AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Development and Validation of Difference Spectrophotometric Method for the Estimation of Fluvastatin Sodium and Bulk Dosage Form

Deepali S. Tuljapure[1]*, Narendra M. Gowekar[1], Savita S.Yadav[1], Aashish S.Mogale[1]

1. Department of Pharmaceutical Chemistry, Sinhgad institute of pharmaceutical sciences, University of Pune, Lonavala, Pune, Maharashtra, India.

2. Bharti Vidyapeeths' Poona College of Pharmacy,Erandwane,Pune-38

3. Sahyadri college of Pharmacy Methwade.Sangola Dist.Solapur

ABSTRACT

A new simple, accurate, precise, highly sensitive and reproducible difference spectrophotometric method for the determination of Fluvastatin in bulk and pharmaceutical dosage form is described. Difference spectroscopic method is based on the principle that Fluvastatin exhibit two different forms; in acidic and basic medium which differs in their absorption spectra. The difference spectra were obtained by reading the absorbance of Fluvastatin in 0.1N HCl in the reference cell and the absorbance of Fluvastatin in 0.1N NaOH in the sample cell and vice versa; in the difference spectrum maxima and minima were seen at 229nm and at 304nm respectively. The amplitude values were calculated, which was plotted against concentration. The method was found to be linear in the concentration range of 10-50 µg/ml. The percentage recovery was found to be between the ranges from 99.44 % to 100.45 %. The LOD & LOQ was found to be 0.215 µg/ml & 0.652 µg/ml respectively. The proposed method was statistically validated and successfully applied for analysis of Fluvastatin in capsule dosage forms. As per ICH guidelines the results of the analysis were validated statistically and were found to be satisfactory.

Keywords: Fluvastatin, Difference Spectrophotometry, Bulk, Validation.

*Corresponding Author Email: deepalitulajapure@gmail.com

Received 20 May 2011, Accepted 2 June 2012

Please cite this article in press as: Tuljapure DS *et al.*, Development and Validation of Difference Spectrophotometric Method for the Estimation of Fluvastatin Sodium and Bulk Dosage Form. American Journal of PharmTech Research 2012.

INTRODUCTION

Fluvastatin sodium is designated chemically as 7-[-3(4-fluorophenyl)-1-(1- methyl ethyl)-1H – indol-2-yl]-3, 5 dihydroxy 6-heptenoic acid monosodium salt [1] (Figure. 1). Fluvastatin sodium is official in USP [2] Fluvastatin Sodium, a fully synthetic cholesterol-lowering agent, is a competitive inhibitor of HMG-CoA reductase, which is responsible for the conversion of HMG-CoA to mevalonate, a precursor of sterols, including cholesterol [3].Several analytical methods have been reported for the analysis of fluvastatin such as few chromatographic[4,5] spectrophotometric[6,7] ,capillary electrophoresis (CE) [8,9,10] and electrochemical as differential pulse voltammetry (DPV) [11,] methods have been reported for the estimation fluvastatin sodium. Literature survey revealed that no difference spectrophotometric method is reported for the analysis of fluvastatin. The purpose of this investigation was to develop and validate a simple, rapid, sensitive, precise, accurate and specific difference spectrophotometric method for the estimation of fluvastatin sodium in bulk and formulation.

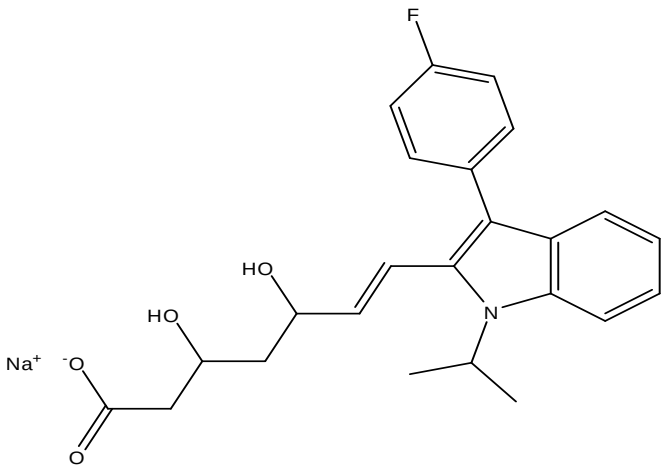

Figure1: Structure of Fluvastatin

MATERIALS AND METHODS

Drugs, Reagents and Chemicals used:

Authenticated standard of Fluvastatin was kindly gift samples from Sandoz Private Limited Mumbai. Sodium hydroxide and Hydrochloric acid were purchased from Poona chemical laboratory and Double distilled water was used throughout the analysis.

Instrumentation

A JASCO V-530 UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements. Commercially available capsules were procured from local market.

Preparation of Solution

0.1N HCl:

4.25ml of HCl analytical grade was taken in 500ml volumetric flask containing 100ml distilled water and diluted with up to the mark with same solvent and then filtered through 0.45µmembrane filter.

0.1N NaOH:

2mg of NaOH was taken in 500ml volumetric flask containing 100ml distilled water and diluted with upto the mark with same solvent and then filtered through 0.45µmembrane filter.

Standard solution:

Standard stock solution containing fluvastatin sodium was prepared by dissolving 100 mg in 100 ml of Distilled water and then diluted with 0.1N NaOH and 0.1N HCl separately to get series of dilution ranging from 10-50 mcg/ml and then absorbance recorded at 229 nm and 304 respectively against reagent blank. Calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range of 10-50µg/ml.

Procedure for capsule dosage form

Twenty Capsules, each containing 20 mg Fluvastatin were weighed. Empty the content of Fluvastatin capsule, a quantity of powder equivalent to 20 mg was weighed and transferred to 10 ml volumetric flask containing about 5 ml methanol, ultrasonicated for 10 min. Finally the volume was made up to mark with methanol. Then it was filtered through Whatman filter paper No. 42. Suitable samples were taken in 10 ml volumetric flasks, and volumes were made up with 0.1N NaOH and 0.1 HCl. The analysis was repeated in triplicate. The possibility of excipient interference in the analysis was studied.

Validation

The proposed method was validated according to ICH (Q2) B guidelines for validation of analytical procedures. As per the ICH guidelines the method validation parameters checked were Selectivity, linearity, precision and accuracy.

Selectivity

The selectivity of the method was assessed by analyzing standard drug, and pharmaceutical product, comparing the maxima and minima of the standard with that of the sample to determine whether the pharmaceutical product and excipient lead to interfere in the estimation.

Limit of Detection and Limit of Quantification:

The Limit of Detection (LOD) is the smallest concentration of the analytes that gives the measurable response. LOD was calculated using the following formula

$$LOD = 3.3\ \sigma / S$$

The Limit of Quantification (LOQ) is the smallest concentration of the analytes, which gives response that can be accurately quantified. LOQ was calculated using the following formula

$$LOQ = 10\ \sigma / S$$

Where,

σ is standard deviation of the response and

S is the slope of the calibration curve.

LOD & LOQ of fluvastatin sodium was found to be 0.215 µg/ml & 0.652 µg/ml respectively.

Linearity

Different volumes of stock solutions were suitably diluted with corresponding medium (10, 20, 30, 40, and 50 µg/ml) to get the desired concentrations. Each solution was analyzed in triplicate. The amplitude values were plotted against the corresponding concentrations to obtain the linear calibration curve.

Precision

Precision of analytical methods were expressed in relative standard deviation (RSD) of a series of measurements. The intra-day and inter-day precisions of the proposed methods were determined by estimating the corresponding responses (i.e. three concentrations / three replicates each) of the sample solution on the same day and on three different days respectively. Precision was calculated as inter-day and intra-day coefficient of variation.

Accuracy:

The accuracy of the method was determined by recovery experiments. A known amount of standard fluvastatin sodium corresponding to 80, 100 and 120% of the label claim (standard addition method) was added to pre-analyzed sample of capsule. The recovery studies were carried out in triplicate at each level.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, percent relative standard deviation and % range of error were found to be within the limits and satisfactory. All of the analytical validation parameters for the proposed method were determined according to ICH guidelines. The method was found to provide high degree of precision and reproducibility. The recovery studies showed that the results were within the limit indicating no interference. The proposed method is simple, sensitive, accurate and precise and can be successfully employed for the routine analysis of the fluvastatin in bulk drugs. Difference spectrum of fluvastatin sodium shown in figure.2

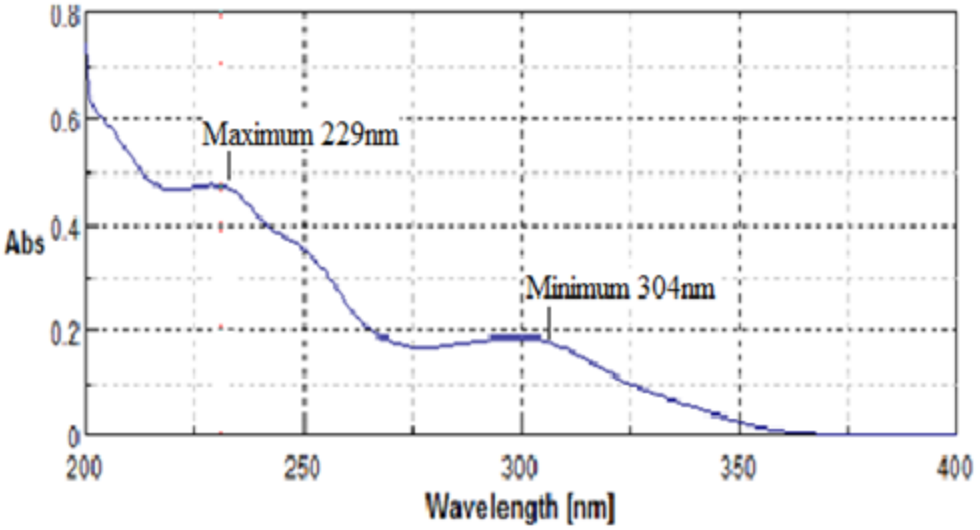

Figure.2: Difference UV spectrum of fluvastatin sodium

The method showed good linear response in concentration range of 10-50 µg/ml (r^2 =0.999) for fluvastatin sodium (Table 1). A typical calibration curve is shown in Figure.3 The characteristic and validation parameter of fluvastatin sodium as shown in (Table 2) The method was found to be precise after quantification of six replicates of fluvastatin sodium and RSD was found to be less than 2.0% (Table 3). The recovery values were 99.44-100.45% with R.S.D. of < 2 (Table 4).

Table 1: Linearity of Fluvastatin sodium by Difference Spectrophotometry

Sr.No.	Concentration Of Fluvastati (µg/ml)	Absorbance at229 nm (0.1N HCl)	Absorbance at304 nm (0.1N NaOH)	Difference in Absorbance
1	10	0.47794	0.20258	0.2754
2	20	1.0664	0.5961	0.4703
3	30	1.5970	0.9175	0.6795
4	40	2.1412	1.2269	0.9143
5	50	2.6147	1.5755	1.0392

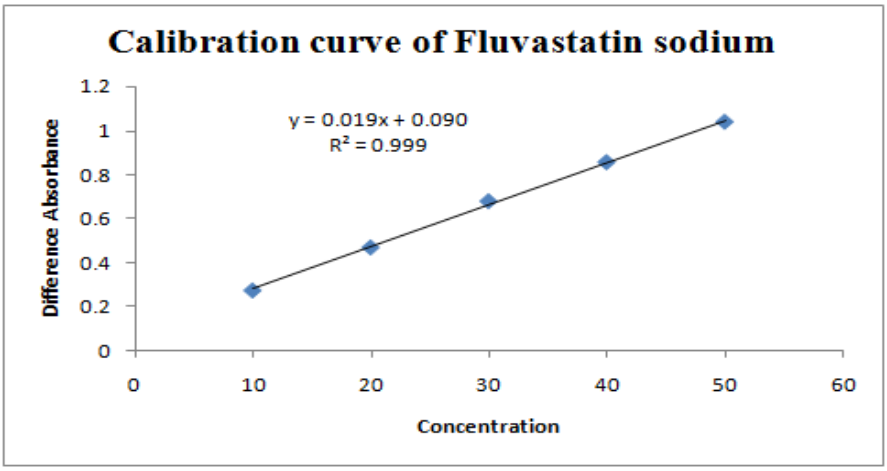

Figure. 3: Calibration curve of fluvastatin sodium

Table 2: Characteristics and validation parameters of fluvastatin sodium

Parameters	Values	
	NaOH (304nm)	HCl (229nm)
Beer's law limit (µg/ml)		
λmax (nm)	304	229
Regression equation (Y=a + bc)	y = 0.019x + 0.090	
Correlation coefficient(r^2)	0.999	
Slope(b)	0.019	
Intercept(a)	0.090	
Linearity (µg/ml)	10-50	
Accuracy range (%)	98-102%	
Precision	< 2	
LOD (µg/ml)	0.215	
LOQ (µg/ml)	0.652	

Table 3. Intra-day and inter-day precision of proposed method

	Intra-day precision			Inter-day precision		
	Observed conc. (µg/ml)	S.D.	% R.S.D.	Observed conc. (µg/ml)	S.D.	% R.S.D.
20	20.23	0.818	0.808	20.56	0.633	0.615
30	31.07	0.883	0.853	30.92	0.787	0.763
40	40.07	0.547	0.546	40.61	0.628	0.618

Table 4. Recovery study of fluvastatin sodium

Drug	Amount of standard spiked (µg/ml	Amount of standard recovered (µg/ml)	Recovery (%)	% R.S.D.
Fluvastatin	18	17.9	99.44	0.18
	20	20.01	100.05	0.32
	22	22.1	100.45	0.15

Mean recovery (± S.D) = 99.98 ± 0.09

CONCLUSION

The developed method was found to be simple, accurate, precise, highly sensitive, reproducible and inexpensive. The proposed method was found suitable for determination of fluvastatin sodium in bulk drug and marketed solid dosage formulation without any interference from the excipients. The method is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine analysis of fluvastatin in bulk drug. Its advantages are low cost of reagents, speed and simplicity of sample treatment, satisfactory precision and accuracy.

ACKNOWLEDGMENT

Authors are grateful to the Dr. S. B. Bhise, Principal of Sinhgad Institute of Pharmaceutical Sciences, for providing necessary facilities to carry out the research work.

REFERENCES

1. Merck & Co. Inc., The Merck Index, 13th ed., Whitehouse station New Jersey; 2001:747–748.
2. United States Pharmacopoeia USP 24/NF 25, US Pharmacopoeia Convention Inc, USA; 2000: 2186-2187.
3. Rang H.P., Dale M.M. Pharmacology 5th ed., Elsevier a division of Reed Elsevier India Pvt. Ltd. 2003:309-311.
4. Saminathan J, Sankar ASK, Anand K. Validated RP-HPLC method for fluvastatin sodium in bulk and its dosage form. J Pharm Sci Res 2009; 1(3):90-96.
5. Marianne A. Mahrouse Spectroscopic and chromatographic determination of fluvastatin sodium in presence of its acid degradate. Int J PharmTech Res 2010;2(1):875-898.
6. Saminathan J, Sankar ASK. Simple UV Spectrophotometric Method for the Determination of Fluvastatin Sodium in Bulk and Pharmaceutical Formulations. E-J Chemistry 2009;6(4):1233-1239.
7. Safwan Ashour, Mahmoud Bahbouh, Mouhammed Khateeb. Kinetic Spectrophotometric Determination of Fluvastatin in Pharmaceutical Preparations. Int J Biomed Sci 2010;6(1):1-26
8. Ozkan SA and Uslu B. Electrochemical study of fluvastatin sodium – analytical application to pharmaceutical dosage forms, human serum and simulated gastric juice. Anal Bioanal Chem 2002; 372(4):582 - 586.
9. Ak DD, Kircali K, Tuncel M, Aboul-Enein HY. Validated analysis of fluvastatin in a pharmaceutical capsule formulation and serum by capillary electrophoresis. Biomedical Chromatography 2001; 15(6):389–392.
10. Yan JL. Determination of fluvastatin sodium by differential pulse voltammetry. Pak J Biol. Sci., 2006, 9(11), 2156 – 2158.
11. Validation of Analytical Procedure: Text and Methodology Q2 (R1), ICH Harmonized Tripartite Guideline 2005:1-13.