Research Article

Quantitative Determination of Rosuvastatin Calcium and Niacin Individually and Combined Tablet Dosage Form by Using UV-VIS Spectrophotometer

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ABSTRACT

Two simple, specific, accurate and economical UV-Spectrophotometric methods were developed and validated for quantitative determination of Rosuvastatin and niacin in combined tablet dosage form. Method I is based on the simultaneous equation and method II is based on the absorbance ratio method. The solvent used to develop the method was Double distilled water. The absorbance maxima were found to be at 241and 262nm in water for the Rosuvastatin and niacin respectively. Beer's law is obeyed in the concentration range 5-40µg/ml with correlation coefficient within range of 0.998 for both the drugs. The accuracy of the method was checked by recovery experiment performed at three different levels i.e., 50%, 100% and 150%.The % recovery was found to be 98-105% for Rosuvastatin and niacin respectively. The low values of % R.S.D are indicative of the accuracy and reproducibility of the method. The % R.S.D value less than 2 indicate that the method is precise. The above method was a rapid and cost-effective quality-control tool for routine analysis of pharmaceutical dosage form.

Keywords: Simultaneous equation method, absorbance ratio method, Rosuvastatin and niacin

Received 3 May 2015 Received in revised form 25 May 2015 Accepted 27 May 2015

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INTRODUCTION

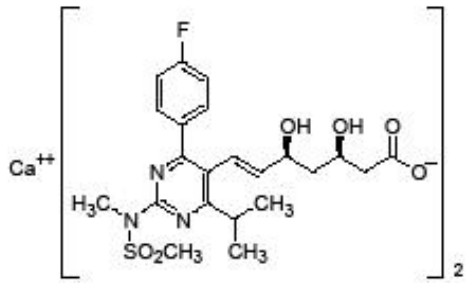
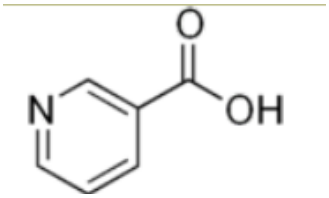
Rosuvastatin (statin) HMG-CoA reductase inhibitor [1]. and niacin (nicotinic acid) are used, in the primary and secondary prevention of coronary heart disease, carotid artery disease and other atherosclerotic vascular diseases. In US guidelines, the lowering of low-density lipoprotein cholesterol (LDL-C) is the primary goal of lipid-modifying therapy in patients with atherosclerotic disease and those at risk for atherosclerotic disease due to dyslipidaemia. However, in patients with primary hyperlipidemia [2] and atherogenic dyslipidaemia [3] and (i.e. those with high triglyceride levels, low high-density lipoprotein cholesterol [HDL-C] levels and small dense LDL particles), LDL-C levels may underestimate the cardiovascular risk. Therefore, the US guidelines recommend lowering both LDL-C and non- HDL-C in patients with hypertriglyceridemia.

In available lipid-modifying drugs, statins are the most effective for lowering plasma LDL-C and are considered the cornerstone of treatment for dyslipidaemia and hyperlipidemias [4].

Niacin at pharmacological doses, displays wide-ranging lipid-modifying activity, reducing levels of all atherogenic lipid and lipoprotein subclasses, including total cholesterol, LDL-C, non- HDL-C, triglycerides, apolipoprotein B, and lipoprotein(a), and also significantly increasing levels of HDL-C and apolipoprotein A. Furthermore, the combination of two lipid-lowering agents in one formulation may potentially improve patient compliance. Niacin is also used in the treatment of hyperlipidemia because it reduces very low density lipoprotein (VLDL), a precursor of low density lipoprotein (LDL) or "bad" cholesterol, secretion from the liver and inhibits cholesterol synthesis [4,5].

Literature survey revealed that numerous methods have been reported for estimation of Rosuvastatin and Niacin in

pharmaceutical formulations individually or with other drug combination but no UV-spectrophotometric method has been reported for this combination. Present study involves development of UV-spectrophotometric method which is simple, economical, sensitive and rapid for quantification of Rosuvastatin and Niacin in individual as well as combined tablet dosage forms as well as subsequent validation of developed method according to ICH guidelines [6-9].

	
Rosuvastatin (bis [(E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl-(methyl-sulfonyl) amino] pyrimidin-5-yl] (3R, 5S)-3, 5-dihydroxyhept-6-enoicacid] calcium salt[4]	**Niacin** (3-pyridinecarboxylic acid) Chemical formula C6H5NO2 Molecular mass 123.11 g/mol Melting point 236.6 °C Boiling point decomposes

MATERIALS AND METHODS:

Instrumentation:

UV-Visible Spectrophotometer instrument

Make: - Shimadzu

Model: - UV 1800

Software: - UV Probe

Shimadzu Ultraviolet-visible spectrophotometer UV 1800 is a computer controlled double beam scanning spectrophotometer. It covers the range from 200-1000 nm with setting accuracy at 0.2nm.

Selection of common solvent:

On the basis of solubility of both the drugs water is selected as common solvent for developing more economical and simple method.

Preparation of Standard Stock Solution

A stock solution of Rosuvastatin and Niacin was prepared by accurately weighed 50mg of drug, transferred to 50ml of volumetric flask, containing 50ml of Double distilled water dissolving it to obtain final standard solution of 1mg/ml of Rosuvastatin and Niacin. Pipette out 10ml and makeup the volume to100ml to get solution of100µg/ml.

Determination of λmax:

The standard solution of Rosuvastatin and Niacin were separately scanned at different concentration in the range of 200-400 nm and the λmax was determined for each drug. The λmax Rosuvastatin and Niacin were found to be 241nm and 262nm respectively and 254 nm as λmax of common absorbance (isobestic wavelength).

METHOD VALIDATION: [2,6-9,12].

Linearity and calibration curve:

A series of standard solution were prepared having concentration in the range of 5-40µg/ml for both Rosuvastatin and Niacin The absorbance of resulting solutions were measured at λmax 241nm , 262nm and 254 nm and calibration curves were plotted. Both the drugs obeyed linearity in the concentration range.

Method I: Simultaneous equation method: [10]

This method of analysis was based on the absorption of Rosuvastatin and niacin at the wavelength maximum of each other. Two wavelengths selected for the development of simultaneous equations [10] were 241nm and 262nm which were λmax of Rosuvastatin and niacin respectively. The

absorbances of Rosuvastatin and niacin measured at selected wavelengths. Absorptivity values were calculated.

The concentrations of both the drugs in mixture can be calculated by using following equations [10,11]:

$$C_x = \frac{A_2 ay_1 - A_1 ay_2}{ax_2 ay_1 - ax_1 ay_2} \qquad eqn-(1)$$

$$C_y = \frac{A_1 ax_2 - A_2 ax_1}{ax_2 ay_1 - ax_1 ay_2} \qquad eqn-(2)$$

Where,

A_1 and A_2 are absorbances of mixture at 241nm and 262nm respectively.

ax_1 and ax_2 are the absorptivities of Rosuvastatin at 241nm and 262nm respectively.

Ay_1 and ay_2 are the absorptivities of Niacin at 241nm and 262nm respectively.

C_x and C_y are concentrations of Rosuvastatin and niacin respectively.

Table No.1: Linearity data of Rosuvastatin

Concentration in µg/ml	Concentration in gm/lit.	Absorbance at 241 nm
5	0.005	0.18755
10	0.010	0.39136
15	0.015	0.54402
20	0.020	0.73745
25	0.025	0.91797
30	0.030	1.127970
35	0.035	1.24234
40	0.040	1.36193

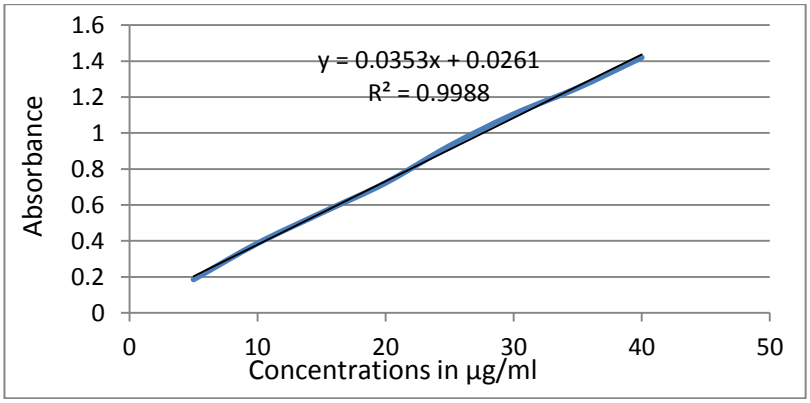


Figure 1: Linearity Graph Rosuvastatin at 254 nm

Table 2: Linearity data of Niacin

Concentration in µg/ml	Concentration in gm/lit.	Absorbance at 262 nm
5	0.005	0.14156
10	0.010	0.28682
15	0.015	0.40744
20	0.020	0.54525
25	0.025	0.67906
30	0.030	0.84407
35	0.035	0.88014
40	0.040	0.91786

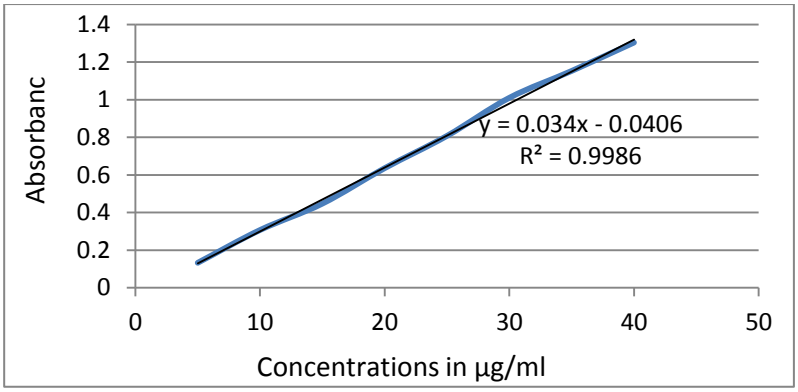


Figure 2: Linearity Graph Niacin at 262 nm

Table 3: Linear regression data for rosuvastatin and niacin

Parameters	Rosuvastatin	Niacin
Linearity range	5-40 µg/ml	5-40 µg/ml
R^2 (Regression coefficient)	0.998	0.998
Slope	0.035	0.034
Intercept	0.026	0.040

Precision:

The intra-day precision study of Rosuvastatin and niacin was carried out by estimating the correspondence responses six times on the same day with 10µg/ml concentration and inter-day precision study of Rosuvastatin and niacin was carried out by estimating the correspondence responses six times next day with 10µg/ml concentration.

Table 4: Results for precision study of tablet dosage form

Component	Concentration (µg/ml)	Mean*	Standard Deviation	Percentage Relative Standard Deviation	Standard Error
Rosuvastatin	10	98%	0.25	0.26	0.14
Niacin	10	102%	0.14	0.13	0.08

Accuracy (recovery test):

The accuracy of the method was done by recovery study. The recovery experiments were performed by adding known amounts of the pure drug to the preanalyzed sample. The recovery was done at three levels: 50%, 100%, and 150% of the label claim. Three samples were prepared for each recovery level.

Table 5: Statistical validation of Accuracy (recovery test)

Component	Percentage	Mean*	Standard Deviation	Percentage Relative Standard Deviation	Standard Error
Rosuvastatin at 241nm	50%	98.01	0.259	0.26	0.14
	100%	100.2	0.58	0.579	0.3
	150%	99.13	0.68	0.68	0.3
Component	**Percentage**	**Mean***	**Standard Deviation**	**Percentage Relative Standard Deviation**	**Standard Error**
Niacin at 262nm	50%	101.2	0.14	0.139	0.081
	100%	103.3	0.47	0.457	0.27
	150%	102.1	0.14	0.138	0.081

Method II: Absorbance ratio method/Q-analysis method:[10]

In quantitative assay of two components by absorption ratio method (Q-analysis)[1], absorbances were measured at the iso-absorptive wavelength (254 nm) and maximum absorption of one of the two components. From overlain spectra of Rosuvastatin and Niacin shown in figure no.4, absorbances were measured at the selected wavelengths of 254 nm (isobestic wavelength) and 262 nm (wavelength of maximum absorption of Niacin). From the following sets of equations, the concentration of each component in sample solution can be calculated [11,12].

$$C_x = \frac{Q_m - Q_y}{Q_x - Q_y} \times \frac{A_1}{ax_1} \qquad eqn-(3)$$

$$C_y = \frac{Q_m - Q_x}{Q_y - Q_x} \times \frac{A_2}{ax_1} \qquad eqn-(4)$$

Where,

C_x and C_y are concentrations of Rosuvastatin and niacin respectively

Q_m =A_2/A_1=absorbance of sample at 254nm/ absorbance ofsample at262nm

Q_x=ax_2/ax_1 =The absorptivity of Ros at 254nm / The absorptivity of Ros at 262nm.

Q_y=ay_2/ay_1 =The absorptivity of Nia at 254nm / The absorptivity of Nia at 262nm.

Table 6: At iso-absorptive point (254nm)

Concentration in µg/ml	Concentration in gm/lit.	Absorbance at 254 nm
5	0.005	0.15508
10	0.010	0.46051
15	0.015	0.68112
20	0.020	0.92300
25	0.025	1.14496
30	0.030	1.40027

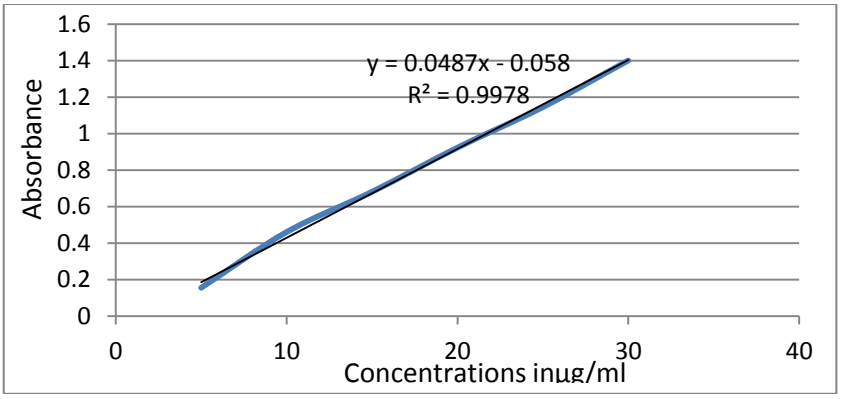
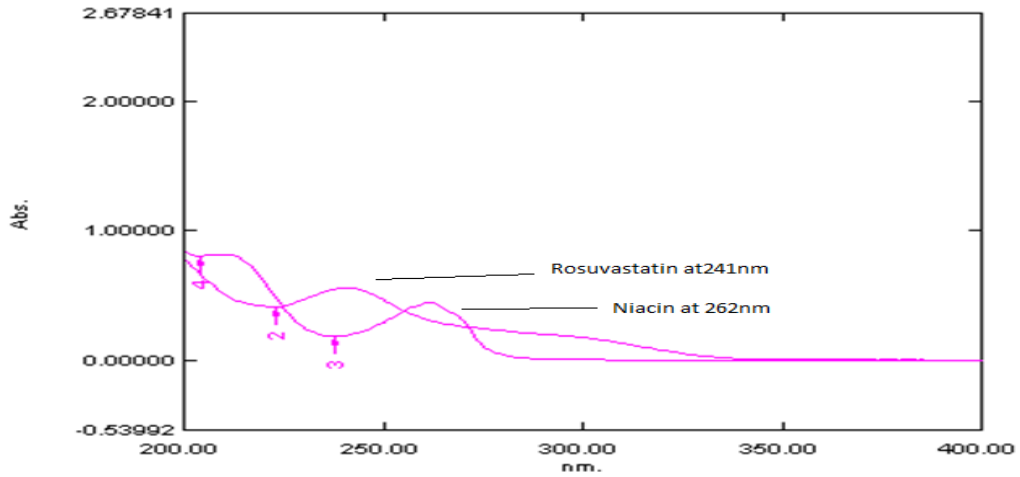


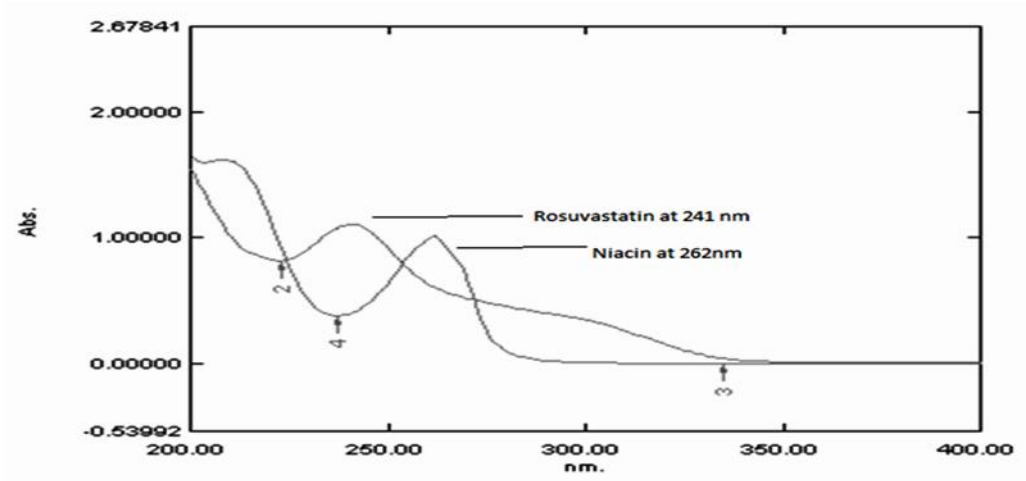
Figure 3: Linearity Graph at iso-absorptive point (254nm)

Table No.7: Statistical validation of Accuracy (recovery test)

Component	Percentage	Mean*	Standard Deviation	Percentage Relative Standard Deviation	Standard Error
Rosuvastatin at 254nm	50%	100.1	0.105	0.105	0.0608
	100%	100.1	0.141	0.141	0.081
	150%	99.6	0.169	0.17	0.9
Component	**Percentage**	**Mean***	**Standard Deviation**	**Percentage Relative Standard Deviation**	**Standard Error**
Niacin at 262nm	50%	100	0.124	0.124	0.072
	100%	100.9	0.105	0.104	0.0608
	150%	100.8	0.38	0.38	0.2



(a)



(b)

Figure 4: Overlain spectra of Rosuvastatin (241nm) and Niacin (262nm)

RESULTS AND DISCUSSION

The proposed method was found to be linear in the concentration range of 5-40 µg/ml and for Rosuvastatin Calcium and Niacin. The method was specific since excipients in the formulation did not interfere in the estimation of Rosuvastatin Calcium and Niacin. Accuracy of the method was indicated by the recovery values 98-105% for Rosuvastatin Calcium and Niacin.Precision is reflected by %RSD as 0.25 for Rosuvastatin Calcium and 0.14 for Niacin which was less than 2.

CONCLUSION

The proposed method is found to be simple, sensitive and reproducible and hence it can be used in routine analysis for simultaneous determination of Rosuvastatin and Niacin in bulk as well as in combined tablet dosage form. Statistical analysis of the results has been carried out revealing linear, high accuracy and good precision. The method provides selective quantification of ROS and FEN without any interference.

ACKNOWLEDGEMENT

Authors are thankful to project guide and Pharmaceutical chemistry department and quality assurance department of Marathwada Mitra Mandal's College of Pharmacy Pune-33, Pune University for providing equipment and facility during entire duration of research /project work.

Words of gratitude also expressed for Ranbaxy lab. Ltd. Gurgaon, India for providing gift sample of Rosuvastatin calcium and Analab fine chemicals, Mumbai-53 for providing niacin as bulk drugs.

REFERENCES

1. Gajjar Anuradha K. and Shah Vishal D. International Journal of Pharmacy and Pharmaceutical Sciences; Simultaneous UV spectrophotometric estimation of Rosuvastatin and Ezetimibe in their combined dosage forms Vol. 2, Issue 1, 2010.
2. Patel Bhoomi B.*, Shah Binal B., Gohil Kirtan N., Patel Piyush M.; International Journal of Research in Pharmacy and Science; Development and Validation of Spectrophotometric Method For Simultaneous Estimation of Rosuvastatin Calcium and Aspirin In Bulk and Pharmaceutical Dosage Form; ISSN: 2249–3522 IJRPS 2012,2(2),115-122.
3. David M. Capuzzi, MD, PhD, John M. Morgan, MD, Christina M. Carey, PA-C, Charles Intenzo, MD, Thomas Tulenko, PhD, Dana Kearney, RD, Kalen Walker, BA, Michael D. Cressman, DO Prev Cardiol; Rosuvastatin Alone or With Extended-Release Niacin: A New Therapeutic Option for Patients With Combined Hyperlipidemia; 2004;7. www:Medscape.com
4. Katherine A. Lyseng-Williamson, Niacin Extended Release (ER)/Simvastatin (Simcor_)A Guide to its Use in Lipid Regulation; Drug and Profile report; Drugs R D 2010; 10 (4): 253-260 1179-6901/10/0004-0253.
5. Vishal V. Rajkondwar, Pramila Maini1 and Monika Vishwakarma2; International Journal of Theoretical & Applied Sciences, Characterization and method development for estimation and validation of Rosuvastatin Calcium by UV – visible spectrophotometry 1(1): 48-53(2009).
6. Michael E. Swartz, Ira S. Krull; Analytical method Developement and Validation, First Indian reprint 2009.Pg.No.54.
7. ICH, Q2(R1) Validation of Analytical Procedures : Text and Methodology, ICH Harmonized tripartite guideline;november.2005.
8. ICH, Q2B Validation of Analytical Procedures: Methodology, Consensus, Consensus Guidelines; ICH Harmonized Tripartite Guidelines, 1996.
9. ICH, Q2A Validation of Analytical Procedures: Consensus Guidelines; ICH Harmonized Tripartite Guidelines, 1994.
10. H. Beckett, J. B. Stenlake; Practical Pharmaceutical Chemistry; Fourth Edition-Part Two.Pg.no.284.
11. Sawant Ramesh Ahmed Rajhan, Ramdin supriya, Darade Sheetal; International Research Journal of Pharmacy; Spectrophotometric methods for simultaneous estimation of Atorvastatin and niacin in tablet dosage forms; 2012,3(5).
12. Prashant S. Mandwal*, Pratik R. Patel, Kapil M. Agarwal, Sanjay J. Surana; Q-Absorbance and Multicomponent UV - Spectrophotometric Methods for Simultaneous Estimation of Rosuvastatin calcium and Fenofibrate in Pharmaceutical Formulation; 2012, 4 (4):1054-1059 ISSN 0975-5071.