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Analytical Method Development for Rosuvastatin and Irbesartan through Simultaneous Equation by UV-Spectroscopy

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ABSTRACT

Development and validation of two samples, rapid precise accurate and sensitive UV spectrophotometric methods using simultaneous equation methods was developed for the simultaneous estimation rosuvastatin calcium and irbesartan combined in dosage forms. Rosuvastatin use in prevent stroke and heart attack and irbesartan used to treat high blood pressure. The absorbance signals in the simultaneous equation method are measured at a λ max 238.99 and 246.5 nm. The linearity ranges for were found rosuvastatin and irbesartan to be 8-20 µg/ml and 12-30 µg/ml respectively. Contraction of each of drugs was obtained by using absorptive value calculated for both the drugs at these two wavelengths. The developed method was validated according to ICH guidelines. The method was validated in terms of linearity, accuracy (% recovery), precision (interday and intraday), reproducibility and robustness. The linearity of the method was with-in range and the % recovery was 99.16% for rosuvastatin and 95.5% for irbesartan therefore the proposed method is suitable for simultaneous equation determination of rosuvastatin calcium and irbesartan from combine pharmaceutical dosage form in routine quality control analysis. Applications of the suggested procedures were successfully applied to the determination of these compounds in active pharmaceutical ingredient and in pharmaceutical preparations, with high percentage of recovery, good accuracy and precision.

INTRODUCTION

Rosuvastatin Calcium [1] is official in Indian Pharmacopeia. It is synthetically (E)- (3R,5S)- 7-{4-(4- fluorophenyl)- 6-isopropyl-2-{methyl(methyl sulphonyl amino)]pyrimidin-5-yl}-3,5-dihydroxyhepten-6-oic corrosive calcium. It is utilized as a lipid bringing down operator act by restraint of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase[2]. Rosuvastatin is orally regulated as calcium salt. The structure of Rosuvastatin is shown in fig. 1

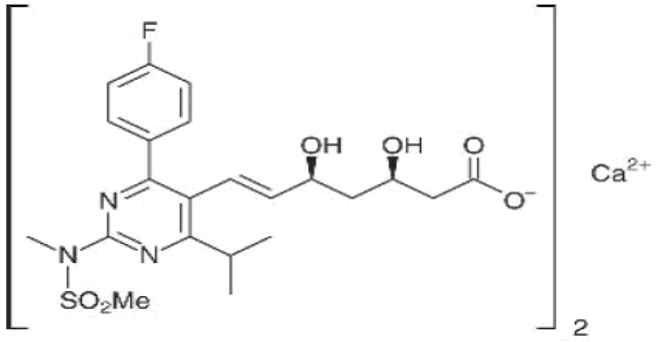

Figure No. 1: Structure of Rosuvastatin calcium

Irbesartan is a non-peptide compound, chemically described as 2-butyl-3-[p -(o -1 H -tetrazol- 5-ylphenyl)benzyl]-1,3-diazaspiro[4.4]non-1-en-4-one[1] used in hypertension[3]. Irbesartan is an angiotensin II receptor antagonist, Irbesartan is indicated for the treatment of hypertension it may also delay progression of diabetic nephropathy and is also indicated for the reduction of renal disease progression in patients with type 2 diabetes, hypertension[4]. Irbesartan is also available in a combination formulation with a low-dose thaizide diuretic, invariably hydrochlorothiazide, to achieve additive antihypertensive effects[5]. The literature study uncovers that there are no strategies for this combination. So we do the simultaneous estimation of Rosuvastatin calcium and Irbesartan definition [10] by UV method. The structure of Irbesartan is shown in fig.2.

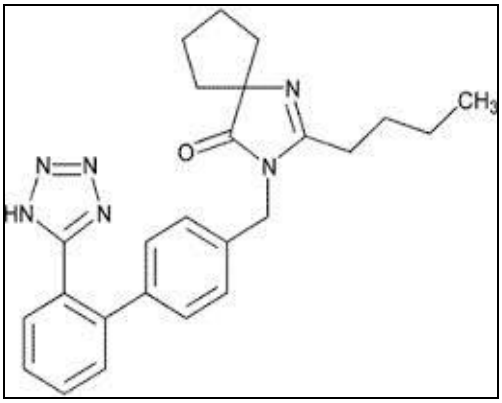

Figure No. 2: Structure of Irbesartan

Validation:

Validation study of Rosuvastatin calcium and Irbesartan: An integral part of analytical method development is validation[6]. Method validation is the process to confirm that the analytical procedure employed for a specific test is suitable for its intended use. UV method was validated as per International Conference on Harmonization (ICH) guidelines for parameters like specificity, system suitability, accuracy, linearity, precision (repeatability), and robustness [7].

MATERIALS AND METHODS

The bulk drugs of Rosuvastatin calcium and Irbesartan were procured available in Cadila pharmaceutical ltd and mankind pharmaceutical ltd. Chemicals and reagents used for the study were of Analytical grade.

Equipment:-The spectrophotometric measurements were carried out using a Shimadzu UV 1800 double beam UV- spectrophotometer (Japan) equipped with 1cm matched quartz cell at the scan speed 100nm per min.

Preparation of standard stock solutions

1. **Standard Stock Solution:** 25 mg each of Rosuvastatin calcium and Irbesartan was accurately weighed and transferred into a clean and dry 25 ml volumetric flask, dissolved with methanol, the flask were shaken, the volume made up to 25 ml with methanol to obtain the concentration of 1000 µg/ml. Filtered the solution with Whatman filter paper.

2. **Working Standard Solution:** 5 ml of the stock solution was diluted in a 100 ml volumetric flask with distilled water to get a concentration 100 µg/ml.

Simultaneous Equation Method

The absorption spectrum shows that Irbesartan has λmax at 246.99 nm whereas Rosuvastatin calcium has at 238.99 nm respectively. For the simultaneous equation method, two wavelengths *i.e.* λmax of the two drugs were selected and the absorbance as well as the absorptivity values were calculated from their individual spectra [8]. Absorbance was noted against each concentration at 238.99 and 246.5 nm. for both the drugs from their individual spectra and their absorptivity values were calculated.

Analysis of marketed formulations

Twenty tablets of formulation were accurately weighed and powdered. A quantity of powder equivalent to 10 mg of both drugs was weighed and dissolves in 100 ml of methanol. The mixture was ultrasonicated for 20 minutes; the solution is filtered through Whatman filter paper no.4 then final dilution was made with methanol to get final concentration.

Determination or estimation of overlay:

The concentration range of 8-20 µg/ml and 12-30 µg/ml The drug Rosuvastatin calcium and Irbesartan and each working standard solution was scanned at 2 different λmax 238.99nm and 246.5 nm with UV spectrophotometer (Japan) equipped with 1cm matched quartz cell and solvent used Methanol(AR grade), manufactured by merck pharmaceutical, shown in figure no:3 and 4.

Determination of λmax by UV

Each working standard solution was scanned between the range 200-400 nm. The calibration curves for RSV calcium and Irbesartan were prepared in the concentration range of 8-20 µg/ml and 12-30 µg/ml respectively. The Linearity graphs of Rosuvastatin calcium and Irbesartan.

Estimation of linearity

The linearity of the response of the drugs Rosuvastatin calcium and Irbesartan was observed in concentration range from 8-20 µg/ml and 12-30 µg/ml were scanned at 2 different λmax 238.99 and 246.5 and it obeyed Beers law[11]. The equation of the calibration curve for Rosuvastatin calcium at 238.99 nm was Y =0.338x+0.077 and at 246.5 Y=0.299x+0.0681, the calibration curve was found to be linear with the correlation coefficient (R2) as 0.997 and

0.996 figure shown in 5 and 6 and table no 1 and 2. Irbesartan at 238.99 nm was Y =0.042x+0.035 and at 246.5 Y=0.038x+0.027, the calibration curve was found to be linear with the correlation coefficient (R2) as 0.995 and 0.996 shown in fig no: 7 and 8 and table no 3 and 4.

Estimation of Precision: The developed UV-spectroscopic method was found to be precise as the % RSD values for system precision[9] was found to be Rosuvastatin calcium at 246.5 nm is 0.439% and 238.99 nm is 0.369% and Irbesartan the percentage RSD for system precision was found to be at 246.5 nm is 0.25% and 238.99 nm is 0.22%. The intra-day precision study of Rosuvastatin calcium and Irbesartan was carried out by estimating the corresponding response different time of same day for different concentrations shown in table no-5, table no-6, table no-7 and table no-8.

Estimation of Robustness:

The evaluation of robustness study of Rosuvastatin calcium in change in temperature shown in table no 9 and 10 and change in pipette shown table no 11 and 12. Irbesartan in change in temperature shown in table no 13 and 14 and change in pipette shown in table no 15 and 16.

RESULT AND DISCUSSION

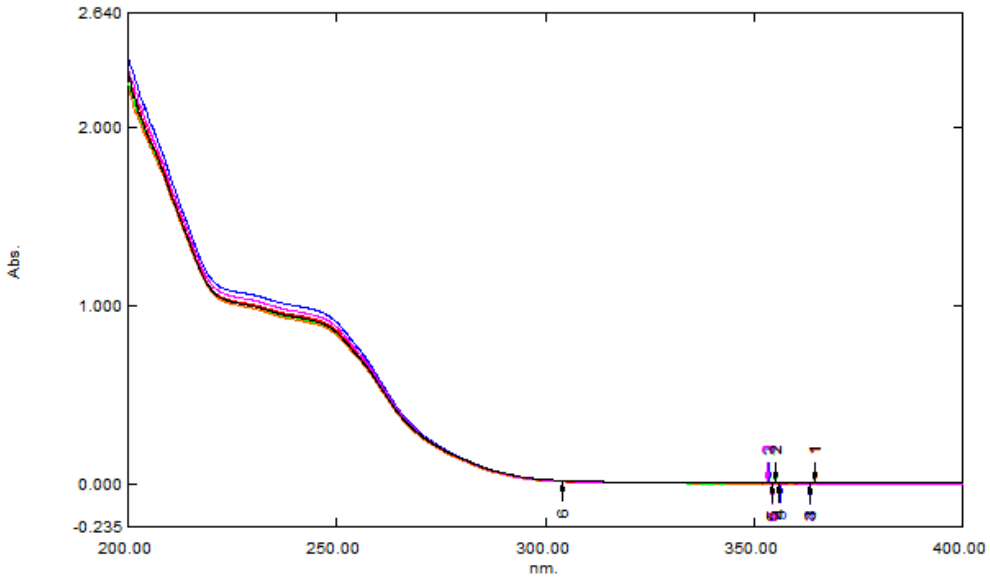

Figure No. 3: Wavelengths (nm) overlay spectra of Irbesartan

The overlay spectrum of Irbesartan and rosuvastatin at different wavelengths is shown in Figures 3 and 4.

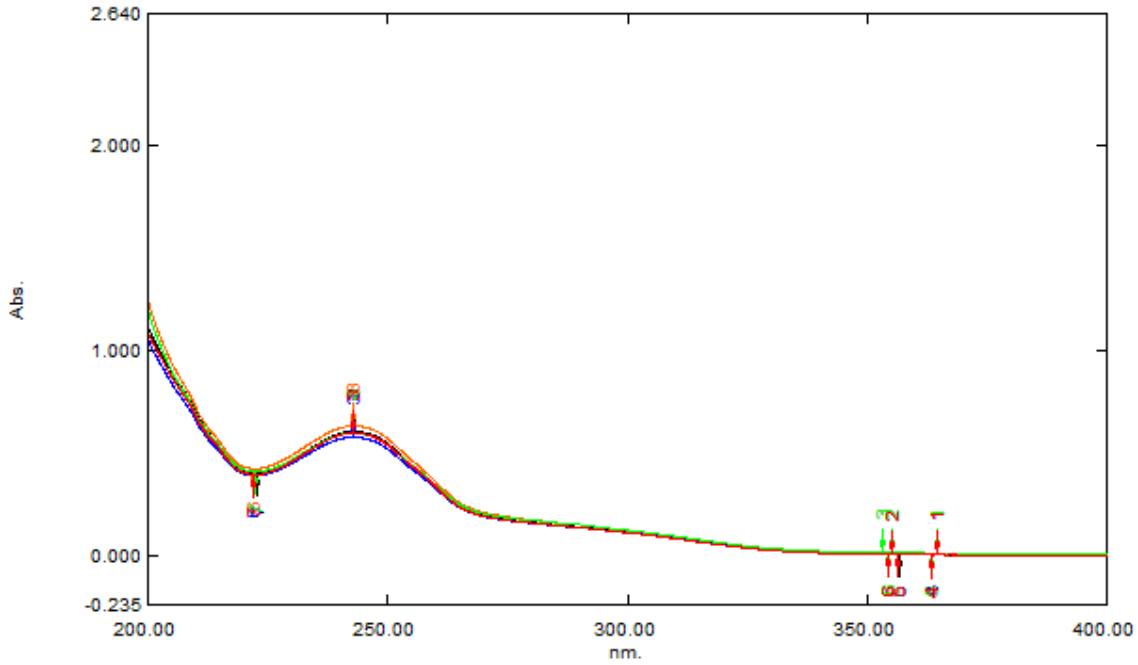

Figure No. 4: Wavelength (nm) overlay spectra of Rosuvastatin

LINEARITY

The linearity range of rosuvastatin at 238.9 nm was found to be in concentration range from 8 µg/ml to 20 µg/ml. Results are highlighted in table 1.

LINEARITY OF ROSUVASTATIN AT 238.9nm

Table No. 1: Linearity data of Rosuvastatin at 238.99 nm

Concentration (µg/ml)	Absorbance (238.9 nm)
8	0.198
12	0.327
16	0.45
20	0.607

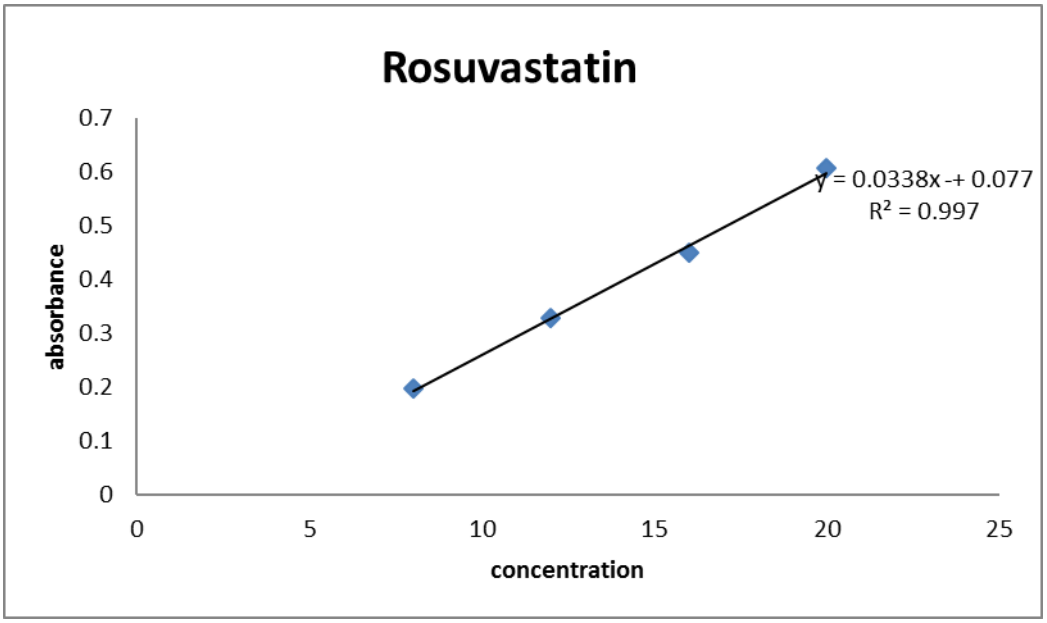

Figure No. 5: Calibration curve of Rosuvastatin at (238.99 nm)

RESULT: Linearity in the response was obtained in the range of 10-100 µ/ml and regression equation was calculated as y=0.033x+0.077 and co-relation value for rosuvastatin were found to be 0.997 which is within acceptance area.

LINEARITY OF ROSUVASTATIN AT 246.5 nm

Table No. 2: Linearity data of Rosuvastatin at 246.5 nm

Concentration (µg/ml)	Absorbance (246.5 nm)
8	0.176
12	0.289
16	0.399
20	0.607

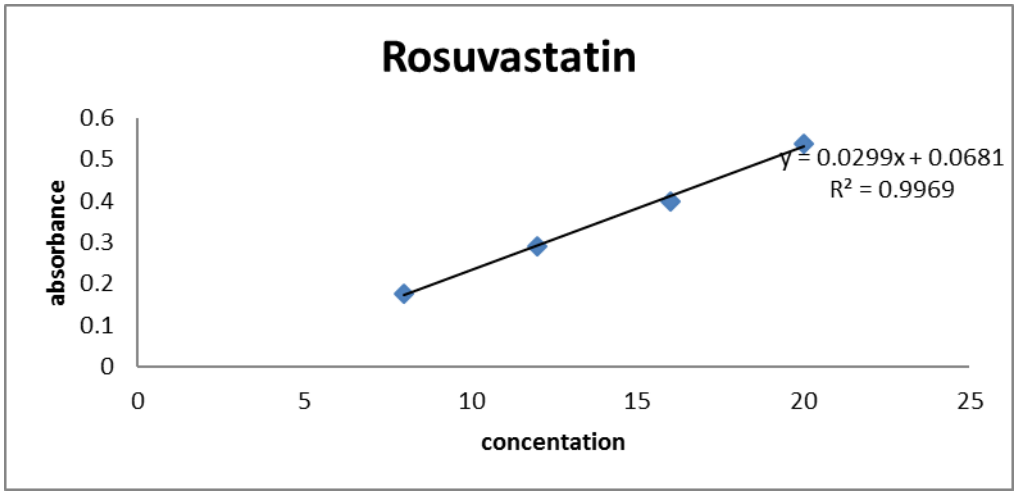

Figure No. 6: Calibration curve of Rosuvastatin at (246.5 nm)

RESULT: Linearity in the response was obtained in the range of 10-100µ/ml and regression equation was calculated as y=0.029x+0.068 and correlation value for rosuvastatin were found to be 0.996 which is within acceptance area.

LINEARITY OF IRBESARTAN AT (238.99 nm)

Table No. 3: Linearity data of Irbesaratan at 238.99 nm

Concentration (µg/ml)	Absorbance (238.99 nm)
12	0.557
16	0.712
20	0.89
24	1.057
28	1.259
30	1.38

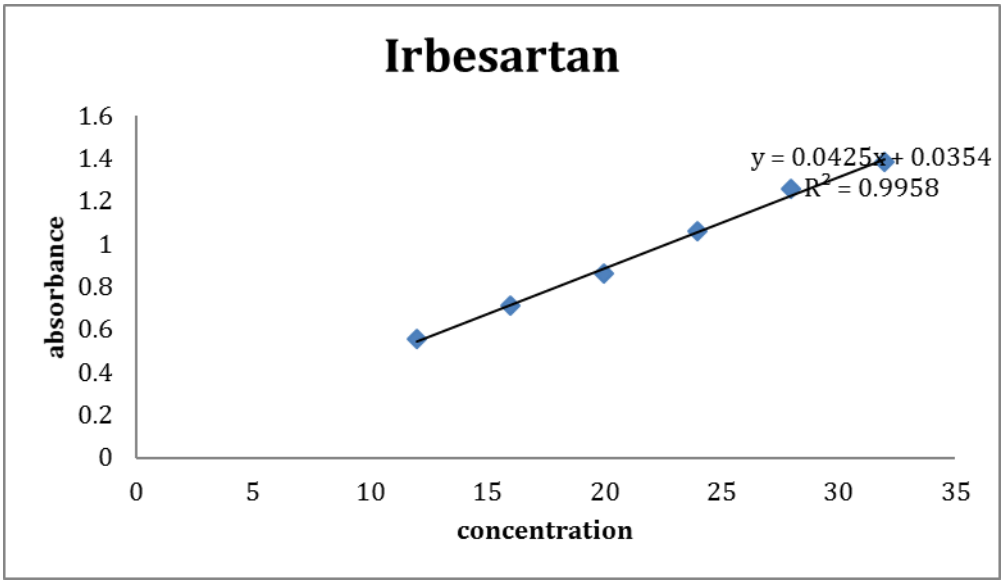

Figure No. 7: Calibration curve of Irbesartan (238.99 nm)

RESULT: Linearity in the response was obtained in the range of 10-100 µ/ml and regression equation was calculated as y=0.042x+0.035 and correlation value for irbesartan were found to be 0.999 which is within acceptance area.

LINEARITY of IRBESARTAN AT (246.5 nm)

Table No. 4: Linearity data of Irbesartan at 246.5 nm

Concentration (µg/ml)	Absorbance (238.99)
12	0.506
16	0.647
20	0.779
24	0.956
28	1.124
30	1.27

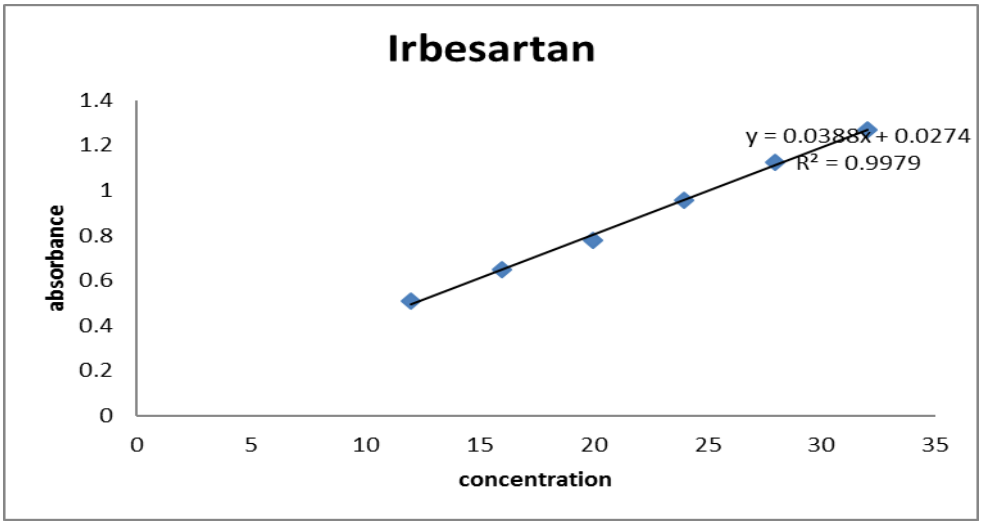

Figure No. 8: Calibration curve of Irbesartan (246.5 nm)

RESULT: Linearity in the response was obtained in the range of 10-100 µ/ml and regression equation was calculated as y=0.038x+0.027 and correlation value for irbesartan were found to be 0.997 which is within acceptance area.

PRECISION

System Precision for Rosuvastatin

Precision is the degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings of a homogeneous sample. Precision is usually expressed as the standard deviation or relative standard deviation.

Table No. 5: Depicting the system precision

Sr. No.	238.99 nm	246.5 nm
1.	0.161	0.134
2.	0.161	0. 138
3.	0.160	0.137
4.	0.160	0.133
5	0.161	0.135
Mean	0.642	0.542
Std dev	0.00057	0.00238
% RSD	0.369	0.439

RESULT: The percentage RSD for system precision was found to be at 246.5 nm is 0.439 and 238.99 nm is 0.369.

System Precision for Irbesartan

Precision is the degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings of a homogeneous sample. Precision is usually expressed as the standard deviation or relative standard deviation.

Table No. 6: Depicting the system precision

S. No	238.99 nm	246.5 nm
1.	1.127	1.078
2	1.127	1.082
3.	1.127	1.083
4.	1.126	1.083
5	1.129	1.085
6	1.128	1.084
Mean	0.938	1.082
Std dev	0.0002429	0.0024
% RSD	0.25%	0.22

RESULT: The percentage RSD for system precision was found to be at 246.5 nm is 0.25 and 238.99 nm is 0.22.

INTRADAY PRECISION

Table No. 7: Intraday data for Rosuvastatin

Time in min	238.99 nm (Absorbance)	246.5 nm (Absorbance)
5	15.3	16.92
10	14.04	15.5
20	12.2	14.09
30	13.01	13.86

The intra-day precision for rosuvastatin at 238.9 nm and 246.5 nm for 30 minutes is depicted in table 7. Also, in case of irbesartan the intra-day precision at 238.9 nm and 246.5 nm for 90 minutes is depicted in table 8.

Table No. 8: Intraday data for Irbesartan

Time in min	238.99 nm (Absorbance)	246.5 nm (Absorbance)
5	7.3	7.6
10	7.5	7.76
20	7.9	7.82
30	7.6	8.18
60	7.8	7.91
90	7.8	8.02

Robustness:

It is the measure of capacity of an assay to remain unaffected by small but deliberate variations in method parameters and provide an indication of its reliability in normal usage. Degradation and variations in chromatography columns, mobile phases and inadequate method development are common causes of lack of robustness.

1. Experiment performed by Analyst 1 and Analyst 2

2. Experiment performed in Room temp and air condition

3. Experiment performed by pipette change

The robustness of rosuvastatin for change in pipette size (2ml) is shown in table 9.

Table No. 9: Robustness data for Rosuvastatin change in pipette

Particular	238.99 nm	246.5 nm
1	0.432	0.427
2	0.537	0.465
3	0.480	0.414
4	0.537	0.465
5	0.480	0.414
Mean	108.3	0.442
Std dev	0.050	0.0026
% RSD	0.046	0.5

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 0.046 and 246.5 nm is 0.5. However, in case of change in pipette size to 5ml; the changes occurred are enlisted in table 10.

Table No. 10: Robustness data for Rosuvastatin change in pipette

Particular	238.99 nm	246.5 nm
1	0.488	0.419
2	0.441	0.378
3	0.419	0.360
4	0.432	0.372
5	0.432	0.372
Mean	1.74	1.8
Std dev	0.0266	0.0226
% RSD	1.8	1.4

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 0.0266 and 246.5 nm is 1.4. Further, the responses for change in temperature (maintained at cool condition) is shown in table 11.

Table No. 11: Depicting the robustness change in temp.

Particular	238.99 nm	246.5 nm
1	0.412	0.351
2	0.415	0.353
3	0.415	0.353
Mean	0.414	1.05
Std dev	0.0017	0.021

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 0.4 and 246.5 nm is 2. Furthermore, when the warm temperature condition was studied; following responses were observed as shown in table 12.

Table No. 12: Robustness data for Rosuvastatin change in temp

Particular	238.99 nm	238.99 nm
1	0.425	0.360
2	0.426	0.360
3	0.421	0.361
Mean	1.27	1.081
Std dev	0.002	0.0005
% RSD	0.15	0.04

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 0.15 and 246.5 nm is 0.04.

In case of robustness of irbesartan; similar conditions as maintained for rosuvastatin; the observation were observed for change in pipette size of 2 ml. The results are shown in table 13.

Table No. 13: Robustness data for Irbesartan change in pipette

Particular	238.99 nm	246.5 nm
1	0.081	0.077
2	0.076	0.072
3	0.075	0.071
Mean	0.22	1.4
Stddev	0.0031	0.0032
%RSD	1.4	0.4

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 1.4 and 246.5 nm is 0.4. Similarly, for change in pipette capacity of 5ml; the following results were observed shown in table 14.

Table No. 14: Robustness data for Irbesartan change in pipette

Particular	238.99 nm	246.5 nm
1	0.081	0.077
2	0.086	0.077
3	0.080	0.078
Mean	0.05	0.15
Std dev	0.0014	0.007
% RSD	0.28	0.4

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 0.28 and 246.5 nm is 0.4.

However, for change in temperature maintained at cool conditions; results are shown in table 15. At warm temperature conditions; the responses are listed in table 16.

Table No. 15: Robustness data for Irbesartan change in temp

Particular	238.99 nm	246.5 nm
1	0.070	0.078
2	0.077	0.072
3	0.075	0.073
Mean	0.04	0.75
Std dev	0.004	0.004
% RSD	0.46	0.46

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 0.46 and 246.5 nm is 0.46.

Table No. 16: Robustness data for Irbesartan change in temp.

Particular	238.99 nm	246.5 nm
1	0.111	0.104
2	0.110	0.103
3	0.110	0.103
Mean	0.110	0.103
Std dev	0.005	0.00115
% RSD	1.3	1.4

RESULT: The percentage RSD for robustness was found be at 238.99 nm is 1.3 and 246.5 nm is 1.4.

Comparative study of our work with other combination available in literature –

Literature reports the use of Rosuvastatin calcium in combination with other drugs and their estimation by UV and HPLC. Some of them are mentioned in table below:

Table No. 17: Comparison of rosuvastatin calcium by UV and HPLC method

Sr. No.	Name of Technique	Drugs use	Parameter estimation	References
1	HPLC	Rosuvastatin calcium and fenofibrate	Linearity, precisions, accuracy robustness, LOD and LOQ	M. Sumalatha*_et. al_, 2013
2	UV	Rosuvastatin calcium and clopidogrel	Assay, accuracy, linearity, Correlation coefficient,% RSD, Slope	Ch. Saikrishnareddy 2013
3	UV	Rosuvastatin calcium and ezetimide	Absorption maxima, beer's law, correlation coefficient, LOD and LOQ	Chirag b. Pandya* _et. al_, 2010

On the basis of table 17, it is clear that UV method is best suited for estimation of rosuvastatin calcium due to its several advantages like ease of application, handy to operate, not require much time *etc.*

CONCLUSION

This method was based on simultaneous equation for estimation of Rosuvastatin calcium and irbesartan literature review revealed that HPLC AND UV –Spectrophotometric method available for estimation of rosuvastatin and irbesartan is selected for analytical method development of rosuvastatin pharmaceutical dosage form. The method is developed and validated. The result is summarized here. The detection wavelength was found to be 238.99 nm and 246.5 nm linearity was observed in the range of 20 µg/ml and system precision and robustness were found within official limit of <2%.

Simultaneous equation method for estimation of rosuvastatin and irbesartan was developed by UV-visible spectroscopy. This method was validated using parameter linearity, system precision and robustness. The linearity range for rosuvastatin calcium was found to 8-32µg/ml and irbesartan was also found to be 8-32 µg/ml. Correlation coefficient value found to be R2 =0.997 and 0.995. For rosuvastatin at 238.99 nm and 246.5 nm and correlation coefficient value found to be R^2=0.996 and 0.997 for irbesartan at 238.99 and 246.5. The method was found to precise and robustness.

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