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First-Order Spectrophotometric Derivative Method for the Estimation of Atorvastatin in Pharmaceutical Preparation

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ABSTRACT

The objective of this research is to describe the optimization, validation, and application of spectrophotometric techniques for the determination of Atorvastatin Calcium in their pharmaceutical formulation (tablets). In this paper simple, rapid, accurate and sensitive spectrophotometric methods have been developed and validated. This method is a direct spectrophotometric analytical method depending on dissolve of atorvastatin calcium in diluted in water and methanol in ratio of (90:10). The maximum absorption wavelength for determination of ATR drug was found to be 241 nanometer (nm), for Beer's law was obeyed in the concentration range from 4 to 32 µg/ml for UV- Spectrophotometric analysis method.

INTRODUCTION:

The development of simple and reproducible analytical methods for estimation of drugs is very important part of quality control and assurance. Chemically Atorvastin is [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. Atorvastatin is a selective, competitive inhibitor of the 3-hydroxy methyl glutaryl coenzyme A (HMG-CoA) reductase enzyme that is involved in the conversion of HMG-CoA to mevalonate (a precursor of sterols, including cholesterol). A reduction of intracellular cholesterol levels promotes an expression of LDL (low-density lipoprotein) receptors on the hepatocyte surface, resulting in an increased extraction of LDL from the blood. As an additional cholesterol-lowering mechanism, HMGCoA reductase inhibitors also decrease the blood concentrations of VLDLs (very low-density lipoproteins) by inhibiting their synthesis and promoting their catabolism. Atorvastatin calcium also inhibits cholesterol synthesis in the liver and increases the hepatic LDL receptors on the cell surface to enhance the uptake and catabolism of LDL. The drug also reduces the LDL production and the number of LDL particles. The structure is shown in fig.1.

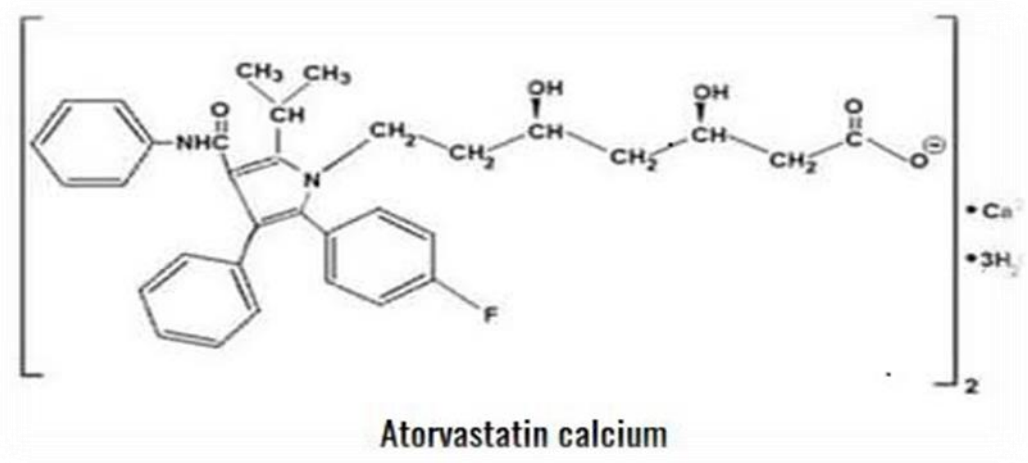

Figure No.1: Structure of Atorvastatin calcium

MATERIAL AND METHODS

Apparatus and software

1. A UV-Visible spectrophotometer (UV-1800 Shimadzu Double Beam Spectrophotometer) computer loaded with Shimadzu UV Probe 2.33 software was used for

all the spectrophotometric measurements. The spectral bandwidth was 1nm and the scanning speed was very fast. The absorbance spectra of the reference and test solutions were carried out in 1cm quartz cells over the range of 200-400 nm.

Reagents and materials

Atorvastatin Calcium (99.5% purity) was received as gift samples from Aurobindo Pharma Ltd. A.R grade Methanol (Merck Index), Pharmaceutical formulation tablets (label claim 10 mg ATR) were used in UV analysis.

Preparation of stock solutions:

Preparation of stock solution- Standard stock solution of Atorvastatin Calcium was prepared by dissolving accurately weighed 10mg of Atorvastatin Calcium in water and methanol in ratio of 90:10 in 10ml volumetric flask to give a concentration of 1mg/ml. which is the standard stock solution.

Determination of Maximum Absorbance (max)

Preparation of stock solution- Standard stock solution of Atorvastatin Calcium was prepared by dissolving accurately weighed 10mg of Atorvastatin Calcium in methanol in 10ml volumetric flask to give a concentration of 1mg/ml. which is the standard stock solution.

From the above stock solution, 0.1ml was pipette out into 10ml volumetric flask and dilution was made with water to obtain concentration 10µg/ml. The samples were then scanned in UV spectrophotometer from a range of 200-400nm against water and methanol in ratio of 90:10 as blank and the wavelength corresponding to maximum absorbance in water and methanol was found at 232.40nm.

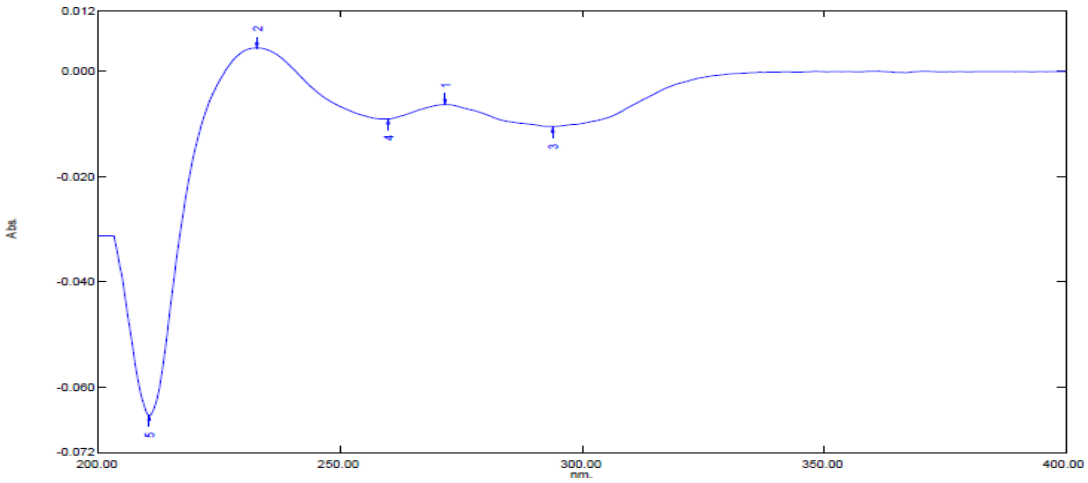

Figure No. 02: UV Spectrum of Atorvastatin Calcium

Selection of analytical concentration ranges:

From the standard stock solution of ATR, appropriate aliquots were pipette out into 10ml volumetric flask and dilutions were made with water and methanol in ratio of 90:10 to obtain working standard solutions of concentrations from 4-32 µg/ml. Absorbance for these solutions were measured at 241nm.

Table No 1: Absorbance of ATR

Sr. No.	Taken concentration (ug/ml)	Absorbance	Find concentration (ug/ml)
1	10	0.0050	10
2	10	0.0049	9.8
3	10	0.0048	9.6

*** Indicates average of three determinations**

Application of the proposed method for estimation of drug in laboratory mixture

Pipetting out 0.1 from the 100µg/ml solution into a 10ml volumetric flask and made up the volume with water and methanol in the ratio of 90:10. The absorbance of each solution was measured at 241nm against water and methanol in ratio of 90:10 as blank.

METHOD VALIDATION

Preparation of standard calibration curve for first derivative method.

For the preparation of the standard calibration curve, concentration of 4-20µg were prepared by pipetting out 0.4, 0.8, 1.2, 1.6, 2ml from the 100µg/ml solution in to a 10ml volumetric flask and made up the volume with water. The absorbance of each solution was measured at 232.40nm against water and methanol in ratio of 90:10 as blank. Calibration curve of the drug was then plotted by taking the absorbance obtained on y-axis and the concentration of the solution on x-axis (Figure). The curve showed linearity in the range of 4-20µg/ml with correlation coefficient 0.9995.

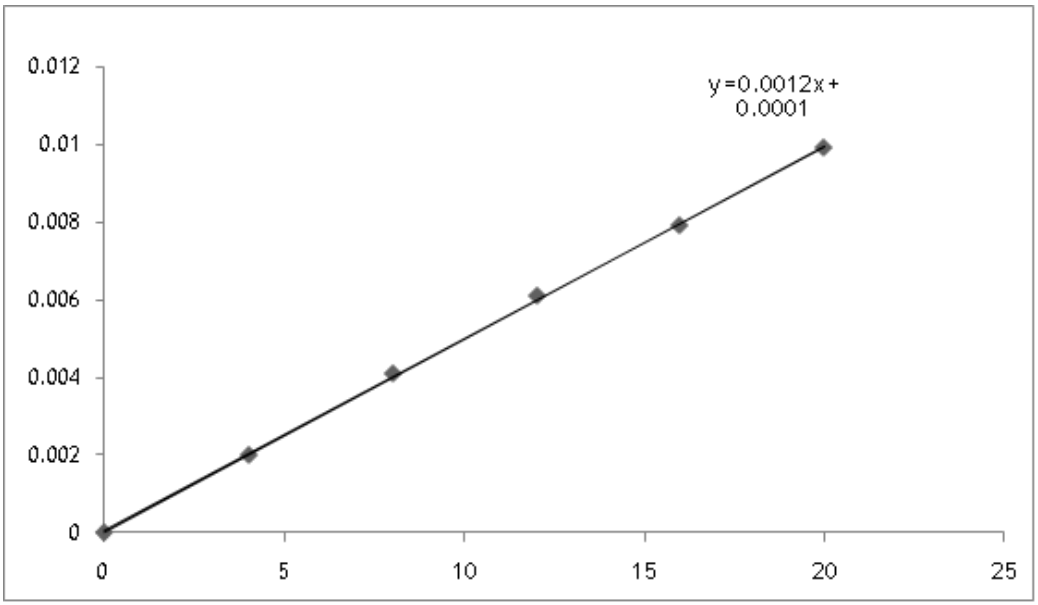

Figure No. 03: Calibration curve Atorvastatin Calcium

Table No.2: Optical and regression characteristics.

sr.no	Parameters	Atorvastatin Calcium
1	Slope	0.0012x
2	Intercept	0.0001
3	Correlation coefficient	0.9995
4	Linearity range (µg/ml)	4-20 µg/ml

Linearity

The linearity of the analytical method was its ability to elicit test results which are directly proportional to analyze concentration in samples within a given range. To establish the linearity of the proposed method, various aliquots of the standard solution of the drug were prepared from the stock solution and analyzed. The drug showed linearity in the range of 4-32µg/ with a correlation coefficient 0.999. Linearity data are shown in Table**.**

Table No.03: Linearity table of Atorvastatin Calcium.

Concentration(ug/ml)	Absorbance(Nm)
4	0.0021
8	0.0042
12	0.0061
16	0.0079
20	0.0098

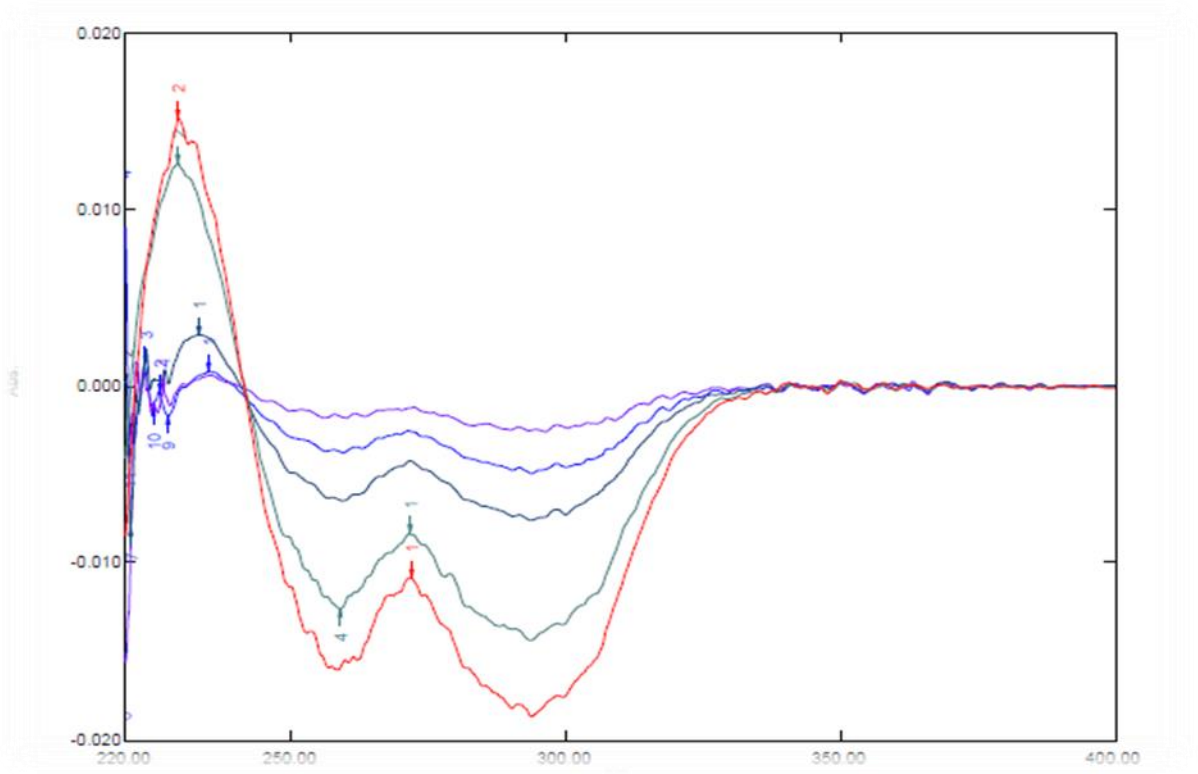

Figure No 04. Overall spectrum for first derivative

Precision

Precision studies were carried out to ascertain the reproducibility of the proposed method. Repeatability was determined by preparing three replicates of the same concentration of the sample and the absorbance was measured. Intraday precision study was carried out by preparing a drug solution of the same concentration and analyzing it at three different times in a day. The same procedure was followed for three different days to determine interday precision. The results were reported as %RSD. The precision result showed a good reproducibility with a percent relative standard deviation less than 2. The results of intraday and interday precision studies are shown in Table.

Table No.04: Precision data.

Sr. No.	Interval of Time	Concentration (µg/ml)	Absorbance	% Purity
I	Intra-day	10	0.0050	100.00
II		10	0.0049	98.00
III		10	0.0050	100.00

Table No.05: Statistical validation of intra-day precision data.

Mean*	SD	%RSD
99.33	1.1547	1.1624

Accuracy

The accuracy of the proposed method was determined using recovery studies. The recovery studies were carried out by adding different amounts (80%, 100% and 120%) of the pure drug to the pre-analysed formulation. The solutions were prepared in triplicates and the % recovery was calculated. The results are shown in Table.

Table No.06: Recovery study data.

Level of Recovery	Amount present(mg)	Added Concentration (mg)	Amount Recovered (mg)	% Recovery
80%	10	08	7.82	97.75
	10	08	7.76	97
	10	08	8.02	100.75
100%	10	10	9.85	98.5
	10	10	10.14	101.4
	10	10	9.85	98.5
120%	10	12	11.97	99.86
	10	12	11.99	99.95
	10	12	12.01	100.04

TableNo.07: Statistical validation of recovery study data

Level of Recovery	%Mean Recovery	SD	% RSD
80%	98.5	1.9843	1.9956
100%	99.46	1.6843	1.6832
120%	99.75	0.09	0.900

3.4 LOD and LOQ

Limit of detection (LOD) is the lowest amount of analyte in the sample that can be detected. The limit of quantification (LOQ) is the lowest amount of analyte in the sample that can be quantitatively determined by suitable precision and accuracy. LOQ nd LOD were determined using the following equation LOQ-10s/m, LOD-3.3s/m where s is the standard deviation of the response and m is the slope of the related calibration curve.

Table No.8: LOD & LOQ.

Name of the drug	LOD µg/ml	LOQ µg/ml
Atorvastatine Calcium	0.84 µg/ml	1.81 µg/ml

3.5Ruggedness.

Ruggedness was determined by carrying out analysis by two different analysts and the respective absorbance was noted and the results were indicated as % RSD. The results are shown in Table.

Table No.9: Ruggedness data

Sr. No.	Analyst	Concentration (µg/ml)	Absorbance	% Purity
I	1st	10	0.244	99.63
II		10	0.246	100.36
III		10	0.244	99.63
I	2nd	10	0.245	100.00
II		10	0.245	100.00
III		10	0.244	99.63

Table No.10: Statistical validation of Ruggedness data (Analyst 1st)

Mean*	SD	%RSD
99.87	0.4214	0.422

Table No.11: Statistical validation of Ruggedness data (Analyst 2nd)

Mean*	SD	%RSD
99.87	0.4214	0.422

Robustness

Analysis was carried out at two different ratio concentrations, Methanol: water; 0.5:9.5 ratio determine the robustness of the method and the respective absorbance was measured. The results were indicated as %RSD.

Table No.12: Robustness data

Sr. No.	Ratio of	Concentration (µg/ml)	Absorbance	% Purity
I	Methanol: water 0.5:9.5	10	0.0050	100.00
II		10	0.0050	100.00
III		10	0.0049	99.00

Table No.13: Statistical validation of Robustness data (Methanol: Water 0.5:9.5)

Mean*	SD	%RSD
99.66	0.5779	0.5792

*** Indicates average of three determinations.**

RESULTS AND DISCUSSION

The solubility of Atorvastin Calcium was studied and Methanol-water (0.5:9.5) is selected as a solvent. For calibration curve method Atorvastin Calcium showed wavelength maxima at 232.40 nm. The drug follows Beer-Lambert's law over the concentration range of 4-20 µg/ml with a correlation coefficient of 0.9995. The present study of proposed method showed precision in terms of the repeatability and reproducibility is found to be not more than 2%. The recovery results are in the range of 98 to 102%. Hence, the results of the analysis are validated as per ICH guidelines. Quantitative determination of Atorvastin Calcium in API and tablet dosage form by employed the method, the assay values found 101.40%.

Table no.14: Optical parameters for first derivative method

Parameters	Result.
Working Wavelength(nm)	232.40nm
Linearity Range(µg/ml)	4-20 µg/ml
Limit of Detection (µg/ml)	0.84 µg/ml
Limit of Quantitation (µg/ml)	1.81 µg/ml
Y= mx+c	y = 0.0012x + 0.0001
Slope ± S.D.	0.0012x
Intercept ± S.D.	0.0001
Regression Coefficient ±S.D.	R^2= 0.9995

CONCLUSION

The newly developed method of Atorvastin Calcium is simple, precise, and validated in terms of linearity, precision, accuracy, and reproducibility. Therefore, the developed spectroscopic method is used for routine analysis of Atorvastin Calcium in bulk & tablet dosage form and can also be used for dissolution, accelerated stability studies or similar studies.

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