm quartz cuvettes was used for all absorbance measurement. All weights were taken on analytical balance. Sonicator was used for dissolving Fluvatatin in DMF.

Experimental

Preparation of standard stock solution

10 mg of Fluvastatin was accurately weighed and it is dissolved in 10 ml of DMF to obtain 1000µg/ml to prepared standard stock solution to Fluvastatin.

Procedure for plotting calibration curve

To a series of 10 ml of volumetric flask, 0.05- 0.3 ml of standard stock solution was pipette out separately. The volume was adjusted using DMF to get concentration 15µg/ml and it was scanned between 200-400 nm which showed the maximum absorbance at 304 nm.

RESULTS AND DISCUSSION

Linearity:

The linearity was confirmed by taking aliquots of concentration of 5-30 µg/ml and absorbance was measured. It was performed in single day only. The obtained absorbance shows good regression coefficient at wavelength 304 nm. The slop and intercept values were recorded. The linearity was plotted against absorbance of Fluvastatin vs concentration of Fluvastatin.

Table 1 Result for Linearity

Sr. no	Concentration (µg/ml)	Absorbance
1	5	0.145
2	10	0.278
3	15	0.395
4	20	0.496
5	25	0.599
6	30	0.713

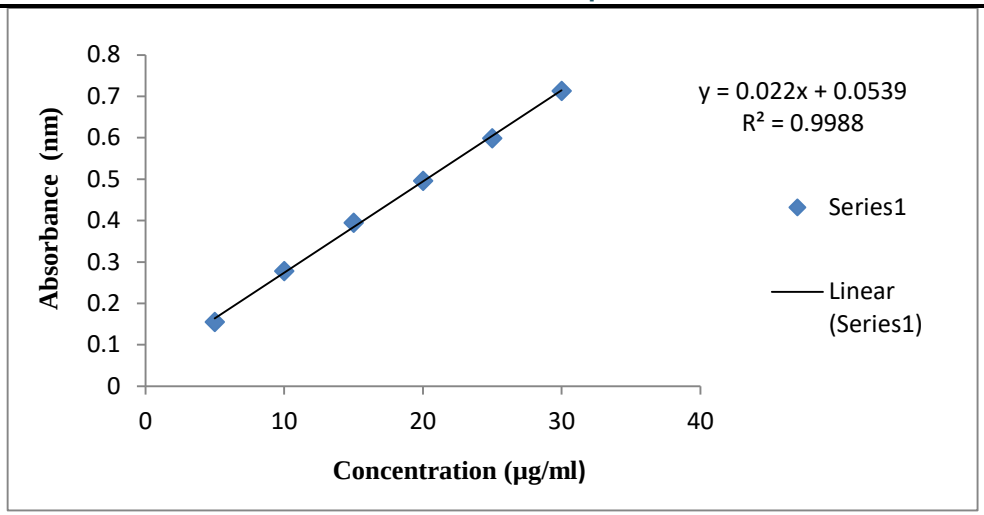


Figure 1 Calibration curve of Fluvastatin

Accuracy

The accuracy of the method was determined by experimentation of recovery. Accuracy is a parameter of an analytical method to which describes the test results of a measurements, calculation or specification conforms to the correct value or a standard. The standard addition method is used to analyze accuracy which is performed by using previous analyzed standard solutions. The percentage relative standard deviation and percentage recovery were analyzed by using standard solutions.

Range

The range is the analytical parameter of interval between lower and upper concentration limit of an analyte i.e. 5-30 µg/ml.

Precision

The precision is performed inter-day and intra-day. Intra-day precision was performed in one day and inter-day precision was performed in two days. Fluvastatin was analyzed at concentration 15 µg/ml. The %RSD for intra-day precision was found to be 0.32% and inter-day precision was found to be 0.32%.

Limit of Detection (LOD)

The limit of detection (LOD) or lower limit of detection is the lowest quantity of a substance that can be able to distinguish from the absence of that substance with a stated experimental level. LOD was calculated using formula;

$$\mathbf{LOD = 3.3\ Sa/b}$$

Limit of Quantification (LOQ)

The limit of quantification (LOQ) is the smallest concentration of the analyst, which gives response that can be accurately quantified. The LOQ was calculated by using formula;

$$\mathbf{LOQ = 10\ Sa/b}$$

Ruggedness

The ruggedness is the study of degree of responsibility of test results obtained by variety of external conditions like different analyst, laboratories, day and reagents. This study shown that there is no any influence of these conditions to test results.

Robustness

The robustness is the small study but deliberate variations in method parameters such as temperature and stability of analytical solution.

Table 2 Regression analysis of the calibration curve for proposed method

Parameters	Results
λ max	304 nm
Beer's law	5-30 µg/ml
Correlation coefficient (R^2)	0.998
Regression equation (y= mx + c)	0.022x + 0.053
Slope (m)	0.022
Intercept (c)	0.053
LOD (µg/ml)	1.501
LOQ (µg/ml)	4.550

Table 3 Results for Recovery (accuracy)

Name of Drug	Recovery level	Concentration (µg/ml)	Amount Recovered	%Recovery with SD
Fluvastatin	50%	10	10.02	100.02±0.6
	100%	20	20.01	100.01±0.2
	150%	30	30.04	100.04±04

Table 4 Results for precision (Intra-day)

Sr. no	Concentration (µg/ml)	Absorbance 1	Absorbance 2	% RSD
1	15	0.378	0.377	
2	15	0.377	0.378	
3	15	0.376	0.376	
4	15	0.378	0.375	
5	15	0.376	0.379	
6	15	0.378	0.378	
Average		0.377	0.377	
SD		0.00098	0.0014	
% RSD		0.26%	0.39%	0.32%

Table 5 Results for precision (Inter-day)

Sr. no	Concentration (µg/ml)	Day 1	Day 2	% RSD
1	15	0.378	0.376	
2	15	0.377	0.378	
3	15	0.376	0.377	
4	15	0.378	0.379	
5	15	0.376	0.375	
6	15	0.378	0.378	
Average		0.377167	0.377167	
SD		0.000983	0.001472	
%RSD		0.260678	0.390268	0.32%

Table 6 Results for Robustness

Concentration	13 µg/ml	13 µg/ml
Absorbance	0.312	0.315
	0.311	0.312
	0.314	0.313
	0.312	0.315
	0.313	0.315
	0.314	0.314
Average	0.312667	0.314
SD	0.001211	0.001265
%RSD	0.387333	0.402838

Table 7 Results of Ruggedness

Concentration	Analyst 1	Analyst 2
13 µg/ml	0.378	0.369
	0.377	0.368
	0.376	0.365
	0.378	0.364
	0.376	0.369
	0.378	0.365
Average	0.377167	0.366667
SD	0.000983	0.002251

Linearity

Six different concentrations of Fluvastatin were prepared and analyzed. Then wavelength was found to be 304nm. The regression coefficient was found to be 0.998. The absorbance was found in limit i.e. 0-2. Hence, the analyzed parameter was found to be validated (Table1).

Precision

- **Intra-day precision**
  The intra-day precision was found within limit i.e. 15 µg/ml at 304 nm. The relative standard deviation is less than 2.0 %. Hence the parameter was found to be validated (Table 4).
- **Inter-day precision**
  Two days are required for the inter-day precision and study was performed. The obtained results of concentration 15 µg/ml at 304 nm shown that the relative standard deviation is less than 2.0 %. Hence the parameter was found to be validated (Table 5).

Robustness

The change in concentration i.e. 13 µg/ml and obtained results shown that there is negligible effect on results. The result of robustness was found to be in boundary i.e. the relative standard deviation is less than 2.0 %. Hence the performed parameter was found to be validated (Table 6).

Ruggedness

The change in analyst at concentration of 13 µg/ml showed that the obtained result does not affected by it (Table 7).

Limit of detection

The limit of detection was found to be 1.501 µg/ml (Table 2).

Limit of quantification

The limit of quantification was found to be 4.550 µg/ml (Table 2).

Recovery values of Fluvastatin

The recovery values of fluvastatin was found to be at concentration 10 µg/ml and 30 µg/ml and it shows that obtained recovery was in limit 100.02±0.6 and 100.04±04 respectively (Table 3).

CONCLUSION

The developed method was simple, precise, accurate, highly sensitive, reproducible and inexpensive. The planned method was found to be appropriate for detection of fluvastatin and it is also gives the satisfactory recovery of analyst, which can be simply applied for the analysis of Fluvastatin in pure form.

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