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Research Article

Development and Validation of UV Spectrophotometric Methods for Simultaneous Estimation of Rosuvastatin and Telmisartan in Pure and Tablet Dosage Form

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Abstract

Simple, sensitive and accurate UV spectrophotometric method for simultaneous determination of Rosuvastatin and Telmisartan has been developed. The new method was developed with Methanol and phosphate buffer (pH 7.2) in proportion of 30:70 as solvent system. The several HPLC and UV spectroscopic methods were reported in literature for estimation of Rosuvastatin and Telmisartan. Therefore need to develop simple, more sensitive and economic method for simultaneous for estimation of Rosuvastatin and Telmisartan in bulk and in combined dosage form is described. Rosuvastatin showed at 276.30 nm and Telmisartan showed at 295.70nm. Linearity range was observed in the concentration range of 5-25μg/ml for Rosuvastatin calcium and 10-50μg/ml for Telmisartan. Percentage purity and recovery study were in the limit of 98-102% for both drugs. Limit of Detection for Rosuvastatin and Telmisartan were found to be 0.508μg/ml and 1.54μg/ml respectively. Limit of Quantitation for Rosuvastatin and Telmisartan were found to be 1.402 μg/ml and 4.25μg/ml respectively. The proposed method can be successfully used for the analysis of pure drug and marketed formulation. The method is found to be precise, simple, and accurate and can be applied for the routine estimation of Rosuvastatin and Telmisartan.

Keywords: Method validation, Rosuvastatin, Telmisartan, Phosphate buffer.

Introduction

Rosuvastatin and Telmisartan are fixed dose combination containing Rosuvastatin 10 mg as Lipid Lowering agent and Telmisartan 40 mg as Anti Hypertensive agent (Figures 1 and 2). Chemically Rosuvastatin is bis[(E)-7-[4(4-fluorophenyl)-6-isopropyl-2[methyl (methylsulfonyl) amino] pyrimidin-5-yl](3R,5S)3,5- dihydroxyhept-6-enoic acid]. Chemically Telmisartan is 4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1,1'-biphenyl]-2-carboxylic acid. Pharmacologically Rosuvastatin is a lipid lowering agent. It is a competitive inhibitor of HMG-CoA reductase. It catalyses the reduction of 3-hydroxyl-3-methylglutaryl coenzyme A to mevalonate, which is a rate limiting step in hepatic cholesterol synthesis [1].

Pharmacologically, Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT1-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland. As angiotensin II is a vasoconstrictor, which also stimulates the synthesis and release of aldosterone, blockage of its effects results in decreases in systemic vascular resistance. Telmisartan does not inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels [1,2,3]. The chemical structure of Rosuvastatin and Telmisartan is shown in Figures 1 and 2.

The several HPLC and UV spectroscopic methods were reported in literature for estimation of Rosuvastatin and Telmisartan. Therefore need to develop simple, more sensitive and economic method for simultaneous for estimation of Rosuvastatin and Telmisartan in bulk and in combined dosage form is described.

Material and methods

Apparatus

UV Spectrophotometer (Shimadzu, model 1800), having two matched quartz cells with 1 cm light path.

Analytical Balance: Wenstar

Sonicator: Ultra sonicator Citizen (Model No- CD4820)

Chemicals and reagents

Rosuvastatin, Telmisartan, methanol and phosphate buffer (pH 7.2). All the materials were purchased from local market of India.

Method development and optimization

Preparation of standard stock solution (100 µg/ml)

The standard stock solution of Rosuvastatin and Telmisartan were prepared by dissolving 50 mg of each drug in mixture of methanol and Phosphate buffer (pH 7.2) in proportion of 30:70. Add this solution when both drug completely soluble. Both drug completely soluble and makeup final volume up to 50 ml with mixture of methanol and Phosphate buffer (pH 7.2) in proportion of 30:70. Final concentration of each drug solution was 1000 µg/ml. From this solution pipette out 1 ml and makeup volume up to 10 ml with distilled water. Concentration of this solution was 100 µg/ml.

Selection of wavelength

The dilution was obtained to the concentration of 10 µg/ml for both Rosuvastatin and Telmisartan Solution. Both the solutions were scanned in UV (200 – 400 nm) range against reagent blank. The study of spectrum revealed that Rosuvastatin and Telmisartan show a well defined λmax at 276.30 nm and 295.70 nm respectively. These two wavelengths selected for development of simultaneous equation. From the overlain isobestic point at 284.80 nm was selected. The overlain spectra for Rosuvastatin and Telmisartan is given Figure 3.

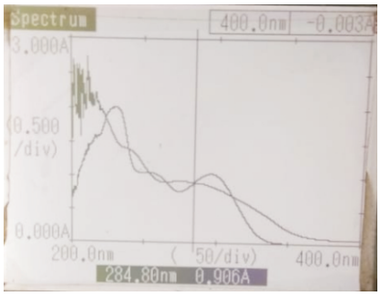

Figure 3: Overlain spectrum of Rosuvastatin and Telmisartan

Construction of calibration curve

From the above stock solution concentration in range of Rosuvastatin 5-25 µg/ml and Telmisartan 10-50 µg/ml were prepared. The absorbance of resulting solution was measured at their respective λmax and isobestic point. A calibration curve as concentration vs. absorbance (Figure 4 and 5) was constructed to study Beer- Lambert's law. Calculate absorptivity value of both drugs at respective wavelengths. The standard calibration curve for Telmisartan and Rosuvastatin are shown in Figures 4 and 5 respectively.

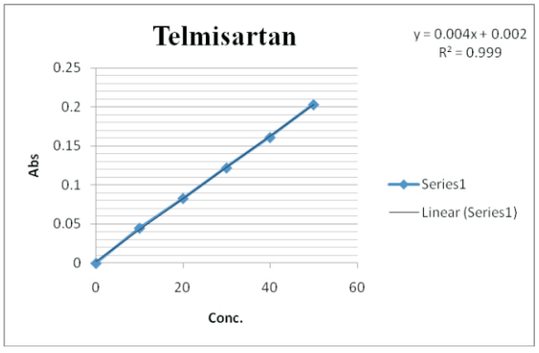

Figure 4: Calibration curve for Telmisartan

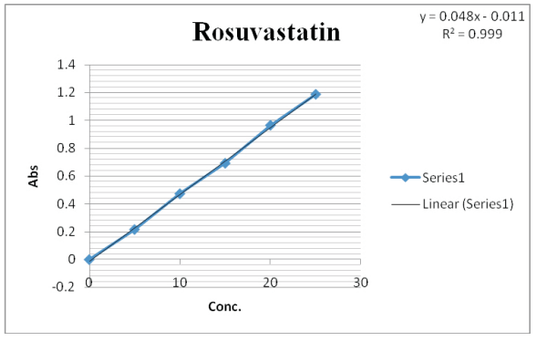

Figure 5: Calibration curve for Rosuvastatin

Analysis of tablet formulation

Twenty tablets of marketed formulation were accurately weighed and powdered. A quantity of powder equivalent to 100 mg of Telmisartan was transferred to 100 ml volumetric flask. Dissolved powder in 25 ml mixed hydrotropic solution and made up the volume up to mark by distilled water. The sample solution was then filter through Whatman filter paper No. 41. From the resulting solution 1 ml of solution was taken and diluted to 10 ml with water to get a solution containing 100µg/ml of Telmisartan and corresponding concentration of Rosuvastatin. From this solution 1 ml of solution was diluted with water in 10 ml volumetric flask to get final concentration of Telmisartan 40 µg/ml and Rosuvastatin 10 µg/ml. Analysis procedure was repeated three times with tablet formulation.

Method validation

The proposed method has been developed and validated for determination of Rosuvastatin and Telmisartan in pharmaceutical dosage forms. The method was validated according to the validation of analytical procedure provided in the ICH guidelines and draft guidance for the industry: analytical procedure and method validation.

Evaluation of linearity

Standard solutions were evaluated for the linearity within the concentration range of 5-25 μg/ml and 10-50 μg/ml for Rosuvastatin & Telmisartan respectively. The absorbance was plotted against drug concentration and the linearity was thus calculated by the linear regression equation $y = mx + c$, where y represent the absorbance and x represent drug concentration in μg/ml. A correlation coefficient of approximately 0.999 or more was considered as desirable for all calibration curve.

Determination of accuracy

Accuracy was determined by performing recovery studies by spiking different concentrations of pure drug in the pre-analysed samples within the analytical concentration range of proposed method at three different set at level of 80%, 100% and 120%. The amount of Rosuvastatin and Telmisartan was calculated at each level and % recoveries were computed. The % recovery study was carried out for 80%, 100% and 120%.

Determination of precision

Inter- day validation was conducted with three sets of three samples of different concentrations of drugs as for the intra-day validation, three sets of three different drug samples were assayed and evaluated with reference to calibration curve on the same run. The precision of the methods were determined for both intra-day and inter day variations using multiple analysis of different concentration of samples on three different days.

Determination of Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection was determined by lower concentration of Rosuvastatin and Telmisartan. The limit of quantification, which is the lowest quantifiable concentration, was also determined from range of concentrations analysed for the LOD determination.

LOD = 3.3*s/S and LOQ = 10*s/S

Where,

s = standard deviation of y-intercept of regression lines.

S = the slope of calibration curve

Results and Discussion

Selection of common solvent:

After assessing the solubility of drugs in different solvents methanol and Phosphate buffer pH 7.2 has been selected as common solvent for developing spectral characteristics.

Selection of wavelength

The study of spectrum revealed that Rosuvastatin and Telmisartan show a well defined λmax at 276.30 nm and 295.70 nm respectively. These two wavelengths selected for development of simultaneous equation. From the overlain isobestic point at 284.80 nm was selected.

Method validation

The method was validated according to the validation of analytical procedures provided in the ICH guidelines and draft guidance for the industry: analytical procedures and methods validation.

Study Beer-Lambert's Law:

Linearity range for Rosuvastatin and Telmisartan are 5-25 µg/ml and 10-50 µg/ml at respective wavelength.

Linearity and range

A linear relationship was obtained between the absorbance for the drug and corresponding concentration. The calibration curves in Figures 4 and 5 exhibit linearity over the concentration range of 5-25 µg/mL for Rosuvastation with regression coefficient 0.999 and 10-50 µg/mL for Telmisartan with regression coefficient 0.999. The

methods provided a good correlation between absorbance and drug concentration. The observations for linearity of Rosuvastatin and Telmisartan are shown in Tables 1 and 2 respectively.

Table 1: Linearity of Rosuvastatin

Sr. No.	Conc.	Abs I	II	III	Average	SD	%RSD
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	5	0.217	0.215	0.216	0.216	0.001	0.46
3	10	0.481	0.468	0.469	0.473	0.007	1.53
4	15	0.698	0.688	0.689	0.692	0.006	0.80
5	20	0.967	0.964	0.965	0.965	0.002	0.16
6	25	1.212	1.174	1.175	1.187	0.022	1.82

Table 2: Linearity of Telmisartan

Sr. No.	Conc.	Abs I	II	III	Average	SD	%RSD
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	10	0.0445	0.0447	0.0456	0.045	0.001	1.30
3	20	0.0823	0.0828	0.0829	0.083	0.000	0.39
4	30	0.1217	01228	01219	0.122	0.001	0.48
5	40	0.16	0.159	0.165	0.161	0.003	1.99
6	50	0.2001	0.2014	0.2075	0.203	0.004	1.95

Optical parameters of both the drugs are given in Table 3.

Table 3: Optical parameters

Parameters	Rosuvastatin at λmax 276.30 nm	Telmisartan at λmax 295.70 nm
Beer's law Range	5-25 μg/ml	10-50 μg/ml
Regression equation (Y)	Y = 0.048x - 0.011	Y = 0.004x + 0.002
Slope (m)	0.048	0.004
Intercept ©	0.011	0.002
Correlation Coefficient (R2)	0.999	0.999

Assay of tablet formulation

Percentage estimation in tablet dosage form was 100.5% and 100.4% (%RSD $<$ 2) for Rosuvastatin and Telmisartan respectively (Table 4).

Table 4: Analysis of tablet formulation

Absorbance reading at selected wavelength			Concentration		% Found	
			ROS	TEL	ROS	TEL
Wavelengths (λmax)	276.30 nm (λ1)	295.70nm (λ2)	10	40	105	101
Rosuvastatin	0.937	0.713	10	40	99.05	98.60
Telmisartan	1.032	0.939	10	40	101.5	101.5
			Average		100.5	100.4
			SD		1.29	1.55

Accuracy

The amount of Rosuvastatin and Telmisartan was calculated at each level and % recoveries were computed. The percentage recovery study was carried out for 80%, 100%, and 120%. The results are shown in Table 5.

Table 5: Accuracy

Level of standard addition	% Recovery ± SD	
	Rosuvastatin	**Telmisartan**
80	100.41±0.20	101.74±0.60
100	99.68±0.21	101.67±1.67
120	100.35±	90.54±0.40

Precision

The intra-day and inter-day precision of the assay method were studied by analyzing replicates at 3 different concentration levels: 5-15 µg/mL and 10-30 µg/mL for Rosuvastatin and Telmisartan respectively. As shown in Table 6.

Table 6: Precision for Rosuvastatin

Precision	Drug	
	Rosuvastatin	**Telmisartan**
Interday (%RSD)	0.005	0.001
Intraday (%RSD)	0.004	0.001

The precision of this method reflected by relative standard deviation (%RSD) of replicates was not more than 2% for interday and intraday precision study.

LOD and LOQ

The limit of detection (LOD) was evaluated by determining the minimum level of concentration for Rosuvastatin and Telmisartan that could be detected using this analytical method. The limit of quantification (LOQ) was studied by estimating the minimum concentration that could be quantified with acceptable accuracy and precision. The LOD and LOQ for Hydrochlorthiazide and Amlodipine were determined (Table 7).

Table 7: LOD and LOQ

Sr. No.	Drug	LOD	LOQ
1	Rosuvastatin	0.508	1.54
2	Telmisartan	1.4025	4.25

Conclusion

The proposed method is simple, precise, and accurate for the rapid for simultaneous determination of Rosuvastatin and Telmisartan in combined tablet dosage forms and this method may be successfully applied in control laboratories for their determination in combined dosage form.

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Conflict of interest

The authors declare that they have no competing interest.

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