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Analytical Method Development And Validation Of Rosavastatin Calcium In Pure Form And Pharmaceutical Formulations By UV Spectroscopy

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Abstract: A simple, specific and economic spectroscopic method has been developed for the estimation of Rosavastatin calcium in bulk and tablet dosage form. In the developed method water was used as the solvent. The absorption maximum of the drug was found to be 241nm. The drug follows a linear Lambert-Beer law relationship with respect to the drug concentration in the range of 5-30µg/mL, with linearity coefficient of 0.9998. Statistical analysis and recovery studies validated the method. The proposed method was found to be rapid, precise and accurate and can be applied for the routine estimation of Rosavastain Calcium in the laboratory.
Key Words: Spectroscopy**,** Rosavastatin Calcium, Water.

INTRODUCTION

Rosuvastatin calcium is chemically bis [(E)-7 [4-(4- fluorophenyl)-6 isopropyl-2-[methyl (methylsulphonyl) amino] pyrimidin-5-yl] (3R, 5S) -3, 5-dihydroxyhept-6-enoic acid] Calcium salt. It is a lipid lowering drug. It inhibits the enzyme 3-hydroxry- 3-methyl glutaryl coenzyme A (HMG-CoA) reductase, the rate limiting enzyme that converts HMG-CoA to mevalonate; a precursor of cholesterol and thereby checks the synthesis of cholesterol. It is used in the treatment of hypercholesterolemia and dyslipidemia[1, 2].It is used to reduce the amounts of LDL cholesterol, total cholesterol, triglycerides and apolipoprotein B in the blood. Rosuvastatin calcium also modestly increases the level of HDL cholesterol in the blood. These actions are important in reducing the risk of astherosclerosis, which in turn can lead to several cardiovascular complications such as heart attack, stroke and peripheral vascular disease[3]. A survey of literature showed few UV spectrophotometric[4-5], HPLC[6], HPTLC[7], chromatography stability indicating method[8, 9], LC-MS method[10] are available for the estimation of Rosuvastatin calcium in pharmaceutical preparation and in biological fluids.

In view of the above fact, some simple analytical methods are in need for its quantitative estimation. So in the present study, a simple, specific, precise, economical, accurate and validated spectroscopic method has been developed for the estimation of Rosuvastatin calcium in bulk and tablet dosage form, using water as the solvent system.

EXPERIMENTAL

Instrumentation

All spectral and absorbance measurements were made on a Shimadzu UV/visible double beam spectrophotometer (model 1700) with 1cm matched quartz cells were used for all the spectral measurements. Shimadzu-AX-200 electronic balance was used for weighing the samples.

Materials and Reagents

Class 'A' volumetric glassware were used. Ultrasonicator was used in the initial steps of extraction. Whatmann filter paper No.41 was used to filter the solution. Double distilled water was used. The pharmaceutical grade of Rosuvastatin calcium was kindly gifted from by Ami Life Science, Baroda, Gujarat. Two commercial formulations, Fenovas (*Micro Labs*) and Novastat-TG 10 (*Lupin*) were purchased from a local pharmacy**.**

Preparation of standard solution of Rosuvastatin calcium

Accurately weighed 100mg of Rosuvastatin calcium was transferred to 100mL volumetric flask. Drug was then dissolved and made up to the volume to 100mL with distilled water. It was further diluted to a concentration of 100µg/mL with distilled water, which was then used as the stock solution for the further dilutions.

Determination of wavelength of maximum absorbance of Rosuvastatin calcium

The above prepared solution was further diluted to 10µg/mL solution with distilled water and the absorbance of standard Rosuvastatin calcium was scanned in the range 190-400nm against distilled water as blank. The λ_{max} of drug was found to be 241 nm (fig.1).

Preparation of calibration curve for Rosuvastatin Calcium

Dilutions of the standard Rosuvastatin calcium solution were prepared (0.5,1.0,1.5,2.0,2.5 and 3.0mL) diluted to 10mL using distilled water in the range of 5 to 30µg/mL in a series of six dilutions in volumetric flasks of capacity 10mL.The absorbance of the solutions were measured at 241nm using distilled water as blank (fig.2).

Estimation of from tablets Rosuvastatin Calcium

Twenty tablets of Rosuvastatin calcium of marketed formulations were taken and the average weights of these tablets were determined. Then these tablets were finely powdered and triturated well. A quantity of powder equivalent to 10mg of Rosuvastatin calcium was transferred to 100mL volumetric flask and dissolved the drug by sonication with distilled water and there after the volume was made up to 100mL with the same. The solution was filtered through whatmann filter paper No.41. From the filtrate, further dilutions were made with distilled water to obtain a concentration range of 5-30µg/mL. The absorbance of this solution was measured at 241 nm using distilled water as blank. The amount of drug present in the tablet was calculated using the standard calibration curve of the drug. The experiments were repeated six times to check its reproducibility.

Recovery studies and validation of the method according to ICH guidelines[11, 12]

Precision of the newly developed method was studied by carrying out intraday, interday analysis and expressed as percent relative standard deviation. Specificity of the method was checked by adding few excipients with in the range as specified in standard literature which are usually added in the preparation such as diluents, lubricant *etc*. to the preanalyzed samples. The absorbance of the solution so obtained after addition of excipients was then measured, compared with that of the absorbance of preanalyzed solution and the specificity was expressed in terms of percent interference, which was found to be less than 2% .Limit of detection (LOD) and limit of quantification (LOQ) were studied based on standard deviation of the response and slope curve. Recovery studies were carried out by adding known amount of pure drug to the analyzed samples of the tablet powder and the mixture was reanalyzed for the drug content using the proposed method. The results of recovery were found to be satisfactory.

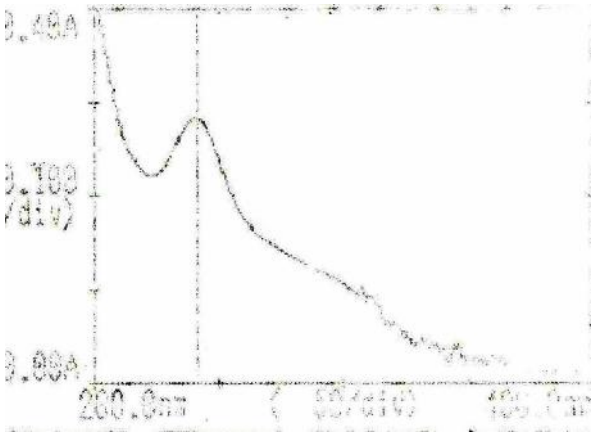

Fig.1.Spectra of Rosavastatin calcium (RC) at 241nm

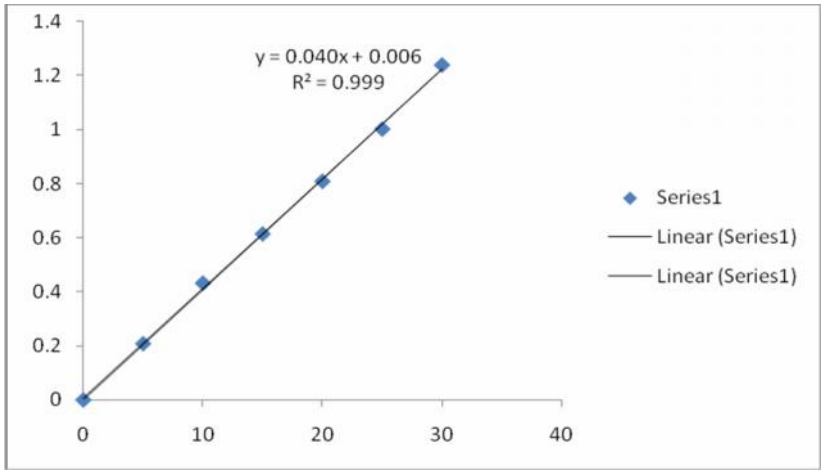

Fig.2. Calibration curve for Rosavastatin calcium at 241 nm by UV Spectroscopy.

RESULTS AND DISCUSSION

The proposed method for determination of Rosuvastatin calcium showed molar absorpitivity of 4.12 × 10^5l/mol/cm. The linear regression of absorbance on concentration obtained the equation y=0.040x + 0.00660 ($R^{2\ =}$ 0.9998) shown in Table 1. Statistical analysis of commercial formulations is presented in Table 2. The recovery experiments indicated the absence of interference from the commonly encountered pharmaceutical additives and excipients Table 3.

Significantly low values of standard deviation, standard error and coefficient of variation indicates the precision of the proposed method. Theses values are compared with the theoretical values of 100 percent by means of unpaired students‘t’ test Table 2.As the calculated ‘t’ values were less than theoretical ‘t’ values, it is calculated that the results of analysis were in good agreement for each brand of tablet. To test the accuracy and reproducibility of the proposed method, recovery experiments were performed adding known amount of pure drug to the analyzed samples and these samples was reanalyzed by the proposed method. The percentage recovery was close to 100% for both methods. The results are summarized in Table 2.The method were found to be good evidenced by low standard deviation.

Table 1: Optical characteristics, precision and accuracy of the proposed methods.

Parameter	Rosuvastatin calcium
Detection wavelength (nm)	241 nm
Beer's law limits (µg/ml)	5-35
Molar absorpitivity ($L\ mol^{-1}\ cm^{-1}$)	4.12×10^5
Regression equation (y*)	y = 0.040 x + 0.006
Slope (b)	0.040
Intercept (a)	0.006
Correlation coefficient (R^2)	0.9998
Precision (%RSD)	0.273
Repeatability	1.07
Intraday	0.247
Interday	0.351
Limit of detection (µg/ml)	0.31
Limit of quantification (µg/ml)	0.95

- Y = bx+ a where x is the concentration of Rosuvastatin calcium in µg/ml and Y* is the absorbance unit

Table 2: Statistical Analysis of Rosuvastatin calcium

Brand name	Label claim(mg)	Amount Estimated (mg/tab) *	SD*	COV*	SE*	't'cal*	't'the*
Fenovas	10	9.70	0.806	0.1214	0.0072	0.6516	3.312
Novastat-TG 10	10	9.84	0.044	0.1246	0.0057	1.4538	

*Mean of six determinations. *Theoretical 't' values were calculated at 95%confidence level with (n-1) degrees of freedom 't'(0.025,5)=3.312. SD=Standard deviation, COV=Coefficient of variance and SE=Standard error.

Table 3: Recovery Studies of Rosavastatin calcium

Brand name	% Recovery ± SD*
Fenovas	100.80±0.67
Novastat-TG 10	100.36±0.75

* Mean of Six determinations.

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