Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Issue 3, 2013

Research Article

FIRST DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF ATORVASTATIN CALCIUM AS BULK AND IN TABLET DOSAGE FORM

SURENDRA SINGH INDA*, SANJAY SHARMA, VISHNU DAS, BHARAT KUMAR, ANIL BHANDARI

Faculty of Pharmaceutical Science, Jodhpur National University, Boranada, Narnadi, Jhanwar Road,Jodhpur, Rajasthan, India.
Email: surendrasinghinda@gmail.com

Received: 05 Apr 2013, Revised and Accepted: 26 May 2013

ABSTRACT

Objective: A simple, economic, sensitive, precise and accurate first derivative spectrophotometric method has been developed for determination of Atorvastatin Calcium as bulk and in tablet dosage form.

Method: The quantitative determination of the drug was carried out using the first derivative values measured at 245.8 nm. The method was validated as per ICH guidelines. Statistical analysis of the result has been carried out revealing high accuracy and good precision. The proposed method was successfully applied to the determination of Atorvastatin Calciumin pharmaceutical formulations without any interference from common excipients.

Result: Calibration curve was linear in concentration range of 4-28 µg/ml with correlation coefficient value of 0.9987. The slope of Atorvastatin Calcium was found to be 0.0007.The results of analysis validated statistically and by recovery studies.

Conclusion: The proposed method was found to be sensitive, specific, accurate, precise and cost effective quality control tool for the routine analysis of Atorvastatin Calcium as bulk and in tablet dosage form.

Keywords: Atorvastatin Calcium, First Derivative spectrophotometry, Validation.

INTRODUCTION

Atorvastatin calcium is a drug of statins class. It is used in elevated blood cholesterol levels. It is chemically [R-(R*, R*)]-2-(4-fluorophenyl)-b,d-dihydroxy-5-(1-methylethyl)-3-pheny1-4 [(phenyl amino) carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate (Fig. 1). Its molecular formula is $C_{66}H_{68}CaF_2N_4O_{10}$ and its molecular weight is 1209.42. It is a synthetic cholesterol lowering agent [1]. Atorvastatin 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 catalyzes the conversion of HMG-CoA to mevalonate. Atorvastatin acts primarily in the liver. Decreased hepatic cholesterol levels increases hepatic uptake of cholesterol and reduces plasma cholesterol levels [2].

Literature survey revealed that various analytical methods such as Spectrophotometry [3-4], Extractive Spectrophotometry [5], HPLC [6 - 7], HPTLC [8] and LC-MS [9] methods have been reported for estimation of Atorvastatin Calcium in formulations andbiological fluids.However no derivative spectrophotometricmethod has been reported to the best of our knowledge. So emphasis was given to develop simple,sensitive, precise, accurate and efficient first derivative spectrophotometric method for estimation of Atorvastatin Calcium in tablet dosage form.

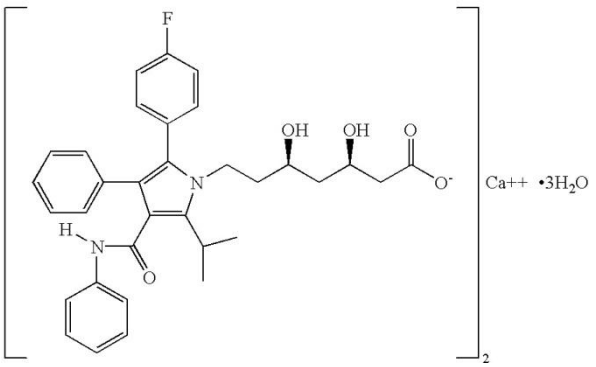

Fig. 1: Chemical structure of Atorvastatin Calcium

Experimental

Chemicals and Reagents

Atorvastatin Calcium was obtained as gift sample from Dr Reddy's, Laboratories Ltd., Andhra Pradesh (India). A commercial tablet formulation was purchased from the local market. Methanolof analytical grade was used.

MATERIALS AND METHODS

Instrument

A double beam UV-VIS Spectrophotometer (UV CE7400, Cecil, UK) Spectral bandwidth of 1 nm and wavelength accuracy of ±0.5 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (XB120A, Precisa, Switzerland).

Preparation of Standard Stock Solution

Accurately weighed Atorvastatin Calcium (10.0 mg) was transferred to 100 ml volumetric flask, dissolved in about 50 ml of methanol and volume was up-to 100 ml with methanol to obtain stock solution of drug concentration of 100 µg/ml.

Determination of wavelength of maximum amplitude (Dvalue) of Atorvastatin Calcium

The 10 ml of standard stock solution was diluted to 100 ml with the help of methanol to get the concentration of 10 µg/ml, scanned in the range of 200 to 400 nm against methanol as a blank. The spectrum was recorded and λ_{max} was found to be 245.8 nm (Fig.2).

Preparation of calibration curve for Atorvastatin Calcium

From standard stock solution of Atorvastatin Calcium 0.4, 0.8, 1.2, 1.6, 2.0, 2.4 and 2.8 solutions were pipetted out in a series of seven 10 ml volumetric flasks. The volumes in each flask were made up to 10 ml with solvent (methanol), to obtain final solutions contained 4, 8, 12, 16, 20, 24 and 28 µg/ml of drug. The spectrum was recorded. The amplitude (D value) was measured at 245.8 nm (Table 1) and Calibration curve was plotted (Fig. 3).

Estimation of Atorvastatin Calcium in Tablet dosage form

The powder of 20 Atorvastatin Calcium tablets (label claim 10 mg) of the same batch no. were triturated and mixed properly.

Accurately weighed 91.1 mg powder (equivalent to 10 mg of Atorvastatin Calcium) was transferred in 100 ml volumetric flask containing small quantity of reference solvent (methanol). Ultrasonic water bath was used for 20 minutes to complete dissolution. The solution were diluted to volume and filtered through Whatman filter paper no. 40. Further suitable dilutions were made to obtain six replicates of 10 µg/ml solutions. These solutions were analyzed and percent recovery of Atorvastatin Calcium tablet was determined.

Method Validation

Specificity

Commonly used excipients present in selected tablet formulation were spiked into a pre-weighed quantity of drug. The amplitude (D value) was measured and calculations were determined the quantity of the drug.

Linearity

A calibration curve was constructed at optimum experimental conditions using Dvalues versus concentration in the range of 4-28 µg/ml. Regression analysis using the method of least square was made for slope (0.0007), intercept (0.0003) and correlation coefficient (0.9987). The regression equation (y = 0.0007x + 0.0003) was obtained, where 'y' is amplitude of the peak at 245.8 nm and 'x' is the concentration of the sample in µg/ml.

From calibration curve data, high value of the correlation coefficient (0.9987) was found and the value of the intercept on ordinate, which is close to Zero, shows very good linearity of the calibration graph and adherence of the method to Beer's law.

Precision

For Intraday and Interday precisions of the method, solutions of Atorvastatin Calcium were prepared at three concentration levels 12.8, 16, 19.2 (µg/ml) each in triplicate. These solutions were analyzed respectively three times within one day and three consecutive days and the result was reported in terms of relative standard deviation (RSD).

Accuracy

The accuracy of the method is based on recovery study. The technique of standard addition was used to assess accuracy of the method. For this purpose a concentration of 10 µg/ml was selected to prepare the sample matrix of the blank drug. Again 10 ml of sample was taken in three, 100 ml volumetric flasks. To these three flasks 8 ml, 10 ml and 12 ml of standard stock solution of API mixture of Atorvastatin Calcium was added and volume was made up to 100 ml. The amplitude of the sample matrix and after standard addition was measured in triplicate. The result was reported in terms of % recovery.

RESULTS AND DISCUSSION

According to the International Conference on Harmonization, the main objective of the validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose, and the parameters that need to be selected are the responsibility of the analyst. The solubility of Atorvastatin Calcium in methanol, so it was used in this method. Atorvastatin Calcium in methanol shows absorption maxima at 245.8 nm in first order derivative spectrum (Fig. 2). The amplitude (D value) was measured at 245.8 nm for calibration curve (Table 1). The response for Atorvastatin Calcium was found to be linear in the concentration range of 4–28 µg/ml (Fig. 3). The % mean recovery data for estimation of Atorvastatin Calcium in Atorvastatin Calcium tablets are summarized in Table 2. The optical characteristics of the method and regression analysis of the calibration curve of Atorvastatin Calcium are shown in Table 3. The results of validation parameters are shown in Table 4. The recovery of Atorvastatin Calcium was found to be satisfactory. Excipients used in the specificity study did not interfere with response of the drug at its analytical wavelength. Also, no significant change in response of Atorvastatin Calcium was observed after 8 hrs. Hence, the method is sensitive, specific and robust for estimation of Atorvastatin Calcium. The proposed spectrophotometric methods were applied to the determination of Atorvastatin Calcium in its pharmaceutical formulations.

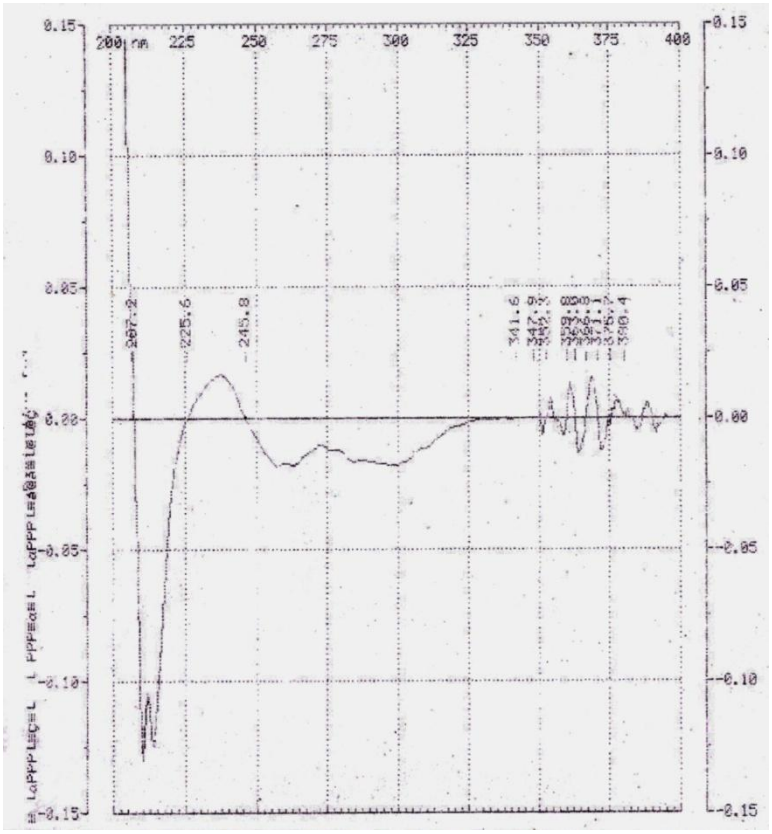

Fig. 2: First derivative UV spectrum of Atorvastatin Calcium

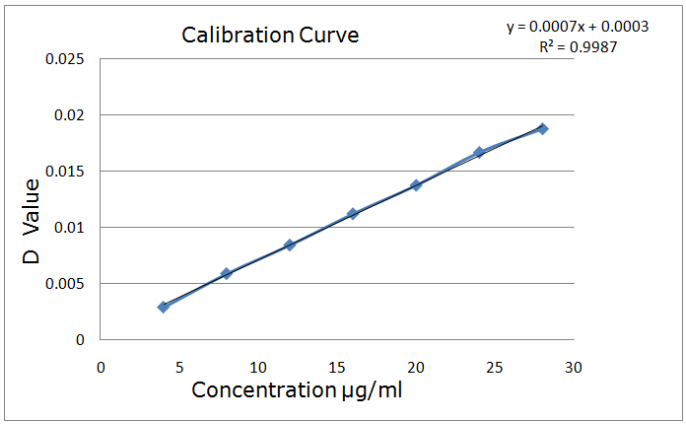

Fig. 3: Calibration curve of Atorvastatin Calcium at 245.8 nm

Table 1: Calibration curve data for Atorvastatin Calcium

S. No.	Conc. (µg/ml)	D value (amplitude)
1.	4	0.002963
2.	8	0.005929
3.	12	0.008093
4.	16	0.011234
5.	20	0.013951
6.	24	0.016667
7.	28	0.018989

Table 2: Assay result of Atorvastatin Calcium in tablets

Label claim	Amount found (mg/tab.)	Standard deviation	% Mean Recovery
10 mg	10.09	1.470600	100.9666

Table 3: Beer's law data and Regression characteristic of Atorvastatin Calcium

S. No.	Parameters	Values
1.	Beer's law limit	4-28 (µg/ml)
2.	Molar absorptivity	391.0479 (lit. gm^{-1} cm^{-1})
3.	Regression equation (Y = a + bc)	0.0007x+0.0003
4.	Correlation coefficient (r^2)	0.9987
5.	Slope (b)	0.0007
6.	Intercept (a)	0.0003

Table 4: Validation parameters of Atorvastatin Calcium

Validation parameters		Inference
Specificity		% Agreement 100.22714
Range (µg/ml)		4-28 (µg/ml)
	Repeatability	0.1864832 %
Precision (% RSD)	Intraday	0.089638296 %
	Interday	1.552240875 %
Range	Working Range	0.00149124 to 28 µg/ml
	Linearity Range	4 µg/ml to 28 µg/ml
	Target Concentration	16 µg/ml
	Target Range	12.8 µg/ml, 16 µg/ml, 19.2 µg/ml
Accuracy(% recovery)		99.37 to 100.416 %
LOD (µg/ml)		0.00044737
LOQ (µg/ml)		0.00149124
Percent mean recovery for Atorvastatin Calcium tablets		100.966667

CONCLUSION

The method was validated and found to be sensitive, specific, economic, accurate and precise. Hence, the method can be used successfully for routine analysis of pharmaceutical dosage form of Atorvastatin Calcium.

ACKNOWLEDGMENT

Authors are grateful to the Dean, Faculty of Pharmaceutical Sciences, and Jodhpur National University for providing necessary facilities to carry out the research work and Dr Reddy's Laboratories Ltd., Andhra Pradesh (India) for providing the gift sample of the drug.

REFERENCES

1. The Merck Index. Thirteenth edition. Merck and co., INC., Whitehouse station: NJ; 1997. p. 868.
2. Indian Pharmacopoeia. Vol – II. Govt. of India, Ministry of Health & Family Welfare: Delhi; 2007. p. 132-134.
3. Prajapati KP, Bhandari A. Spectroscopic method for estimation of Atorvastatin Calcium intablet dosage form. Indo Global J Pharm. Sci2011; 1(4): 294-299.
4. Jadhav SD, Bhatia MS, Thamake SL. Spectroscopic methods for estimation of Atorvastatin Calcium intablet dosage form. International JPharm. Tech Research2010; 2(3): 1948-1953.
5. Navin E.Extractive Spectrophotometric Determination of Atorvastatin in Bulk and Pharmaceutical Formulations. Taylor & Francis Group content 2003; 36(12): 2699-2711.
6. Stanisz B, Kania L. Validation of HPLC method for determination of Atorvastatin in tablets and for monitoring stability in solid phase.Acta Pol Pharm 2011; 63(6): 471-476.
7. Khedr A. Stability-indicating high-performance liquid chromatographic assay of Atorvastatin with fluorescence detection. J AOAC Int 2007; 90(6): 1547-1553.
8. Yadav SS. Mhaske DV, Kakad AB, Patil BD,Kadam SS, Dhaneshwar SR. Simple andsensitive HPTLC method for determination of content uniformity of Atorvastatin Calcium tablet. Indian JPharm Sci 2005; 67(2): 182-188.
9. Jani Ashutosh J., Dasandi Bhavesh, Rathnam Shivprakash, Mehta Anita A. Liquid Chromatographic-MS/ MS Determination of Atorvastatin and Metabolites in Human Plasma. Eurasian J Ana Chem2010; 5(1): 46-52.
10. Sharma S, Sharma MC. Method development and validation of AtorvastatinCalcium using $FeCl_3$ by UV-Visible Spectrophotometric method. American – Eurasian J toxi Sci2011; 3(2): 105-110.
11. Validation of Analytical Procedures. Text and Methodology Q2 (R1). ICH Harmonised Tripartite Guideline; 1994. p. 5.
12. Validation of Analytical Procedures. Text and Methodology Q2 (R1). ICH Harmonised Tripartite Guideline; 2005. p. 1-13.