Oriental Journal of Chemistry Vol. **26**(2), 589-593 (2010)

Visible spectrophotometric determination of Rosuvastatin in bulk and pharmaceutical formulations

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(Received: March 16, 2010; Accepted: April 20, 2010)

ABSTRACT

Two simple and sensitive methods have been developed for the estimation of rosvastatin in bulk and in pharmaceutical dosage forms. Method A is based on the oxidative coupling of rosvastatin with MBTH in presence of oxidant cerric ammonium sulphate and the λmax of the colored species was found to be 658 nm. Method B is based on the formation of co-ordination complex between rosvastatin and cobalt thiocyanate and the blue colored complex formed is extracted into nitrobenzene which posses characteristic absorption maxima 626 nm. The colored species obeyed Beer's Law in the concentration range 2-14 µg/mL and 50-250 µg/mL for method A and method B respectively. Marketed pharmaceutical preparations were analyzed and the results obtained by the proposed methods were in agreement with labeled amount. Recovery studies were carried out by standard addition method. The results of analysis have been validated by application of statistical principles to the data obtained and the methods were found to be satisfactory. Both the proposed methods were simple, rapid, and economical and can be used for routine analysis of rosvastatin in bulk and pharmaceutical dosage forms.

Key words: Rosuvastatin, Cobalt thiocynate, 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH).

INTRODUCTION

Rosuastatin is a member of the drug class of statins, used to treat high cholesterol and related conditions, and to prevent cardiovascular diseases. Chemically rosuvastatin is (3R,5S,6E)-7-[4-(4-Flourophenyl)-2-(N-methyl methane sulphonamido) -6-(propan-2-yl) pyrimidin-5-yl]-3,5-dihydroxy hept-6- enoic acid. Rosuvastatin is a synthetic statin that represents an advance on the pharmacological and clinical properties of other agents in this class. Relative to other statins, rosuvastatin possesses a greater number of binding interactions with HMG-CoA reductase and has a high affinity for the active site of the enzyme. Rosuvastatin is relatively hydrophilic and is selectively taken up by, and active in, hepatic cells. Rosuvastatin has the longest terminal half-life of the statins and is only minimally metabolized by the cytochrome P450 (CYP450) enzyme system with no significant involvement of the 3A4 enzyme. Consistent with this finding is the absence of clinically significant drug interactions between rosuvastatin and other drugs known to inhibit CYP 450 enzymes. In patients with hypercholesterolemia, rosuvastatin 10–40 mg has been shown to reduce low-density lipoprotein cholesterol (LDL-C) levels by 52–63%, as well as increase high-density lipoprotein cholesterol (HDL-C) levels by up to 14% and reduce triglycerides (TG) by up to 28%. Studies have

shown that rosuvastatin is superior to atorvastatin, simvastatin and pravastatin in reducing LDL-C and favorably modifying other components of the atherogenic lipid profile. The significant decreases in LDL-C with rosuvastatin treatment should help to improve attainment of lipid goals and reduce the requirement for dose titration. In addition, the effects of rosuvastatin on HDL-C and TG levels will be of benefit in treating patients with abnormalities such as mixed dyslipidemia and the metabolic syndrome. Rosuvastatin is well tolerated, with a safety profile comparable with that of other currently available statins formulations. The structural formula of rosuvastatin is as follows; as shown in Fig.1.

Few analytical methods [1-6] are available in the literature which includes UV, extractive, simultaneous spectrophotometric and HPLC for the analysis of rosuvastatin but there is no simple and sensitive visible spectrophotometric method. Therefore the principle objective of this study is to develop two simple, sensitive and rapid visible spectrophotometric methods for determination of rosuvastatin in bulk and pharmaceutical formulations.

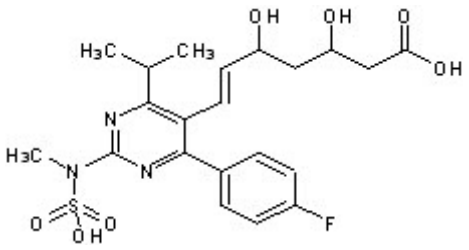

Fig. 1: Structure of Rosvastatin

EXPERIMENTAL

Materials and Methods

Instrument

A Shimadzu UV-1800 double beam UV-Visible spectrophotometer with 10 mm matched quartz cells was used. Pharmaceutical grade rosuvastatin was provided by M/S Aurobindo Pharmaceuticals, Ltd., Hyderabad, India. All the chemicals used were of analytical grade, procured from S.D.fine chemicals Ltd., Mumbai, and distilled water was used through out the work. For the present study 2 brands of commercial tablets designated as Tablet-1 and Tablet-2 containing 5 mg and 10 mg of rosuvastatin respectively, procured from the local drug store.

Preparation of Reagents

3-Methyl-2-benzothiazolinone hydrazone hydrochloride (0.2 % w/v): 200 mg of MBTH was dissolved in 100 mL of distilled water.

Cerric ammonium sulphate (1 % w/v)

1 gm of Cerric ammonium sulphate was dissolved in 0.1 N sulphuric acid and the volume was made upto 100 mL.

Cobalt thiocyanate solution

Prepared by dissolving 7.25 gm of cobalt nitrate and 3.8 gm of ammonium thiocyanate in 100 mL of distilled water.

Buffer solution (pH 2.0)

Prepared by mixing 25 mL of potassium chloride (0.2 M) and 13 mL of hydrochloric acid (0.2 M) and made upto 100 mL with distilled water and pH was adjust- ted to 2.

Nitrobenzene

Analytical grade nitrobenzene was used.

Procedure for Assay

Preparation of standard drug solution

100 mg of rosuvastatin was accurately weighed and dissolved in 100 mL distilled water (1 mg/mL) and from this working standard solution was prepared by taking 10 mL of standard drug solution into 100 mL volumetric flask and made up to 100 mL with distilled water (100 µg/mL) which was used for both the methods.

Analysis of pure sample

Method A

Volumes of standard rosuvastatin (0.2-1.4 mL of 100 µg/mL) were transferred into a series of 10 mL volumetric flasks the total volume in each flask was brought to 3 mL with distilled water. Then 1 mL of MBTH and 1mL of cerric ammonium sulphate solutions were added and the flasks were kept aside for 5 min at room temparature.The solutions in each flask was made up to the mark with distilled water and absorbances were measured at 658 nm against the reagent blank. The optimum conditions are shown in the Table 1.

Method B

Aliquots of standard rosuvastatin (0.5-2.5 mL of 1mg/mL) were delivered into a series of 60 mL separating funnels. Then 2mL of pH 2.0 buffer and 3 mL of cobalt thiocyanate solutions were added and the total volume of aqueous phase in each funnel was adjusted to 10 mL. To each separating funnel 10mL of nitro benzene was added and the contents were shaken for 2 min. Then the two phases were allowed to separate and the absorbance of the separated nitrobenzene layer was measured immediately at 626 nm against the reagent blank. The optimum conditions obtained are reported in Table-1.

Analysis of pharmaceutical formulations

Twenty tablets were taken and grounded to fine powder. An amount of tablet powder equivalent to 25 mg of active ingredient was weighed accurately and transferred into 25 mL of volumetric flask. Then dissolved with 10 mL of distilled water and filtered through whatmann filter paper and volume was made up to 25 mL with distilled water. The solution was assayed as under the assay procedure by method A and method B.

RESULTS AND DISSCUSSION

The absorbance spectra of the reaction products in method A and method B show characteristic λ_{max} values. The reaction conditions were established by variation of one variable at a time (OVAT). In method A, MBTH on oxidation with Ce (IV) loses two electrons and one pro ton to form an electrophillic intermediate, which is the active coupling species. The active species reacts with drug by electrophilic attack on the most nucleophilic site of drug and a colored complex is formed, which has absorption maxima at 630 nm.

The method B is based on the formation of co-ordination complex between drug and cobalt thiocyanate. In order to establish optimum sensitivity of the complex formed between Rosuvastatin (electron donor) and the central neutral atom of cobalt thiocyanate, the author has studied the various parameters such as type of buffer, shaking time, volume of cobalt thiocyanate, stability of the colored complex formed, for a series of solution varying one and fixing the other parameters. The method was validated according to ICH guidelines[7]. The optical characteristics such as Beer's law limit, molar absorbivity, and other parameters for the proposed method are summarized in Table-2. The linearity, regression equation of absorbance on concentration gave the equation, Y= ax+b with a correlation coefficient (r) 0.998 for method A and 0.999 for method B which indicates a good linearity between absorbance and concentration in the range 2-14 µg/mL method A and 50-250 µg/mL for method B. The value of percentage RSD is less than 1% and low range of error confirm the high degree of precision and accuracy of the proposed method. The assay results obtained by proposed methods were found to be in good agreement with the labeled amounts (Table-3). Recovery studies were carried out by addition of standard drug solution to the preanalyzed sample. Results of recovery studies were found to be satisfactory and are presented in Table-3.The percentage recovery values, which are close to 100%, indicate the reproducibility of the methods and absence of interference of the exicipients present in the formulation. The values obtained by the proposed methods were compared with the reference method statistically by means of F and T-tests and found that they did not differ significantly at the 95% confidence level.

Table 1: Optimum conditions and results of the proposed method for the determination of Rosvastatin for method A and method B

Reagent	Method A	Method B
Drug solution taken (µg/mL)	2-14	50-250
Volume of pH 2 buffer (mL)	-	2.0
Volume of CAS solution (mL)	1.0	-
Volume of reagent employed (mL)	1.0	3.0
λ max (nm)	658	626

Table 2: Optical characteristics and precision of the proposed methods

Parameter	Method A	Method B
λ max	658	626
Beer's law limits(mcg/mL)	2-14	50-250
Sandell'ssensitivity (mcg/cm^2/0.001A.U)	0.0147	0.2493
Molar Absorptivity(L mol^{-1}cm^{-1})	0.3269×10^6	0.0193×10^6
Correlation coefficient(r^2)	0.998	0.999
Regression equation (y=b+ax)**	0.06542 x + 0.00732	0.00203 x + 0.19480
Slope(a)	0.06542	0.00203
Intercept(b)	0.00732	0.19480
Range of errors*		
Confidence limit with 0.05 level	0.19680.2912	0.45150.6680
Confidence limit with 0.01 level		
% Relative Standard deviation*	0.2354	0.540

** y is the absorbance and x is the concentration in µg/mL

*Average of six determinations

Table 3: Assay and recovery of rosvastatin in pharmaceutical formulations

Pharmaceutical formulations	Labeled amount found(mg)	Amount found in[a](mg) using proposed methods ±S.D		Found by reference method [c] ±S.D	%Recovery by proposed methods[b] ±S.D	
		A	B		A	B
Tablet-1	5.0	5..011 ±0.0211 F=0.9638 T=0.8796	5.0 ±0.0216 F=1 T=0.4817	5.01 ±0.0216	100.04 ±0.1143	99.90 ±.2549
Tablet-2	10	9.995 ±0.0275 F=0.4029 T=0.1025	10.048 ±0.1108 F=0.0477 T=0.3040	10.03 ±0.0409	100.06 ±0.093	99.80 ±0.2236

[a]Average ± stadard deviation of eight determinations, T and F-values refer to comparison of proposed method with reference method .Theoretical values at 95% confidence limits T=2.365 and F=4.88.

[b] Recovery of 5 mg added to the pre analyzed pharmaceutical formulations (average of three determinations).

[C] U.V method using methanol as solvent at ë max 244nm.

CONCLUSION

The authors conclude that the proposed spectrophotometric methods for the estimation of Rosuvastatin are simple, convenient, accurate, precise and reproducible. The methods do not require any separation of the soluble excipients in pharmaceutical preparations. The methods can be used for routine analysis of rosuvastatin in bulk as well as in pharmaceutical formulations.

ACKNOWLEDGEMENTS

The authors are thankful to M/S Aurobindo Pharmaceuticals, Ltd., Hyderabad, India for sending rosuvastatin as gift samples and to the Principal and management of Sarojini Naidu Vanitha Pharmacy Maha Vidyalaya, Hyderabad for their constant support and encouragement for this work.

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