International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.4, No.3, pp 999-1003, July-Sept 2012

Validated Spectrophotometric Method for Simultaneous Estimation of Atorvastatin and Nicotinic acid in Combined Pharmaceutical dosage form

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Abstract: A simple, precise and cost effective spectrophotometric method have been developed for the estimation Atorvastatin and Nicotinic acid in combination in tablet dosage form by UV spectroscopy, using multi-component mode of analysis. Methanol used as solvent λmax of Atorvastatin and Nicotinic acid was found to be 248nm and 261.5nm respectively. The method shows linearity in the Atorvastatin and Nicotinic acid the Beer-Lamberts concentration range was found to be 2-12 µg/ mL and10 – 60 µg/ mL respectively.The proposed methods are found to be free from interference of excipients and are successfully applied to estimation of the amount of Atorvastatin and Nicotinic acid in bulk and pharmaceutical dosage forms.
Key words: Atorvastatin and Nicotinic acid, Simultaneous estimation, UV spectrometry.

Introduction

Atorvastatin is chemically (3R,5R)-7-[2-(4-fluorophenyl) -3-phenyl-4-(phenylcarbamoyl)-5-(propan-2yl)1H-pyrrol-1-yl -3,5-dihydroxyheptanoic acid calcium salt trihydrate **fig 1.** Atorvastatin is selectively and competitively inhibits the hepatic enzyme HMG-CoA reductase. As HMG-CoA reductase is responsible for converting HMG-CoA to mevalonate in the cholesterol biosynthesis pathway. HMG-CoA reductase is responsible for converting HMG-CoA to mevalonate in the cholesterol biosynthesis pathway. Nicotinic acid is chemically pyridine-3-carboxylic acid **fig 2.** The main purpose of the present study was to establish a relatively simple, sensitive, validated and inexpensive spectrophotometric method for the determination of Atorvastatin and Nicotinic acid in pure form and in pharmaceutical dosage form. Several studies for the estimation of the drug using various techniques have been carried out for Atorvastatin and Nicotinic acid, some of them being: Simultaneous Estimation of Atorvastatin Calcium and Amlodipine Besylate from Tablets[3]. Development and Validation of RP-HPLC Method for Simultaneous Estimation of Atorvastatin Calcium and Fenofibrate in Tablet Dosage Forms[4].Simultaneous determination of Nicotinic acid and meclozine hydrochloride in tablet by RP-HPLC[5].

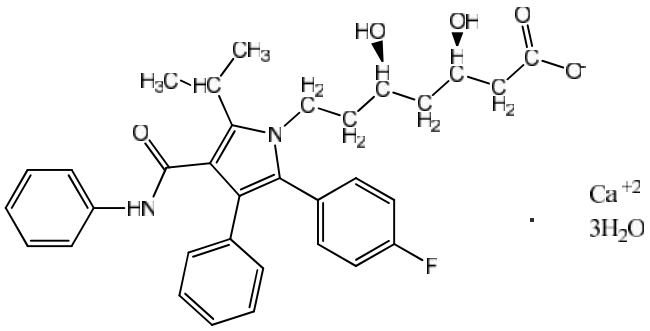

Figure 1. Chemical structure of Atorvastatin calcium

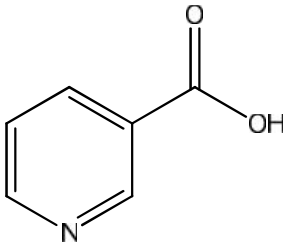

Fig 2.chemical structure of Nicotinic acid[2]

Experimental

Instrument:

A Jasco V630 double beam UV-Visible spectrophotometer equipped with 10mm matched quartz cells was used in the present study. All weights were taken on electronic balance (Denver, Germany).

Chemicals and Reagents:

Atorvastatin and Nicotinic acid working standards were generous gifts from Lupin Laboratory Limited Aurangabad and Aurobindo labs hydrabad, India respectively. Combination drug products of Atorvastatin and Nicotinic acid (Label claim: Atorvastatin calcium equivalent to Atorvastatin 10mg, and Nicotinic acid 375 mg), TONACT plus (Lupin Ltd.mumbai, India), purchased from local pharmacy. Methanol used was of analytical reagent grade.

Preparation of Standard Stock Solution:

weigh 10mg each of Atorvastatin and Nicotinic acid in 100 ml of methanol in separate volumetric flask, first dissolved in 25ml and then volume is make up to mark to obtain final concentration of 100mcg/ml of each component.

Preparation of Mixture of Atorvastatin and Nicotinic acid:

The standard solutions of Atorvastatin were prepared in the concentration range of 2µg/mL to 12 µg/mL, and that of Nicotinic acid were prepared in the range of 10 µg/mL to 60 µg/mL in Methanol.All the mixed standard solutions were scanned over the range of 200- 400nm; using two sampling wavelengths 248nm for Atorvastatin and 261.5nm for Nicotinic acid respectively. The spectral data from these scans were used to determine the concentration of these drugs in tablet formulation.

Procedure for Analysis of Tablet Formulation

Twenty tablets were weight accurately and triturated to powder form and quantity of powder equivalent to 10 mg of the drug was transferred to a 100 mL volumetric flask and dissolved first in about 50 mL methanol and volume is make up to the mark. The solution is ultrasonicated for 30 minutes and then filtered through Whatman filter paper (No. 41). After suitable dilution, the spectrum of the final sample corresponding to 2 µg /mL of Atorvastatin and 75ug/ml of Nicotinic acid was recorded against methanol as blank.

Validation of the Method

The following validation parameters; linearity, range, accuracy, precision, LOD and LOQ were studied as per ICH guidelines[6]. The accuracy of the method was ascertained by carrying out recovery studies using Dual wave length method. The recovery study was performed to determine if there was any positive or negative interference from excipients present in the formulation. The precision of an analytical method is expressed as standard deviation and relative standard deviation of a series of measurements. It was ascertained by triplicate estimation of drug by the proposed method. LOD and LOQ were calculated by using the formula 3.3S.D/S and 10S.D/S where S.D is the standard deviation of Y-intercept and S is the slope of the calibration curve.

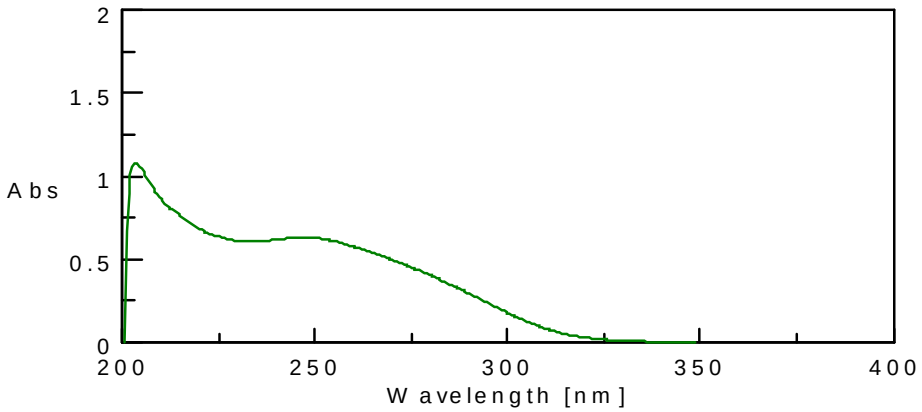

Fig3.Spectrum of Atorvastatin

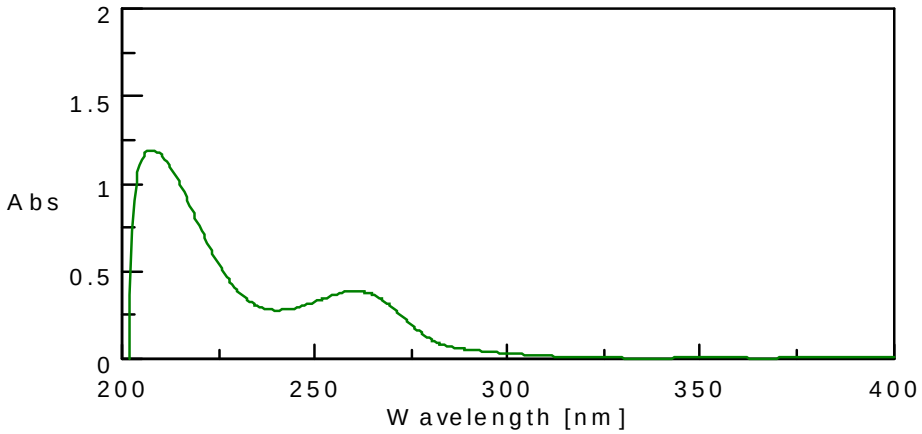

Fig4.Spectrum of Nicotinic acid

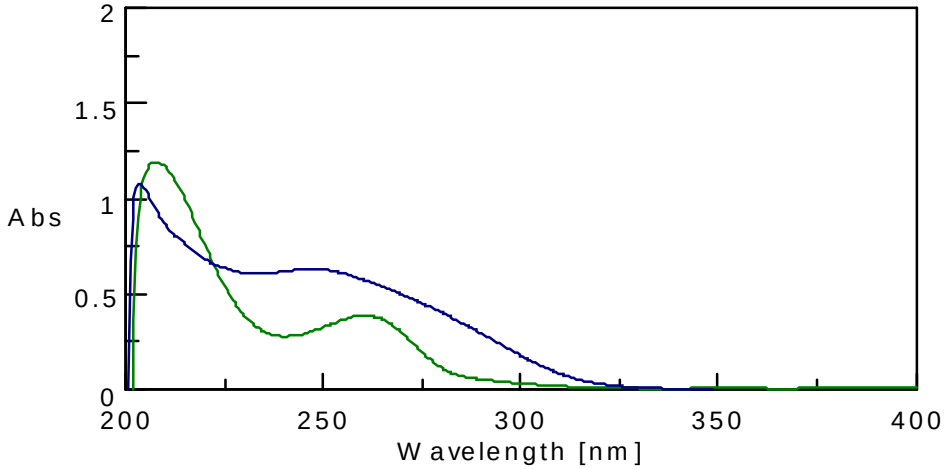

Fig5.Overlay Spectrum of Atorvastatin and Nicotinic acid

Table- 1: Validation Parameters

Parameters	**Atorvastatin**	**Nicotinic acid**
Beer's law limit (µg/ ml)	2-12 µg/ mL	10 – 60 µg/ mL
λmax	248nm	261.5nm
Regression Equation (y = mx+c)	y = 0.090x + 0.041	y = 0.042x + 0.013
Slope (m)	0.090	0.042
Intercept ®	0.041	0.013
Correlation coefficient ®	0.999	0.998
LOD	1.503	1.021
LOQ	4.555	3.095

y= mx+c, where x is concentration in µg/mL, y is amplitude (Absorbance and ΔA) for Methods, LOD= limit of Detection, LOQ= limit of Quantitation

Table-2: Analysis of Commercial Formulation

		Atorvastatin	**Nicotinic acid**
Sr. NO		**% Label claim**	**% Label claim**
1		99.3	99.0
2		99.5	99.3
3		99.3	98.3
4		99.8	98.6
5		99.0	99.3
6		98.7	99.66
	MEAN	99.26667	99.02667
	S.D	0.382971	0.502262
	%RSD	0.3858	0.50719

n= 6, S.D. = standard deviation, R.S.D. = Relative standard deviation,

Table-3: Accuracy

	Atorvastatin			**Nicotinic acid**		
	Level of % Recovery (λ_{max} = 248 nm)			**Level of % Recovery (λ_{max} = 261.5)**		
	80	100	120	80	100	120
Amount present(mg)	10	10	10	375	375	375
Amount of standard added(mg)	8	10	12	300	375	450
Total amount recovered(mg)	17.88	19.77	21.88	672.97	742.27	823.92
% Recovery	99.38	98.88	99.49	99.70	98.97	99.87
% mean	99.25			99.51		
SD	0.325115			0.478156		
%RSD	0.3275			0.4805		

SD: Standard deviation, R.S.D: Relative standard derivation (n=3).

Table-4: Precision

Drug	**Precision**	**S.D**	**%RSD**
Atorvastatin	Intra-day	0.011348	0.013
	Inter-day	0.016404	0.018
Nicotinic acid	Intra-day	0.055943	0.056
	Inter-day	0.115972	0.118

Results and Discussion

A UV-spectroscopic, multicomponent mode of analysis, method was developed for the simultaneous estimation of Atorvastatin and Nicotinic acid in tablet dosage forms. Solvent used was methanol. The absorbance was recorded at 248 and 261.5 nm respectively. The UV-Visible absorption spectra of Atorvastatin, Nicotinic acid and overlay are shown in fig 3, 4 and 5 respectively. The developed validated method is simple, rapid, precise and accurate. The newly developed method can be used for routine analysis as method for the simultaneous estimation of Atorvastatin and Nicotinic acid in tablet dosage forms. The linearity of measurement was evaluated by analyzing different concentration of standard solution of Atorvastatin and Nicotinic acid the Beer-Lamberts concentration range was found to be 2-12 µg/ mL and10 – 60 µg/ mL respectively (Table 1). In accordance with the formula given by International Conference on Harmonization (ICH), LOD is defined as 3 s/b and LOQ is defined as 10 s/b, where s is the standard deviation of replicate determination values under the same conditions as for the sample analysis in the absence of the analyte and b is the sensitivity, the slope of the calibration curve. LOD were calculated as1.503 µg/mL for Atorvastatin, and 1.021ug/mL for Nicotinic acid and LOQ were calculated as 4.55 µg/ mL for Atorvastatin, and3.095 ug/mL for Nicotinic acid (Table 1).Analysis of commercial formulation is as shown in Table2. In this study accuracy was determined by analyzing the recoveries of known amount of Atorvastatin and Nicotinic acid added into preanalyzed sample of Atorvastatin and Nicotinic acid tablet. To determine the precision of the methods, each method was studied for three levels. The percent recoveries (Accuracy) were found as 99.25and 99.51 for Atorvastatin and Nicotinic acid respectively and the developed methods had good precision (Table 3). Precision was calculated as repeatability, intra and inter day variations for Atorvastatin and Nicotinic acid, RSD was found to be less than 1 (Table 4). The robustness of the proposed methods was tested by changing wavelength range and scanning speed. None of these variables significantly affect the absorbance of Atorvastatin and Nicotinic acid that the proposed methods could be considered as robust. The ruggedness of the developed methods was tested by changing operators on different days for developed methods.

Conclusion

A new spectrophotometric method for estimation of Atorvastatin and Nicotinic acid can be estimated by using the UV Spectrophotometric methods. All the procedures have the advantages of simplicity, precision, accuracy, and convenience. Moreover, the methods use simple reagents with minimum sample preparation, which allows them to be used for routine analyses and quality-control assays of Atorvastatin and Nicotinic acid in bulk and tablets.

Acknowledgement

The authors thankful to the Mrs. Fatima Rafiq Zakaria Chairman Maulana Azad Educational Trust and Dr. M.H.G. Dehghan, Principal, Y. B. Chavan College of Pharmacy, Dr. Rafiq Zakaria Campus, Aurangabad 431 001 (M.S.), India for providing the laboratory facility.

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