SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF ROSUVASTATIN IN BULK DRUG AND ITS DOSAGE FORM

B.Suvartha Rani

III BSc,BZC. CH.S.D.ST.Theresa's College for Women (Autonomous)
Eluru, Andhra Pradesh, India

K.J.Subhashini

MSc.B.Ed, CH.S.D.ST.Theresa's College for Women (Autonomous)
Eluru, Andhra Pradesh, India
Email: khandavalli.subha@gmail.com

Received: Jul. 2019 Accepted: Aug. 2019 Published: Sep. 2019

Abstract: Simple, accurate, precise, sensitive and highly selective spectrophotometric methods were developed for the estimation of rosuvastatin. The estimation of rosuvastatin was carried out by various solvents like ethanol (method I) at 236 nm, 2-propanol (method II) at 230nm and conc.H_2SO_4 (method III) at 415 nm. And these methods were found to be linear in the range of 1-6µg/ml, for method I and II and 10-60µg/ml for method III. And **B**eers law range were found to be 1-15µg/ml, 1-15µg/ml, and10-250µg/ml, and with mean recovery of 97.5 %, 97.5 % and 103.5 % of rosuvastatin for methods I, II and III respectively. The method developed found to be accurate and was validated according to the guidelines of ICH. Thus the proposed method can be successfully applied for simultaneous determination of rosuvastatin and in routine analysis work.

Keywords: Rosuvastatin, Spectrophotometre, Validation, Beer's Law.

Introduction: Rosuvastatin butanoic acid, 2, 2-dimethyl-, 1, 2, 3, 7, 8, 8a-hexahydro-3, 7-dimethyl-8- [2(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester, is a lipid-lowering agent that is derived synthetically from fermentation products of Aspergillus terreus. After oral ingestion, it is hydrolyzed to corresponding b-hydroxy acid leading to the inhibition of 3-hydroxy 3-methyl glutaryl – coenzyme A. (HMG- CoA) reductase. It is responsible for catalyzing the conversion of HMG CoA to mevalonate. It is an early and rate limiting step in cholesterol biosynthesis. Ezetimibe (EZ), 1- (4-Fluorophenly) – 3 (R) - [3-(4-fluorophenyl) - 3 (S) hydroxyl propyl]-4 (S) – (4-hydroxy phenyl) – 2 azetidinones is a therapeutically beneficial drug that works by inhibiting the protein transporters on small intestinal microvilli, which brings about this active transport of cholesterol. In addition, it also inhibits phytosterol absorption[3]. This distinct mechanism of action results in a overall cholesterol lowering effect when used together with statins

inhibits cholesterol synthesis by liver. This statin may be determined by several methods including gas chromatography–mass spectrometry (GC–MS)[5], liquid chromatography with UV detection (LC–UV)[6-8]. Literature survey revealed that there is few UV-visible methods have been reported.

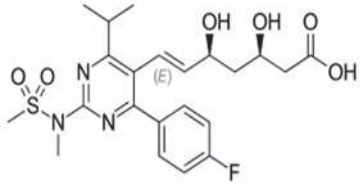

Fig. 1: Chemical Structure of Rosuvastatin

Experimental:

Instrumentation: The present work was carried out on UV- visible spectrophotometer having double beam detector configuration. The absorption spectra of test solution and the reference were carried out in a 1 cm quartz cell over the range of 200-800 nm.

Chemicals: All the chemicals used are of analytical grade.

Preparation of Standard Solution: A stock solution was prepared in methanol as 1 mg/ml. This solution is diluted with methanol to obtain required concentrations.

Preparation of Sample Solutions: 10 tablets were weighed and powdered. An amount equivalent to 100mg of rosuvastatin was weighted and transferred to the 100ml volumetric flask. To it 50 ml of methanol was added and shake until the drug is dissolved. The solution was filtered and made up to 100ml with ethanol. This solution was suitably diluted to obtain the required concentration. The same procedure is followed in other methods with respective solvents.

Procedure: Aliquots of working standard solution of rosuvastatin 1-6ml (100µg/ml) were transferred into a series of 10ml volumetric flask. The volumetric flasks are made up to the volume with the respective solvents (i.e. ethanol (method-I), 2-isopropanol (method-II), conc.HCL (method-III). Then the absorbance of the samples are measured spectrophotometrically at 236nm for method using methanol, at 240nm for method using 2-propanol and at 415nm for method using conc.H_2SO_4 against a reagent blank.

Validation: Validation of the developed method was done according to ICH guideline

Linearity: The linearity of the method is its ability to elicit test results that are directly proportional to the concentration of the analyte in samples. The calibration curve was taken in the range of 4-14 µ/ml at the respective λmax for method I and Method II, and 10-60 µg/ml. The correlation coefficient of the linearity were found for three methods and reported in table No.1

Precision and Accuracy: The precision of the analytical method was determined by assaying a sufficient number of aliquots of a homogeneous sample to be able to calculate statistically valid estimate of % Relative Standard Deviation (%RSD). Intermediate precision was done to express within laboratory variation, on different days. Five replicates of 12 µg/ml concentration of the working standard mixture and sample solution were analyzed %RSD and was found to be less than 2%. Accuracy were determined for three methods and results were reported in table no.2

Specificity: Results of sample tablet solution showed that there is no interference of the inert substance when compared with the working standard solution. Thus, the method was said to be specific

Result and Discussions: The optimum conditions for methods I, II and III have been established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of products on the absorbance of the sample and colored species. Beer's law limits, molar absorbivity, Sandal's sensitivity, % range of error and % relative standard deviation are summarized in Table I. The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation coefficient (r)obtained from different concentrations are given in Table I The results showed that these methods have reasonable precision.

To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical dosage forms and the mixtures were analyzed by the proposed methods. The percentage recoveries are given in Table - 2. The interference studies revealed that the common excipients and other additives that are usually present in the injection dosage forms did not interfere at their regularly added levels.

Conclusion: The proposed spectrophotometric methods were accurate, precise and reliable for the measurement of SIM in dosage form. The developed spectrophotometric method was validated for estimation of SIM using linearity, range, accuracy and precision. The RSD for all parameters was found to be less than one, which indicates the validity of method and assay results obtained by this method are in fair agreement. The developed method can be used for routine quantitative estimation of SIM in pharmaceutical Preparation.

Table 1: Optical Regression Characteristics, Precision and Accuracy of the Proposed Methods

Parameter	Method -I	Method - II	Method - III
λmax (nm)	236nm	240nm	415nm
Beer's law limits (μg.ml^{-1})	0.5-15μg/ml	0.5-15μg/ml	10-250μg/ml
Molar absorbivity (lit . mole^{-1},cm^{-1})	125.4x10^3	137.94 x 10^3	8.36x10^3
Sandell's sensitivity (μg.cm^{-2}/0.001 abs.unit)	0.0033	0.00303	0.05
Regression equation (y*=a+bx) slope (b)	0.0601	0.0662	0.00398
Intercept (a)	2.7 x10^{-4}	-1.9 x10^{-4}	1.3 x10^{-4}
Correlation Co-efficient (r)	0.995	1.05	0.994
R.S.D.	0.488	0.85	0.491
Range of error** (confidence limits) 0.05 level	0.041	0.0714	0.041
0.01 level	0.60512	1.054	0.60884

Y = a+ bx where x is the concentration of rosuvastatin μg/ml and Y is the absorbance at the respective λ max.

**Average of six determinations considered.

Table 2: Assay of Rosuvastatin in Pharmaceutical Formulation

Formulation	Labeled amount in mg	Amount found by proposed MethodM_I	Amount found by proposed Method M_{II}	Amount found by proposed MethodM_{II}	%Recovery* proposed by methods M_I	%Recovery* proposed by methods M_{II}	%Recovery* proposed by methods M_{III}
Tablet-I	10	10.13	9.67	9.6	101.3	96.7	96
Tablet-II	10	9.67	9.47	10.9	96.7	94.7	109
Tablet-III	10	9.47	10.13	10.4	94.7	101.3	104

R. Reference was UV method developed in the laboratory.

*Recovery amount is the average of six determinations

References:

1. Merck index, Maryadele J.O.Neil Edu. In: 13th ed. Published by Merck Research lab., NJ, USA. 2001, 868.
2. Ochiai H, Uchiyama N, Imagaki K, Hata S, Kamei T. Determination of rosuvavastatin and its active metabolites in human plasma by column-switching high performance liquid chromatography with fluorescence detection after derivatization with 1-bromoacetylpyrene. J Chromatogram B Biomed Sci. 1997; 694(1):211-217.
3. Merck index, Maryadele J.O.Neil Edu. In: 13th Ed. Published by Merck Research Lab., NJ, USA.2001, 148.
4. Darkes MJ, Poole RM, Goa KL. Ezetimibe. Am J. Cardio Vasc.Drugs. 2003; 3(1): 67-76.

5. Morris MJ, Gilbert JD, Hsieh JY,Matuszewski BK, Ramjit HG, Bayne WF. Determination of the HMG- CoA reductase inhibitors rosuvastatin, lovastatin and pravastatin in plasma by gas chromatography/chemical ionization mass spectrometry. Biol Mass Spectrom. 1993; 22(1):1-8.174
6. Tan L, Yang LL, Zhang X, Yuan YS, Ling SS. Determination of rosuvastatin in human plasma by high performance liquid chromatography. Se Pu. 2000; 18(3):232-234.
7. Curlucci G, Mazzeo P, Biordi L,Bologna M. Simultaneous determination of rosuvastatin and its hydroxy acid form in human plasma by high performance liquid chromatography with UV detection. J Pharm Biomed Anal. 1992; 10(9):693
8. Wang L, Asgharnejad M. Second-derivative UV spectrometric determination of rosuvastatin in tablet dosage form. J Pharm Biomed Anal. 2000; 21(6):1243-1248.

***