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SIMULTANEOUS QUANTIFICATION OF ROSUVASTATIN AND TELMISARTAN IN BULK AND TABLET - A VALIDATED UV-SPECTROPHOTOMETRIC TECHNIQUE

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Keywords:

Antihypertensive, ICH Guidelines, Rosuvastatin, Spectrophotometric telmisartan

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ABSTRACT: Rosuvastatin and Telmisartan are used together as a fixed dosage combination to treat hypertension associated with dyslipidemia. **Objective:** To develop and validate a simple, sensitive, precise, ecofriendly and cost-effective method for the determination of Rosu-vastatin and Telmisartan in bulk and pharmaceutical formulation as per ICH Guidelines. **Methods:** an effort has been made to develop a simple double beam UV Spectrophotometric method and validate the same with different parameters such as Linearity, Precision, Repeat-ability, Limit of Detection (LOD), Limit of Quantification (LOQ), Accuracy, Robustness, and Ruggedness. **Results:** Rosuvastatin and Telmisartanin Ethanol: Water 60: 40% v/v shows maximum absor-bance at 244 nm and 296 nm, respectively. Beer's law was obeyed in the concentration range of 2-10µg/mL and 3-15µg/mL; The LOD and LOQ were found to 0.35µg/mL and 1.06 µg/ Rosuvastatin mL for Rosuvastatin and 0.54 µg/mL and 1.64 µg/mL for Telmisartan respectively. Recovery of Rosuvastatin and Telmisartan in tablet formulation was observed in the range of 80.00-120.00%. **Conclusion:** The proposed method is precise, accurate, eco-friendly and reproducible and can be used for routine analysis of Rosuvastatin and Telmisartan in bulk and pharmaceutical dosage form.

INTRODUCTION: Rosuvastatin is a HMG-CoA reductase used widely for the treatments related to cardiovascular diseases [1]. The chemical name of Rosuvastatin is calcium; (E, 3R, 5S)-7-[4-(4-fluorophenyl) - 2 - [methyl (methylsulfonyl) amino] -6 propan-2-ylpyrimidin-5-yl] - 3, 5-dihydroxyhept-6-enoate with molecular formula $C_{44}H_{54}CaF_2N_6O_{12}S_2$, as shown in **Fig. 1** [2].

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Rosuvastatin competitively inhibits the enzyme hydroxymethylglutaryl coenzyme A Reductase, which catalyzes the conversion of HMG-CoA to mevalonic acid and is the rate-limiting step in a sequence of metabolic reactions involved in the production of several compounds involved in lipid metabolism and transport including cholesterol, low-density lipoprotein (LDL) [1, 3].

Telmisartan is an angiotensin II receptor antagonist (ARB) used in the management of hypertension [4]. The chemical name (IUPAC) of Telmisartan is 2-[4-[[4-methyl-6 - (1 - methylbenzimidazol - 2 - yl) - 2 -propylbenzimidazol - 1 - yl] methyl] phenyl] benzoic acid with molecular formula $C_{33}H_{30}N_4O_2$, as shown in **Fig. 2** [5]. Telmisartan binds to the

angiotensin II type 1 (AT1) receptors with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle, ultimately leading to a reduction in arterial blood pressure [4, 5]. Hypertension and dyslipidemia are comorbid disorders, and thus, antihypertensive drugs and lipid-lowering agents are prescribed together. Rosuvastatin and Telmisartan are available as a fixed-dose Combination to treat the same [6]. As per the literature survey, simultaneous analysis of the drugs is estimated by various chromatographic techniques such as UV and HPLC. The aim of the present work was to develop and validate a simple, precise, sensitive, and eco-friendly spectroscopy method for simultaneous estimation of Rosuvastatin and Telmisartan in bulk and tablet dosage form.

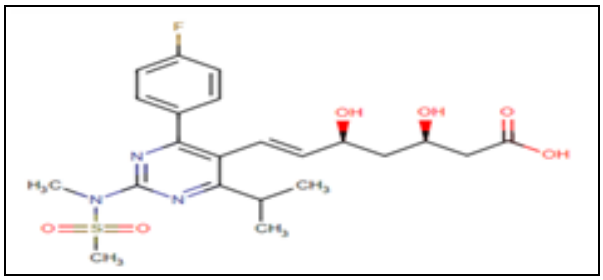

FIG. 1: STRUCTURE OF ROSUVASTATIN

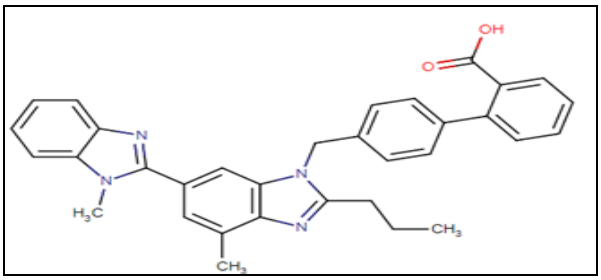

FIG. 2: STRUCTURE OF TELMISARTAN

MATERIALS AND METHOD: [7, 8, 9]

Drug Samples: Rosuvastatin and Telmisartan were obtained as a gift sample from Apotex, Bangalore.

Reagents and Chemicals: All the chemicals and reagents used for the experiment were of analytical grade. Ethanol was obtained from Molychem, Mumbai, and HPLC Grade Ethanol from S D Fine-Chem Limited, Mumbai.

Instruments and Apparatus: UV-Spectrophotometer of Shimadzu UV-1900 with Lab solutions software& Shimadzu UV-1800 with UV probe were used for determination of Rosuvastatin and Telmisartan.

Method Development: [8] Development of UV-Spectrophotometric method involved, determination of λ_{max} of Rosuvastatin and Telmisartanin suitable solvent. Various solvents were employed, out of which ethanol and water were selected. Different ratios were tried out; analytes exhibited best results in Ethanol: Water 60:40% v/v. Solutions containing both the analytes were scanned for single and in combination, between the range of 800-200 nm, respectively. Rosuvastatin and Telmisartan showed maximum absorbance at 243 nm and 296 nm wavelength, respectively.

Preparation of Standard Stock Solution: [7, 8] 10 mg of Rosuvastatin calcium and 10 mg Telmisartan were accurately weighed and transferred to a 100 ml volumetric flask. Ethanol was added to dissolve the drugs, and the solution was sonicated for 10 min. Volume made up to 100 ml with Ethanol: Water 60: 40% v/v to obtain a 100 ppm solution.

Method Validation: [7, 8, 9] According to ICH guidelines, the newly developed UV-Spectrophotometric method was validated in order to prove the suitability of the method using optimized method parameters.

Specificity and Selectivity: [9, 10, 11] UV-spectrum of blank solvent Ethanol: Water 60: 40% v/v and solution containing Rosuvastatin and Telmisartan were scanned between the range of 800 nm-200 nm. The spectrum obtained was compared for any interference at the maximum wavelength of absorbance of respective analytes by the solvent.

Linear Range Response: [9] Linearity was performed using the above stock solution, serial dilutions containing a concentration of Rosuvastatin 2, 4, 6, 8, 10 µg/mL and Telmisartan 3, 6, 9, 12, 15 µg/mL were prepared. The solutions were analyzed in triplicates, and absorbance was measured at 243 nm and 296 nm, respectively. A calibration curve was plotted as Concentration on X-axis and Absorbance on Y-axis, and a linear regression equation was calculated.

Detection and Quantification Limit of Analyte: [7, 9] Limit of Detection and Limit of Quantification (LOD and LOQ) were calculated from linear curve by statistical calculations using following formulae

LOD = 3.3 × Standard deviation of y - Intercept / Slop of the calibration curve

LOQ = 10 × Standard deviation of y - Intercept / Slop of the calibration curve

Precision: Precision was carried out using.

System Precision: Six replicates of a solution containing 2 µg/mL of Rosuvastatin and 3 µg/mL of Telmisartan were prepared. Each solution's absorbance was measured at 243 nm and 296 nm, respectively and % RSD was calculated.

Intraday Precision: Six replicates of solutions containing 2 µg/mL of Rosuvastatin and 3 µg/mL of Telmisartan were analyzed, and % RSD was calculated at different time intervals on same day.

Interday Precision: Six replicates of solutions containing 4µg/mL of Rosuvastatin and 6 µg/mL of Telmisartan were analyzed, and % RSD was calculated on three consecutive days.

Accuracy: [12] Accuracy was determined by performing recovery experiments in which determination of % mean recovery of the sample by percentage method at three different levels. 80 to 120% of the sample solutions were prepared as per the procedure given in the methods from the dilutions used for linearity. For the analysis, Rosuvastatin was taken in the concentrations of 4.8, 6, 7.2 µg/mL and Telmisartan in the concentrations of 7.2, 9, 10.8 µg/mL, respectively. At each level, three analyses were performed. Percent mean recovery was calculated. The accepted limits of recovery are 98%-102%, and all observed data are within the required range, which indicates good recovery values and hence the accuracy of the method developed.

Ruggedness and Reproducibility: [9, 12, 13] In order to prove ruggedness and reproducibility of the method, six replicates of solutions containing both the analytes were prepared and absorbance of each replicate solution containing 6 µg/mL of Rosuvastatin and 9 µg/mL of Telmisartan was measured by the different analyst. Also, a different instrument (UV Spectrophotometer: UV-1800) was used wherein 8 µg/mL and 12 µg/mL of Rosuvastatin and Telmisartan were analyzed, and % RSD was calculated, Change in maker of solvent was also employed in order to prove robustness.

Solvent and Standard Stock Solution Stability: [13, 14] In order to obtain the stability of solvent and stock solution, the fresh stock was prepared, and dilutions were made using fresh solvent, absorbance of each dilutions containing both analytes were compared with that of old stock dilutions and % RSD was calculated.

RESULTS AND DISCUSSION:

Development: For simultaneous estimation, both the analytes must be soluble in a single solvent system. Rosuvastatin and Telmisartan, both were found to be soluble in Ethanol: Water 60:40% v/v. Detection wavelength for both the analytes was obtained by scanning analyte solution in spectrophotometer. The spectrum showed the maximum absorbance at 243 nm and 296 nm for Rosuvastatin and Telmisartan, respectively. Developed method parameters are presented in **Table 1.**

Validation:

Specificity and Selectivity: The solvent spectrum obtained displayed no interference of absorbance at of Rosuvastatin and Telmisartan. Both the analytes selectively showed maximum wavelength at 243 nm and 296 nm, respectively. The method was found to be specific and selective. UV spectrum of Rosuvastatin and Telmisartanis presented in **Fig**. **3** and **4**.

Linear Range Response: Linear relationships were observed by plotting drug concentration against absorbance. Each showed linear absorbance range between a range of 2, 4, 6, 8, 10 µg/mL and 3, 6, 9, 12, 15 µg /mL with regression equation of 0.999 and 0.999 for Rosuvastatin and Telmisartan, respectively. Linearity range data is discussed in **Table 2**. The overlay spectrum of linearity of Rosuvastatin and Telmisartanis presented in **Fig. 5,** and the standard calibration curve is presented in **Fig. 6** and **Fig. 7.**

Limit of Detection and Limit of Quantification: LOD of Rosuvastatin and Telmisartan was found to be 0.35 µg/mL and 0.54 µg/mL, LOQ of Rosuvastatin and Telmisartan was found to be1.06 µg/mL and 1.64 µg/mL respectively.

Precision: Method was found to be precise as the % RSD calculated for six replicates solution of both analytes at each precision level was found to be less than 2% **Table 3, 4, 5.**

Accuracy: At each level, three analyses were performed. Percent mean recovery was calculated as shown in **Tables 6** and **7**. The accepted limits of recovery are 98%-102%, and all observed data are within the required range, which indicates good recovery values and hence the accuracy of the method developed.

Ruggedness and reproducibility: % RSD values obtained for each analyte was found to be less than 2% which indicates the method was rugged with change in the maker of solvent system and also found to be reproducible as %RSD obtained for absorbance of each replicate of solution was within the acceptance criteria by a change in the analyst and instrument. It is represented in **Tables 8** and **9**.

Solution and Standard Stock Solution Stability: The %RSD for absorbance obtained by fresh and old dilutions containing Rosuvastatin and Telmisartan was found to be within the acceptance criteria, and the data obtained showed that the standard stock solution and solvent system were stable for 10 days. It is represented in **Table 10**.

TABLE 1: DEVELOPED METHOD PARAMETERS

S. no.	Parameters	Specifications
1	Analytes	Rosuvastatin and Telmisartan
2	Solvent	Ethanol: Water (60:40% v/v)
3	Max. Absorbance of Rosuvastatin	243nm
4	Max. Absorbance of Telmisartan	296 nm

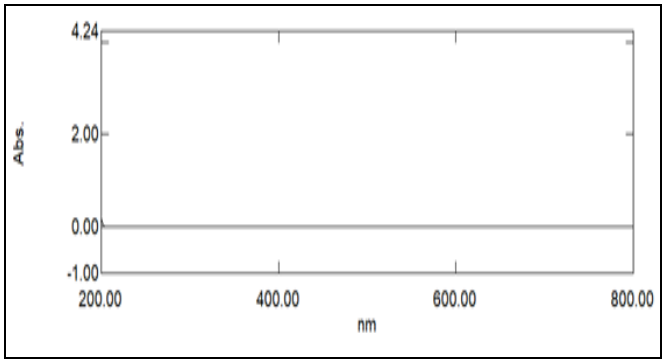

FIG. 3: UV-SPECTRUM OF SOLVENT (ETHANOL: WATER (60:40% V/V)

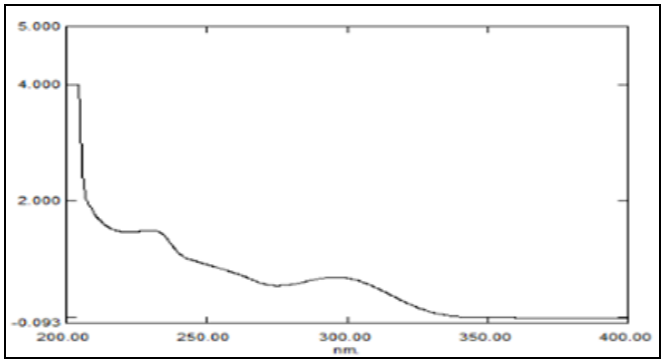

FIG. 4: UV-SPECTRUM OF ROSUVASTATIN AND TELMISARTAN

TABLE 2: LINEARITY AND RANGE DATA OF ROSUVASTATIN AND TELMISARTAN

S. no.	Rosuvastatin (244 nm)		Telmisrtan (296 nm)	
	Concentration	Absorbance	Concentration	Absorbance
1	2 µg/mL	0.188	3 µg/mL	0.219
2	4 µg/mL	0.372	6 µg/mL	0.428
3	6 µg/mL	0.549	9 µg/mL	0.612
4	8 µg/mL	0.765	12 µg/mL	0.822
5	10 µg/mL	0.937	15 µg/mL	1.01
	r^2	0.999	0.999	
	Slope	0.094	0.067	
	LOD	0.35 µg/mL	0.54 µg/mL	
	LOQ	1.06 µg/mL	1.64 µg/mL	

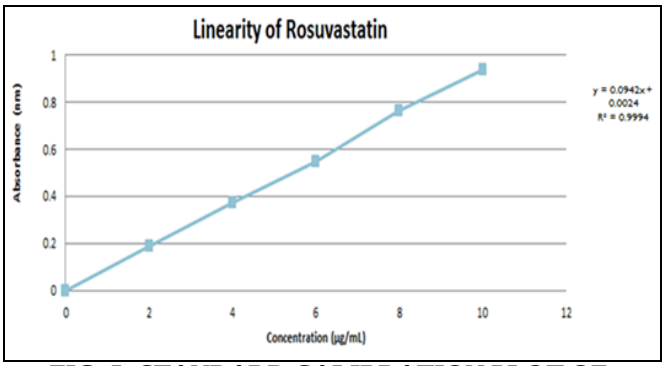

FIG. 5: STANDARD CALIBRATION PLOT OF ROSUVASTATIN

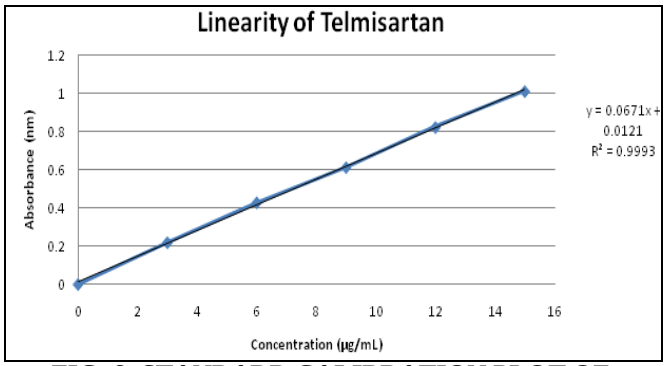

FIG. 6: STANDARD CALIBRATION PLOT OF TELMISARTAN

TABLE 3: SYSTEM PRECISION

Replicates	Rosuvastatin (2 µg/mL)	Telmisartan (3µg/mL)
	Absorbance	Absorbance
1	0.158	0.217
2	0.160	0.221
3	0.154	0.215
4	0.160	0.218
5	0.159	0.217
6	0.162	0.211
% RSD	1.709%	1.539%

TABLE 4: INTRADAY PRECISION (INITIAL HOUR, 1STHOUR, 5TH HOUR)

Replicates	Rosuvastatin (2 µg/mL)	Telmisartan (3 µg/mL)	Rosuvastatin (2 µg/mL)	Telmisartan (3 µg/mL)	Rosuvastatin (2 µg/mL)	Telmisartan (3 µg/mL)
	Initial Hour		1st Hour		5th Hour	
	Absorbance	Absorbance	Absorbance	Absorbance	Absorbance	Absorbance
1	0.159	0.226	0.156	0.215	0.163	0.218
2	0.158	0.225	0.161	0.218	0.164	0.216
3	0.161	0.224	0.160	0.221	0.165	0.216
4	0.156	0.228	0.159	0.223	0.159	0.221
5	0.161	0.229	0.163	0.226	0.158	0.223
6	0.156	0.219	0.157	0.222	0.161	0.224
% RSD	1.425%	1.574%	1.620%	1.752%	1.735%	1.594%

TABLE 5: INTERDAY PRECISION

Replicates	Rosuvastatin (4 µg/mL)	Telmisartan (6 µg/mL)	Rosuvastatin (4 µg/mL)	Telmisartan (6 µg/mL)	Rosuvastatin (4 µg/mL)	Telmisartan (6 µg/mL)
	Day 1		Day 2		Day 3	
	Absorbance	Absorbance	Absorbance	Absorbance	Absorbance	Absorbance
1	0.369	0.455	0.358	0.448	0.360	0.451
2	0.371	0.457	0.362	0.459	0.358	0.449
3	0.370	0.459	0.363	0.456	0.361	0.453
4	0.373	0.463	0.361	0.449	0.360	0.441
5	0.372	0.463	0.358	0.451	0.360	0.452
6	0.370	0.469	0.362	0.455	0.362	0.459
% RSD	0.397%	1.098%	0.599%	0.957%	0.369%	1.304%

TABLE 6: ACCURACY (ROSUVASTATIN)

Level (%)	Absorbance	% Recovery	Mean % Recovery
80	0.402	98.25	98.78
80	0.419	98.59	
80	0.407	99.52	
100	0.545	99.14	99.84
100	0.551	99.87	
100	0.548	100.51	
120	0.682	101.60	101.91
120	0.687	102.02	
120	0.681	102.13	

TABLE 7: ACCURACY (TELMISARTAN)

Level (%)	Absorbance	%Recovery	Mean % Recovery
80	0.501	98.16	98.93
80	0.504	99.71	
80	0.502	98.93	
100	0.610	101.11	100.79
100	0.613	100.93	
100	0.611	100.31	
120	0.791	101.14	101.44
120	0.793	101.17	
120	0.787	102.03	

TABLE 8: RUGGEDNESS (CHANGE IN INSTRUMENT AND CHANGE IN ANALYST)

Replicates	Rosuvastatin (6 µg/mL)	Telmisartan (9 µg/mL)	Rosuvastatin (6 µg/mL)	Telmisartan (9 µg/mL)
	Change in Instrument		Change in Analyst	
	Absorbance	Absorbance	Absorbance	Absorbance
1	0.550	0.681	0.549	0.684
2	0.542	0.680	0.541	0.682
3	0.548	0.674	0.547	0.683
4	0.547	0.671	0.553	0.679
5	0.546	0.688	0.547	0.681
6	0.563	0.690	0.559	0.685
% RSD	1.311%	1.098%	1.114%	0.317%

TABLE 9: ROBUSTNESS (CHANGE IN SOLVENT MAKE)

Replicates	Rosuvastatin (8 µg/mL)	Telmisartan (12 µg/mL)
	Absorbance	Absorbance
1	0.763	0.879
2	0.760	0.887
3	0.762	0.888
4	0.741	0.890
5	0.758	0.881
6	0.751	0.878
% RSD	1.115%	0.579%

TABLE 10: SOLUTION STABILITY

Replicates	Rosuvastatin (10 µg/mL) Absorbance		Telmisartan (15µg/mL) Absorbance	
	Fresh	Old	Fresh	Old
1	0.937	0.951	1.01	1.03
2	0.948	0.943	1.02	1.04
3	0.956	0.959	1.00	1.04
%RSD	0.861%		1.596%	

TABLE 11: VALIDATION PARAMETERS

S. no.	Validation Parameters		Values of Rosuvastatin (243 nm)	Values of Telmisartan (296 nm)
1	Linearity range		2-10 µg/mL	3-15 µg/mL
2	Precision	System Precision	1.709%	1.539%
		Interday Day-1	0.397%	1.098%
		Interday Day-2	0.599%	0.957%
		Interday Day-3	0.369%	1.304%
		Intraday Initial hour	1.425%	1.574%
		Intraday 1st hour	1.620%	1.752%
		Intraday 5th hour	1.735%	1.594%
3	Robustness (Change in solvent make)	1.115%	0.579%	
4	Ruggedness	By change in analyst	1.114%	0.317%
		By change in instrument	1.311%	1.098%
5	LOD	0.35 µg/mL	0.54 µg/mL	
6	LOQ	1.06 µg/mL	1.64µg/mL	
7	Solution Stability	10 days at room temperature (0.861%)	10 days at room temperature (1.596%)	

CONCLUSION: The present research concluded that the newly developed spectrophotometric technique was found to be simple, eco-friendly, specific, selective, linear, precise, robust, rugged, and reproducible for the simultaneous quantification of Rosuvastatin and Telmisartan in bulk and tablet dosage form.

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CONFLICTS OF INTEREST: We declare no conflicts of interest of any kind with anybody

REFERENCES:

1. Arjun S, Karthik S, Arjunan K, Hariharan S, Seenivasan P and Sankar V: Preparation and Evaluation of Rosuvastatin Calcium Nanosuspension and Solid Dispersion Tablets by Wet Granulation and Direct Compression Techniques using Tamarind Gum as a Binder. Indian Journal of Pharmaceutical Sciences 2020; 82(1).
2. Ângelo M, Moreira F, MoraisRuela A, Santos A, Salgado H and de Araújo M: Analytical Methods for the Determination of Rosuvastatin in Pharmaceutical Formulations and Biological Fluids: A Critical Review. Critical Reviews in Analytical Chemi 2018; 48(4): 317-29.
3. Dudhipala N and Veerabrahma K: Improved anti-hyperlipidemic activity of Rosuvastatin Calcium *via* lipid nanoparticles: Pharmacokinetic and pharmacodynamic evaluation. Eur J Pharm Biopharm 2017; 110: 47-57.
4. Hong S, Jeong H, Cho J, Chang K, Pyun W and Ahn Y: Efficacy and Safety of Triple Therapy With Telmisartan, Amlodipine and Rosuvastatin in Patients With Dyslipidemia and Hypertension: The Jeil Telmisartan, Amlodipine and Rosuvastatin Randomized Clinical Trial. Clinical Therapeutics 2019; 41(2): 233-48.
5. Fang D, Jin Q, Jin Z, Wang F, Huang L and Yang: Folate-Modified Liposomes Loaded with Telmisartan Enhance Anti-atherosclerotic Potency for Advanced Atherosclerosis in ApoE–/– Mice. J of Biom Nanotech 2019; 15(1): 42-61.
6. Oh G, Han J, Han K, Hyon M, Doh J, Kim M: Efficacy and Safety of Fixed-dose Combination Therapy With Telmisartan and Rosuvastatin in Korean Patients With Hypertension and Dyslipidemia: Telsta-YU (TELmisartan-rosuva Statin from Y Uhan), a Multicenter, Randomized, 4-arm, Double-blind, Placebo-controlled, Phase III Study. Clinical Therapeutics 2018; 40(5): 676-91.
7. Janardhanan SV, Manavalan R and Valliappan K: Chemometric technique for the optimization of

chromatographic system: Simultaneous HPLC determination of Rosuvastatin, Telmisartan, Ezetimibe and Atorvastatin used in combined cardiovascular therapy. Arabian Journal of Chemistry 2016; 9: 1378-87.
8. ICH guidance, validation of analytical method: definition and terminology. Internat Confere on Harmo Q2A Geneva.
9. ICH guidance, validation of analytical Procedures: Methodology. Inter Confer on Harmonizati Q2B Geneva.
10. Tekin K, Hao N, Karagoz S and Ragauskas A: Ethanol: A Promising Green Solvent for the Deconstruction of Lignocellulose. Chem Sus Chem 2018; 11(20): 3559-75.
11. Pacheco-Fernández I and Pino V: Green solvents in analytical chemistry. Current Opinion in Green and Sustainable Chemistry 2019; 18: 42-50.
12. Kaur I, Wakode S and Singh HP: Development and Validation of UV Spectroscopic Method for Determination of Canagliflozin in Bulk and Pharmaceutical Dosage Form. Pharmaceutical Methods 2015; 6(2): 82-86.
13. Pancham Y and Patil N: Development and Validation of Analytical Method for Determination of Andrographolide in Bulk Powder. International Journal of Pharma Research and Health Sciences 2019; 7(1): 2899-903.
14. Pancham Y, Patil N and Girish BSB: Validated UV-Spectrophotometric Method for Simultaneous Estimation of Curcumin and Gallic Acid In Bulk Powder. World Journal of Pharmacy and Pharmaceutical Sciences 2020; 9(4): 1255-66.

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