Development and Validation of A Cerium (Iv)–Indigo Carmine-Based Indirect Spectrophotometric Method for The Quantitative Determination of Selected Pharmaceutical Formulations

Dr. Rajitha Balusani

Department of Chemistry
Government Degree College, Ibrahimpatnam, Rangareddy (Dist), Telangana, India – 501506.

Abstract:
A simple, sensitive, and cost-effective indirect spectrophotometric method was developed and validated for the quantitative determination of Ciprofloxacin, Pantoprazole Sodium Sesquihydrate, Atorvastatin Calcium, and Rosuvastatin Calcium in bulk drugs and pharmaceutical formulations. The method is based on the oxidation of the selected drugs with a measured excess of Cerium (IV) Ammonium Sulphate in Sulphuric acid medium, followed by the spectrophotometric determination of the residual oxidant using indigo carmine dye. Experimental conditions, including acid concentration and reaction time, were systematically optimized to achieve maximum sensitivity and stable analytical response. The proposed method exhibited excellent linearity within the respective Beer's law ranges and was validated according to International Council for Harmonisation (ICH) guidelines for accuracy, precision, limit of detection, limit of quantification, robustness, and ruggedness. Recovery studies demonstrated excellent accuracy and confirmed the absence of interference from common pharmaceutical excipients. Owing to its simplicity, rapid analysis, low operational cost, and reliable performance, the proposed method provides an efficient alternative to sophisticated instrumental techniques and is well suited for routine quality control analysis of pharmaceutical formulations.

Keywords: Indirect Spectrophotometry; Cerium (IV); Indigo Carmine; Pharmaceutical analysis; Method validation.

I. INTRODUCTION

The development of simple, rapid, and reliable analytical methods for pharmaceutical quality control remains an important area of research in pharmaceutical and analytical chemistry. Although chromatographic techniques such as High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), and Liquid Chromatography–Mass Spectrometry (LC–MS/MS) provide excellent sensitivity and selectivity, their routine application is often limited by expensive instrumentation, complex sample preparation, high solvent consumption, and longer analysis time. Consequently, visible spectrophotometric methods continue to attract considerable interest because of their simplicity, affordability, operational convenience, and suitability for routine quality control laboratories.

Ciprofloxacin (CIP) [1-6]], Pantoprazole Sodium Sesquihydrate (PNT),[1-6] Atorvastatin Calcium (ATV)[1-2], and Rosuvastatin calcium (ROSU) [1-2, 34-35]are widely prescribed therapeutic agents used for the

treatment of bacterial infections, acid-related gastrointestinal disorders, hypercholesterolemia, and dyslipidemia, respectively. Owing to their extensive clinical use, the development of accurate and reliable analytical methods for their quantitative determination in bulk drugs and pharmaceutical formulations is essential to ensure product quality, efficacy, and patient safety.

Several analytical procedures have been reported for the estimation of these drugs, including UV-Visible Spectrophotometry[8, 16-19,32,39-42] HPLC[7, 24-26, 30-31, 43-46, 52]] RP-HPLC[9,20,21,53-56 27-29,43-46,47-48]] HPTLC[22,49], UPLC[11], LC–MS/MS, spectrofluorimetry[23], FTIR spectroscopy[12,13], Voltammetry[14,50] Turbiditry Method [10], Microbiological assays[15,33] and LC–MS/MS with Electrospray ionization method [36-38], Although these methods offer satisfactory analytical performance, many require sophisticated instrumentation, skilled personnel, lengthy analytical procedures, or high operational costs, which restrict their routine application in laboratories with limited resources.

Oxidation-based spectrophotometric methods offer a simple, sensitive, and reproducible approach for pharmaceutical analysis. Cerium(IV), owing to its high oxidation potential and stable reaction kinetics in acidic medium, is an effective oxidising agent for indirect spectrophotometric determination using chromogenic dyes such as Indigo Carmine. Although several analytical methods have been reported for Ciprofloxacin, Pantoprazole Sodium Sesquihydrate, Atorvastatin Calcium, and Rosuvastatin Calcium, a validated Cerium(IV)–Indigo Carmine method for their quantitative estimation has not been reported. Therefore, the present study develops and validates a rapid, economical, and sensitive indirect spectrophotometric method in accordance with ICH guidelines and demonstrates its applicability for the routine analysis of pharmaceutical formulations.

Table 1: Comparison Of Various Existing Methods Used For Quantification Of Four Drugs

S.No.	Drug	Method	Quantification limit	%RSD
1	Ciprofloxacin	HPLC	4.0-24.0 (µg ml^{-1})	1.00
		HPLC	150-900 (µg ml^{-1})	0.19
		UPLC	6.33-50.69 (µg ml^{-1})	0.18
		Turbidimetry	14.0-56.0 (µg ml^{-1})	1.85
		RP-HPLC	3.0-18.0 (µg ml^{-1})	1.50
		UV Spectrophotometry	10.0-35.0(µg ml^{-1})	0.75
2	Pantoprazole Sodium Sesquihydrate	HPLC	1.0-10.0 (µg ml^{-1})	1.82
		RP-HPLC	15.0-75.0(µg ml^{-1})	0.73
		RP-HPLC	2.6-13.0 (µg ml^{-1})	0.
		UV Spectrophotometry	10.0-50.0(µg ml^{-1})	0.64
		UV Spectrophotometry	2.5-50.0 (µg ml^{-1})	1.85
		UV Spectrophotometry	2.0-20.0 (µg ml^{-1})	0.75
3	Atrovastatin Calcium	HPLC	4.0-24.0 (µg ml^{-1})	1.69
		HPTLC	200-1200(ng/spot)	0.38
		RP-HPLC	50.0-150.0(µg ml^{-1})	0.57
		RP-HPLC	8.13-23.77 (µg ml^{-1})	0.63

		UV Spectrophotometry	4.0-24.0 (µg ml^{-1})	0.39
4	Rosuvastatin Calcium	RP-HPLC	3.0-1602 (µg ml^{-1})	0.92
		RP-HPLC	1-160 (µg ml^{-1})	0.84
		HPLC	5-20 (µg ml^{-1})	0.79
		HPTLC	11-33.56(µg ml^{-1})	0.93
		UV Spectrophotometry	5-30 (µg ml^{-1})	0.56
		UV Spectrophotometry	5-35 (µg ml^{-1})	0.29

II.PRINCIPLE OF THE METHOD

Cerium(IV) is a strong oxidizing agent (E° = 1.44 V) widely used in pharmaceutical analysis because of its high oxidation efficiency and stability in acidic medium. The proposed indirect spectrophotometric method is based on the oxidation of the selected drugs with a measured excess of Cerium(IV) Ammonium Sulphate in Sulphuric acid medium, followed by the determination of the residual oxidant using Indigo Carmine dye. Unreacted Cerium(IV) oxidizes Indigo Carmine

, and the absorbance of the remaining dye is measured at 610 nm. As the concentration of the drug increases, more Cerium(IV) is consumed during oxidation, leaving less oxidant available to react with the dye, resulting in a proportional increase in absorbance. This relationship forms the basis for the quantitative determination of the selected pharmaceutical compounds.

Among the chromogenic dyes commonly employed in Cerium(IV)-based spectrophotometric methods, indigo carmine was selected because of its superior sensitivity, colour stability, and reproducibility, making the proposed method simple, accurate, and suitable for routine pharmaceutical quality control analysis.

Structure of Drugs

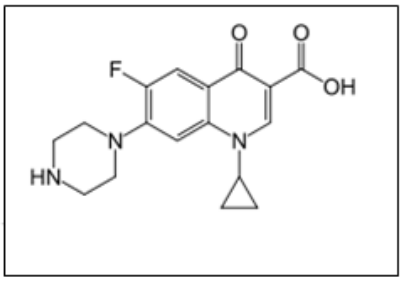

Fig 1 Ciprofloxacin

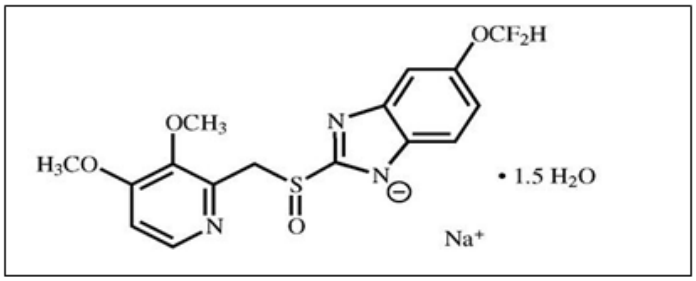

Fig. 2 Pantoprazole Sodium Sesquihydrate

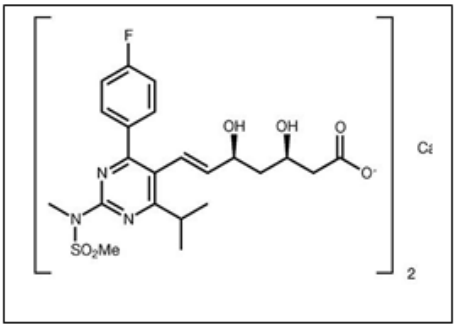

Fig.3 Atrovastatin Calcium

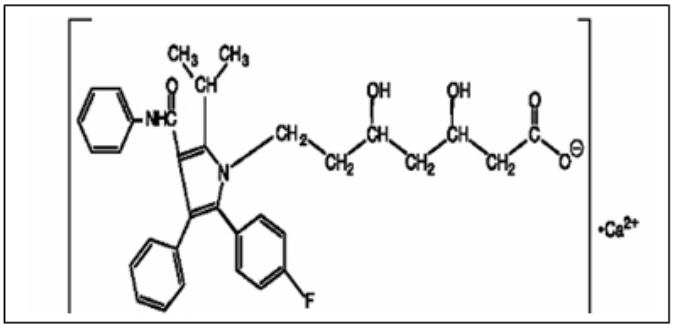

Fig.4 Rosuvastatin Calcium

III. EXPERIMENTAL

3.1. Instrumentation

Absorbance measurements were carried out using ELICO SL-210 double-beam, Thermo Nicolet 1000, and ELICO SL-159 UV–Visible spectrophotometers equipped with 10 mm quartz cells. Sample weighing was performed using a Dhona 200 single-pan electronic balance.

3.2. Chemicals and Reagents

All chemicals and reagents were of analytical reagent (AR) grade, and bidistilled water was used throughout the study.

Cerium(IV) solution: Cerium(IV) Sulphate (750 mg, $CeSO_4 \cdot 2H_2O$, 99.9%; Merck, Mumbai, India) was dissolved in 2 M Sulphuric acid with gentle heating, filtered through glass wool, diluted to 250 mL with the same acid, and standardized using Ferrous Ammonium Sulphate with Ferroin indicator. A working solution of 4.0×10^{-3} M (0.25%) was prepared by appropriate dilution.

Indigo Carmine solution: A stock solution (1000 μg mL^{-1}) was prepared by dissolving 112 mg of Indigo Carmine (Sigma-Aldrich, 90% purity) in bidistilled water and diluting to 100 mL. A working solution of 200 μg mL^{-1} was obtained by suitable dilution.

Sulphuric acid: A 2 M H_2SO_4 solution was prepared by diluting concentrated Sulphuric acid (Merck, Mumbai, India; 98%, sp. gr. 1.84) with distilled water.

3.3. Preparation of Standard Drug Solutions

Standard stock solutions (200 μg mL^{-1}) of Ciprofloxacin (CIP), Pantoprazole Sodium Sesquihydrate (PNT), Atorvastatin Calcium (ATV), and Rosuvastatin Calcium (ROSU) were prepared by accurately dissolving 20 mg of each drug in an appropriate solvent and diluting to 100 mL in volumetric flasks. Working standard solutions were prepared by further dilution of the respective stock solutions with the corresponding solvent.

IV. ANALYTICAL PROCEDURE

Appropriate aliquots of standard drug solutions corresponding to concentration ranges of **1.2–8.4 μg mL^{-1} (CIP), 1.6–11.2 μg mL^{-1} (PNT), 1.8–12.6 μg mL^{-1} (ATV), and 1.5–10.5 μg mL^{-1} (ROSU)** were transferred into separate 10 mL volumetric flasks. To each flask, **1.0 mL of Cerium(IV) Ammonium Sulphate (CAS)** solution and **1.0 mL of 2 M Sulphuric acid** were added, and the mixtures were thoroughly shaken. After allowing the oxidation reaction to proceed for **15 min** at room temperature, **1.0 mL of 0.02% Indigo Carmine solution** was added, and the solutions were diluted to volume with distilled water and mixed well. The absorbance was measured at **610 nm** against a corresponding reagent blank. The concentration of each drug was determined from the respective calibration curve constructed under the optimized experimental conditions.

V. ASSAY OF PURE DRUG SAMPLE

The accuracy and precision of the proposed method were evaluated by analyzing pure drug samples within their respective Beer's law concentration ranges: **1.2–8.4 μg mL^{-1} for Ciprofloxacin (CIP), 1.6–11.2 μg mL^{-1} for Pantoprazole Sodium Sesquihydrate (PNT), 3.0–21.0 μg mL^{-1} for Atorvastatin Calcium (ATV), and 1.5–10.5 μg mL^{-1} for Rosuvastatin Calcium (ROSU).** Each solution was treated with **1.0 mL of Cerium(IV) Ammonium Sulphate solution (250 μg mL^{-1})** and **1.0 mL of 2 M Sulphuric acid**, and the residual Cerium(IV) was determined using the optimized indigo carmine procedure described above. Calibration curves were constructed by plotting absorbance against drug concentration for each analyte.

All measurements were performed in six replicates to evaluate the repeatability of the method. The relative response (absorbance-to-concentration ratio) was calculated for each determination, and responses within **95–105%** of the mean value were considered acceptable for constructing the calibration curves and assessing the analytical performance of the method.

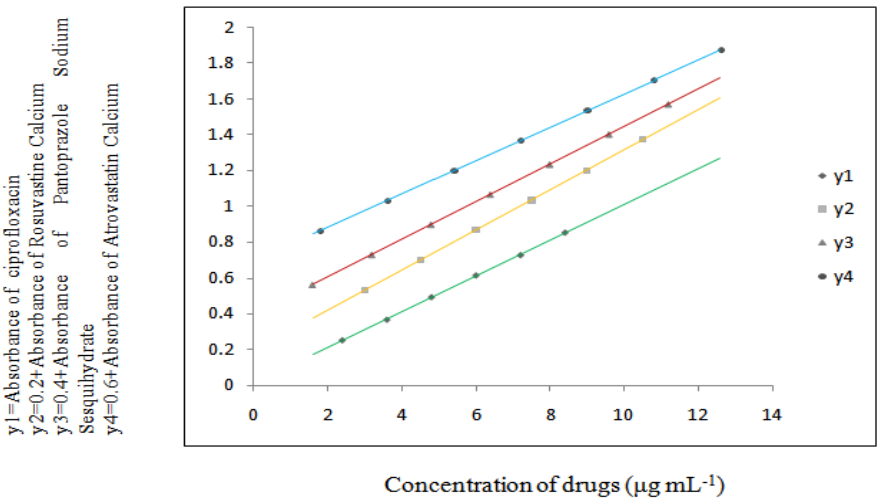

Fig.5 Calibration curves of CIP, ROSU, PNT and ATV

5.1 Procedure For Assay Of Pure Drug

Pure drug samples within their respective Beer's law concentration ranges were analyzed to evaluate the accuracy and precision of the proposed method. Recovery studies were performed at selected concentration levels, and the results are presented in **Table 3**. Precision was assessed from six replicate determinations and expressed as %RSD. Recovery values close to 100% and %RSD values below 2% confirmed the excellent accuracy, precision, and reliability of the developed method.

VI. ANALYSIS OF PHARMACEUTICAL FORMULATIONS

6.1 Commercial tablet formulations of Ciprofloxacin (CIPRO, 250 mg), Pantoprazole Sodium Sesquihydrate (40 mg), Atorvastatin Calcium (10 mg), and Rosuvastatin calcium (ROSUVAS, 20 mg) were accurately weighed and finely powdered. An amount of powder equivalent to 10 mg of the respective drug was transferred to a 100 mL volumetric flask and extracted with an appropriate solvent (double-distilled water for CIP and PNT; methanol for ATV and ROSU). For Atorvastatin and Rosuvastatin, the solutions were sonicated for 10 min to ensure complete dissolution.

The resulting solutions were diluted to volume, mixed thoroughly, and filtered through Whatman No. 42 filter paper to obtain stock sample solutions. Appropriate aliquots were further diluted with the corresponding solvent to prepare working solutions for spectrophotometric analysis under the optimized experimental conditions.

VII. METHOD OF VALIDATION

The proposed method was validated according to ICH guidelines[51] for linearity, accuracy, precision, LOD, LOQ, selectivity, robustness, and ruggedness. Calibration curves were constructed by plotting absorbance against drug concentration. Accuracy and precision were assessed from six replicate analyses, yielding recoveries close to 100% with %RSD values below 2% (Table 3). LOD and LOQ were calculated using **LOD = 3.3σ/S** and **LOQ = 10σ/S**. Selectivity studies confirmed the absence of interference from common pharmaceutical excipients, while robustness and ruggedness evaluations under minor experimental variations showed no significant changes in analytical response, demonstrating the reliability and reproducibility of the proposed method.

VIII.OPTIMIZATION OF EXPERIMENTAL CONDITIONS

4.1. Selection of Acid

The influence of different acids, namely Sulphuric acid (H_2SO_4), Phosphoric acid (H_3PO_4), and Acetic acid (CH_3COOH), on the oxidation reaction was investigated. Among the acids tested, Sulphuric acid provided the highest and most stable absorbance and was therefore selected as the reaction medium for subsequent studies.

4.2. Effect of Acid Concentration

The effect of sulphuric acid concentration was evaluated using different acid strengths (0.5–2.5 M) and volumes (0.5–2.5 mL). Maximum absorbance was obtained with **1.0 mL of 2 M H_2SO_4** in the presence of **1.0 mL of 4.0×10^{-3} M Cerium(IV)** solution. Higher acid concentrations resulted in a decrease in absorbance; therefore, these optimized conditions were adopted for all measurements.

4.3. Effect of Reaction Time

The influence of reaction time was examined over the range of **2.5–20 min**. The oxidation reaction reached completion within **15 min**, producing maximum and stable absorbance. Hence, a reaction time of **15 min** was selected for the proposed method.

IX. ANALYSIS OF PHARMACEUTICAL FORMULATIONS

The applicability of the proposed method was evaluated by analyzing commercial tablet formulations within their respective Beer's law concentration ranges. Each analysis was performed in six replicates, and the results were expressed in terms of percentage recovery and relative standard deviation (%RSD). As summarized in **Table 4**, recovery values close to 100% and %RSD values below 2% confirmed the accuracy, precision, and suitability of the method for routine pharmaceutical quality control.

X. RESULTS AND DISCUSSION

The proposed indirect spectrophotometric method is based on the oxidation of the selected drugs by a measured excess of Cerium(IV) Ammonium Sulphate in an acidic medium, followed by the determination of the residual oxidant using indigo carmine dye. The remaining Cerium(IV) oxidizes Indigo Carmine, resulting in a decrease in dye concentration, while the unreacted dye exhibits a characteristic absorbance at **610 nm**.

As the concentration of the drug increases, a larger amount of Cerium(IV) is consumed during the oxidation process, leaving less oxidant available to react with indigo carmine. Consequently, the concentration of the residual dye increases, producing a proportional increase in absorbance. Under the optimized conditions, a linear relationship between absorbance and drug concentration was observed over the respective Beer's law ranges for all four analytes.

The oxidation reaction was efficiently carried out using **1.0 mL of 2 M sulphuric acid**, which provided maximum and stable absorbance. The proposed reaction mechanism can be represented as follows:

Drug + Excess Ce(IV) → Oxidized Drug + Ce(III) + Unreacted Ce(IV)
Unreacted Ce(IV) + Indigo Carmine → Oxidized Dye + Residual Indigo Carmine

The absorbance of the residual Indigo Carmine was measured at **610 nm**, forming the basis for the quantitative determination of the selected pharmaceutical compounds.

XI. ANALYTICAL DATA

The analytical performance of the proposed method was evaluated by constructing calibration curves over the respective Beer's law concentration ranges. A good linear relationship was observed between absorbance and drug concentration for all the selected drugs. The sensitivity of the method was assessed in terms of Sandell's

Sensitivity, Limit of Detection (LOD), and Limit of Quantification (LOQ), which were calculated according to ICH guidelines and are summarized in **Table 2**.

Regression analysis of the calibration data was performed using the least-squares method to determine the slope (b), intercept (a), and correlation coefficient (r). The high correlation coefficients obtained confirm the excellent linearity and reliability of the proposed spectrophotometric method for the quantitative determination of the selected pharmaceutical compounds.

XII. ACCURACY AND PRECISION

The accuracy and precision of the proposed method were evaluated using pure drug samples at six concentration levels. Accuracy was expressed as percentage recovery and relative error (%RE), while precision was assessed by relative standard deviation (%RSD). The results (Table 3) showed high recovery values and %RSD below 2%, confirming the accuracy, precision, and reproducibility of the method.

XIII. ROBUSTNESS AND RUGGEDNESS

The robustness of the proposed method was evaluated by introducing minor variations in Sulphuric acid volume and reaction time, while ruggedness was assessed using different analysts and spectrophotometers. No significant changes in absorbance or analytical performance were observed, confirming the robustness, ruggedness, and reproducibility of the method.

XIVAPPLICATION TO PHARMACEUTICAL FORMULATIONS

The proposed method was successfully applied to the analysis of commercial tablet formulations, yielding assay results in good agreement with the labeled claims and without interference from common excipients (Table 4). Statistical comparison with reported methods using Student's *t*-test and *F*-test (Table 5) showed no significant difference at the 95% confidence level. Standard addition studies (50%, 100%, and 150% levels) produced satisfactory recoveries, confirming the accuracy, reliability, and suitability of the method for routine pharmaceutical quality control.

XV.CONCLUSION

A simple, sensitive, and validated indirect spectrophotometric method was developed for the quantitative determination of Ciprofloxacin, Pantoprazole Sodium Sesquihydrate, Atorvastatin Calcium, and Rosuvastatin Calcium in bulk drugs and pharmaceutical formulations. The proposed Cerium(IV)–Indigo Carmine system demonstrated excellent accuracy, precision, selectivity, and robustness, with no interference from common pharmaceutical excipients. Owing to its simplicity, rapid analysis, low cost, and reliable analytical performance, the method provides a practical alternative to sophisticated instrumental techniques and is well suited for routine quality control applications in pharmaceutical laboratories.

Acknowledgement

The authors thank Prof. M. Sayaji Rao (Retd.), Department of Chemistry, University College of Science, Osmania University, for guidance.

Table 2: Analytical And Regression Parameters Of Spectrophotometric Method

Name of drug Property	CIP	PNT	ATV	ROSU
λ_{max}, nm	610	610	610	610
Beer's law limits (μg mL^{-1})	1.1-8.3	1.7-11.3	1.3-12.3	1.4-10.6
Molar absorptivity	$5.12x10^4$	$4.31x10^4$	$7.25x10^4$	$1.27X10^4$

Sandell's sensitivity (µg cm^{-2})	0.0370	0.3229	0.017627	0.101525
Variance $(S_a)^2$	0.0310	0.0023	0.00089	0.0011
Limit of detection µg mL^{-1}	1.8062	1.5102	1.8255	1.1682
Limit of quantification µg mL^{-1}	5.4736	4.5756	5.5323	3.8127
Regression equation, Y**				
Intercept, (a)	0.0027	0.0032	0.0215	0.0938
Slope, (b)	0.0278	0.1016	0.0557	0.0114
Correlation coefficient, (r)	0.9998	0.9999	0.9945	0.9903
Standard deviation of intercept (S_a)	0.0144	0.0461	0.0312	0.0324
Standard deviation of slope (S_b)	0.0013	0.0103	0.0073	0.0012

*Limit of determination as the weight in µg per mL of solution, which corresponds to an absorbance of A = 0.001 measured in a cuvette of cross-sectional area 1 cm2 and path length of 1 cm. Y** = a+bX, where Y is the absorbance and X concentration of drugs in µg per mL.

Table 3: Determination Of Accuracy And Precision Of The Methods On Pure Drug Samples

Drug	Taken (µg/ml)	Found (µg/ml)	error (%)	Recovery (%)	RSD (%)	Proposed method Mean ± SD
CIP	1.2 2.0 3.0	1.18 2.0 3.02	1.66 0.00 0.66	98.33 100.00 100.66	1.200	99.66 ±1.201
PNT	2.0 4.0 6.0	2.01 3.9 6.02	0.50 2.50 2.00	100.50 97.50 100.33	1.382	99.44 ±1.375
ATV	3.0 6.0 9.0	2.95 6.01 9.02	1.66 0.16 0.22	98.33 100.16 100.22	1.074	99.57 ±1.074
ROSU	1.5 3.0 6.0	1.51 2.98 5.92	0.66 0.66 1.33	100.66 99.33 98.66	1.018	99.55 ±1.018

Table 4 Results of Assay of Tablets By The Proposed Methods And Statistical Evaluation And Recovery Experiments By Standard Addition Method.

Tablets	Drug in tablet µg mL^{-1}	Drug added µg mL^{-1}	Total found µg mL^{-1}	Error (%)	Recovery (%)	RSD (%)	Reference method Mean± **SD**	Proposed method ± **SD**
CIPRO (CIP)	0.50 0.50 0.50 1.2 2.4 3.0	1.0 2.0 3.0 0.0 0.0 0.0	1.47 2.48 3.48 1.21 2.40 3.02	0.66 0.80 0.57 0.83 0.00 0.66	99.33 99.20 99.43 100.83 100.00 99.33	0.66285	100.15 ±0.18	99.69 ±0.6265

PANTO PRAZOLE (PNT)	0.50 0.50 0.50 2.0 4.0 6.0	0.3 0.6 0.9 0.0 0.0 0.0	0.78 1.11 1.39 2.00 3.01 5.97	0.00 0.90 0.71 0.00 0.25 0.50	100.00 100.90 99.29 100.00 100.25 99.50	0.5704	98.16 ±1.15	99.99 ±0.5703
ATRO VASTATIN CALCIUM (ATV)	0.50 0.50 0.50 3.0 6.0 9.0	1.0 2.0 3.0 0.0 0.0 0.0	1.49 2.48 3.50 2.98 6.01 8.97	0.66 0.80 0.00 0.66 0.16 0.33	99.33 99.20 100.00 98.33 100.16 99.66	0.6822	100.03 ±0.409.	99.62 ±0.6784
ROSUVAS (ROSU)	0.50 0.50 0.50 2.0 3.0 4.5	1.0 2.0 3.0 0.0 0.0 0.0	1.503 2.52 3.48 1.985 3.02 4.45	0.20 0.80 0.57 0.75 0.66 1.11	100.20 100.80 99.43 99.25 99.33 98.88	0.7137	100 ±1.070	99.65 ±0.7112

Table 5: F-Test And t-Test Values

	CIPRO (CIP)	PANTOPRAZOLE (PNT)	ATROVASTATIN CALCIUM (ATV)	ROSUVAS(ROSU)
F-test*	1.426 (3.182)	1.313 (2.571)	0.157 (2.262)	0.535 (2.447)
t-test**	0.28 (4.75)	0.17 (4.38)	0.18 (4.09)	0.63 (4.28)

*t- test and **F-test values from literature.

REFERENCES:

1. The Merck index. An encyclopedia of Chemicals, Drugs and biologicals. 2006;14th ed., 6291.
2. Balfour JAB, Lamb HM. Drugs. 2000;59:115–39.
3. Muijsers RBR, Jarvis B. Drugs. 2002;62:967–73.
4. Cazedey, Edith Cristina Laignier; Salgado, Herida Regina Nunes, Spectrophotometric determination of Ciprofloxacin hydrochloride in ophthalmic solution, Advances in Analytical Chemistry (2012), 2(6), 74-79, 6 pp.
5. The Merck index, 13th edn., Merck and Co Inc., White house station, N.J., USA ,779.
6. Mathew, Das Gupta V., Bailey R.E., Drug Dev. Ind.Pharm.(8), 1995.
7. Najla Mohamad Kassab, AnilKumar singh, Erika Rosa aria Kedor-Hackmam, Maria Ines Rocha Miriello Santoro, Quantitative determination of Ciprofloxacin and Norfloxacin in pharmaceutical preparations by high performance liquid chromatography, Brazillian Journal of pharmaceutical Sciences,Vol.41, n.4, out / dez, 2005.
8. *Sowjanya Gummadi1 , Devi Thota1 , Sri Valli Varri1 , Pratyusha Vaddi1 , Venkata Lakshmi Narasimha Seshagiri Rao Jillella2, Gummadi et al., Development and validation of UV spectroscopic methods for simultaneous estimation of Ciprofloxacin and tinidazole in tablet formulation International Current Pharmaceutical Journal 2012, 1(10): 317-321
9. Urvish H. Desai* , Arpit H. Patwari, Jaydeepkumar K. Maradiya, Mehul K. Sathawara, Bhanubhai N. Suhagia, Ishwarsinh S. Rathod, RP-HPLC Method for Simultaneous Estimation of Ciprofloxacin and

Dexamethasone in Eye/Ear Drops International Journal of Pharmaceutical Sciences and Drug Research 2013; 5(2): 62-66, ISSN 0975-248X.

10. ELaignier Cazedey, Herida Regina Nunes Salgado, A novel and rapid microbiological assay for Ciprofloxacin hydrochloride, Journal of Pharmaceutical Analysis Volume 3, Issue 5, October 2013, Pages 382–386.
11. Subhakar Nandipati1* , Krishna Reddy Vanka1, Sreenivas Uba2, The Separation And Quantitative Determination Of Ciprofloxacin In A Pharmaceutical Formulation By Ultra Performance Liquid Chromatograph, International Journal Of Pharmacy And Pharmaceutical Sciences Issn- 0975-1491 Vol 5, Issue 3, 2013.
12. Tablets S. Pandey,* P. Pandey, G. Tiwari, R. Tiwari, and A. K. Rai, FTIR Spectroscopy: A Tool for Quantitative Analysis of Ciprofloxacin in Indian J Pharm Sci. 2012 Jan-Feb; 74(1): 86–90.
13. Skoulika, Stavroula G.; Georgiou, Constantinos, A.Rapid Quantitative Determination of Ciprofloxacin in Pharmaceuticals by Use of Solid-State FT-Raman Spectroscopy, Volume 55, Number 9 (Sept. 2001) Page 1259-1265.
14. Erk N. Differential pulse anodic voltammetric determination of pantoprazole in pharmaceutical dosage forms and human plasma using glassy carbon electrode, Analytical Biochemistry,323(1), 2003, 48-53
15. Castro S, Neto O, Santos S, Medeiros E, Araujo M, Josue C, Korn M. for determination of pantoprazole in pharmaceutical tablets, Journal A flow-injection biamperometric method of AOAC international, 88(4), 2005, 1064-1068.
16. Basavaiah K, Anilkumar U, Tharpa K, Spectrophotometric Determination of Pantoprazole Sodium in Pharmaceuticals Using N-Bromosuccinimide, Methyl Orange and Indigo Carmine as Reagents, Iranian Journal of Chemistry and Chemical engineering, 28(1), 2009, 31-36.
17. Okram Zenita Devi and Kanakapura Basavaiah*, Validated spectrophotometric determination of pantoprazole sodium in pharmaceuticals using ferric chloride and two chelating agents International Journal of ChemTech Research, CODEN(USA): IJCRGG ISSN : 0974-4290, Vol.2, No.1, pp 624-632, Jan-Mar 2010.
18. Nejal M. Bhatt,1 Vijay D. Chavada,1 Mallika Sanyal,2 and Pranav S. Shrivastav1, Manipulating Ratio Spectra for the Spectrophotometric Analysis of Diclofenac Sodium and Pantoprazole Sodium in Laboratory Mixtures and Tablet Formulation, The Scientific World Journal Volume 2014 (2014), Article ID 495739.
19. Mohamed M. Baraka*1, Mohamed E. El-Sadek , Lobna M. Abdel-Aziz, Samar S. El-Bermawi, Mohamed M Baraka. Et Al. / Validated Spectrophotometric Determination Of Panto Prazole Sodium In Tablets Using 2, 4-Dinitrofluorobenzene Through Nucleophilic Substitution Reaction Asian Journal Of Pharmaceutical Analysis And Medicinal Chemistry. 2(1), 2014, 26 - 36.
20. Rishna R. Gupta*, Rajesh B. Chawla and Sudhir G. Wadodka Stability indicating RP-HPLC method for simultaneous determination of pantoprazole sodium and itopride hydrochloride in bulk and capsule, ISSN 1984-6428, |Vol 2, No. 3, July-September 2010
21. Kampati Anil Kumar*, Ree.V. Janadharanan, Yarasi Surendranath Reddy, Vanam Naveen Kumar, Method Development And Validation For Simultaneous Estimation Of Pantoprazole Sodium And Itopride Hydrochloride In Its Bulk Dosage Forms By Rp-Hplc, Inernational Journal Of Pharmacy And Pharmaceutical Sciences, Vol 5, Suppl 1, 2013.
22. A validated stability indicating HPLC method for the determination of process-related impurities in pantoprazole bulk drug and formulations. *Braz. J. Pharm. Sci. vol.49 no.1 São Paulo Jan./Mar. 2013*
23. Fathalla Belal, Mohie Sharaf EL-Din,Manar M. Tolba and Heba Alaa, Enhanced spectrofluorimetric determination of esomeprazole and Pantoprazole in dosage forms and spiked human plasma using

organized media, The Journal of Biological and chemical Luminescene, Volume 30, Issue 3, Pages 343-351, JUL 2014.

24. BG Chaudhari, NM Patel, PB Shah, Development and validation of a HPTLC method for the simultaneous estimation of Atorvastatin Calcium and ezetimibe, Indian journal of Pharmaceutical science, 2007 Apr;**23**(4):445-51. 9.
25. SB Wankhede, NR Dixi, Stability indicating HPTLC method for quantitative determination of Atorvastatin Calcium and metoprolol succinate in capsules, - Der Pharmacia Sinica Journal, 5(1), 89-93. 3. 2011.
26. Ginoya Charmi G, Dinesh V. Thakkar, Ginoya Charmi G Et Al, Development And Validation Of HPTLC Method For Simultaneous Determination Of Metoprolol Succinate And Atorvastatin Calcium In A Pharmaceutical Dosage Form International Research Journal Of Pharmacy, . Irjp 2013, 4(2) Page 102
27. DA Shah, KK Bhatt, RS Mehta, MB Shanka , Development and validation of a RP-HPLC method for determination of Atorvastatin Calcium and aspirin in a capsule dosage form - Indian journal of pharmacuetical science, 69 (4), 546, **2007**.
28. Suresh Kumar GV1*, Rajendraprasad Y, Chandrashekar SM, Development and validation of reversed-phase HPLC method for Simultaneous Estimation of Atorvastatin Calcium and Telmisartan in Tablet dosage form, International Journal of PharmTech Research, ISSN : 0974-4304, Vol.2, No.1, pp 463-470, Jan-Mar 2010.
29. RP-HPLC method development and validation for the simultaneous estimation of Atrovastatin and Ezetimibe in pharmaceutical dosage form. Saroj Kumar Raul, Atna Bhaskar Aravelli, Durgasi Jhansi, *Asian Journl of Pharmaceutical and clinical research, Vol 8, Issue 2, 2015.*
30. Mohammadi, A., N. Rezanour, M. Ansari, F. Dogaheh, G. Bidkorbeh, M. Hashem and R.B. Walker. A stability-indicating high performance liquid chromatographic (HPLC) assay for the simultaneous determination of atrovastatin – amlodipine in commercial tablets. J. Chrom. B., 846: 215-22, 2007.
31. Stability-indicating HPLC method for the simultaneousdetermination of pantoprazole, rabeprazole, lansoprazole and domperidone from their combination dosage form, Vaithiyanathan Sree Janardhanan*, Rajappan Manavalan and Kannappan Valliapp, International Journal of Drug Development & Research October-December 2011, Vol. 3, Issue 4, ISSN 0975-9344.
32. Capsules Sagar B. Wankhede*, Nitin R. Dixit, Sohan S. Chitlange, Validated spectrophotometric methods for quantitative determination of Atorvastatin Calcium and Metoprolol succinate in, Der Pharma Chemica , 2010, 2(1): 134-140 ISSN 0975-413X , 134,
33. Xiu-Sheng, M. and C.D. Metcalfe, Determination of cholesterol-lowering statin drugs in aqueous samples using liquid chromatography-electrospray ionization tandem mass spectrometry. J. Chrom B., 998: 133-14,2003.
34. Journal of Pharmaceutical and Biomedical Analysis 2000 Feb;22(1):45-58.
35. S.C. Sweetman Martindale-The Complete Drug Reference (thirty-sixth ed.), 1The Pharmaceutical Press, London, UK (2009) pp. 1218–1219, 1238–1239, 1284–12851310, 1307–1310.
36. Trivedi R.K. Kallem R.R. Mullangi R. Srinivas N.R., Simultaneous determination of rosuvastatin and fenofibric acid in human plasma by LC–MS/MS with electrospray ionization: Assay development, validation and application to a clinical study, J Pharma Biomed Anal., 2005, 39, 661-669.
37. Xu D.H. Ruan Z.R. Zhou Q. Yuan H. Jiang B., Quantitative determination of rosuvastatin in human plasma by liquid chromatography with electrospray ionization tandem mass spectrometry, Rapid Commun Mass Spectrom., 2006, 20, 2369-2375.
38. Kallem R.R. Karthik A. Chakradhar L. Mullangi R. Srinivas N.R., Development and validation of a highly sensitive and robust LC-MS/MS with electrospray ionization method for quantification of

rosuvastatin in small volume human plasma samples and its application to a clinical study, Arzneimittel forsch., 2007, 57, 705-11.

39. Uyar B. Celebier M. Altinoz S., Spectrophotometric determination of rosuvastatin calcium in tablets, Pharmazie., 2007, 62, 411-413.
40. Rekha, Rajeevkuma, *, S. Anbazhagan1, P. Rajeev Kumar2and K. Nimesh , Novel Simultaneous Determination of Rosuvastatin Calcium and Fenofibrate in Tablet Formulation by Derivative Spectrophotometry, International Journal of Research in Pharmaceutical and Biomedical Sciences, ISSN:2229-3701,2011.
41. G. Sre, Chandini Saha, elatha, Md. Nazeeruddin,, Spectrophotometric Estimation Of Rosuvastatin Calcium In Bulk & Pharmaceutical Formulations, Int.J. Pharmacy and Analytical Research vol-2(3) 2013.
42. Ramnath Y. Lahare*, Ashish N. Phuge, Ajit L. Gite3 and Arjun K. Jadhav3, A Review on Ultraviolet Spectrophotometric Determination of Rosuvastatin Calcium in Marketed Formulation, International Journal Of Pure & Applied Bioscience, ISSN: 2320 – 7051 Int. J. Pure App. Biosci.2 (6): 169-174 (2014).
43. Singh S.S. Sharma K. Patel H. Jain M. Shah H. Gupta S. Thakkar P. Patel N. Singh S.P. Lohray B.B., Estimation of Rosuvastatin in human plasma by HPLC tandem mass spectroscopic method and its application to bioequivalence study, J. Braz. Chem. Soc., 2005, 16, 944-950.
44. Vittal S. Shitut N.R. Kumar T.R. Vinu M.C. Mullangi R. Srinivas N.R., Simultaneous quantitation of rosuvastatin and gemfibrozil in human plasma by high-performance liquid chromatography and its application to a pharmacokinetic study, Biomed chromatography., 2006, 20, 1252-1259.
45. Validated High-Performance Liquid Chromatographic Method for the Estimation of Rosuvastatin Calcium in Bulk and Pharmaceutical Formulations, Int J Biomed Sci. 2011 Dec; 7(4): 283–288.
46. TRIPTI SHARMA1*, SUDAM C SI, DANNANA G SANKAR, Development and Validation of HPLC Method for the Simultaneous Estimation of Rosuvastatin Calcium and Olmesartan Medoxomil in Pharmaceutical Dosage Form, International Journal of ChemTech Research, Vol.6, No.2, pp 1115-1123, 2014.
47. D Dipali Tajane*, Amol M.Raurale, Pradeep D. Bharande, Anil N.Mali, Amol V.Gadkari, Vishal R.Bhosale,, evelopment and validation of a RP-HPLC-PDA method for simultaneous determination of Rosuvastatin calcium and Amlodipine besylate in pharmaceutical dosage form Journal of Chemical and Pharmaceutical Research, 20 12, 4(5):2789-2794.12, 4(5):2789-2794 .
48. Muthy TGK and Geethanjali J, Validated RP-HPLC Method for Simultaneous Estimation of Metformin Hydrochloride and Rosuvastatin Calcium in Bulk and In-House Formulation Journal of Chromatography & Separation Techniques ISSN: 2157-7064 J Chromatogr Sep Tech 5:252. December 05, 2014.
49. Rani S. Potawale, Satish Y. Gabhe , HPTLC Method For Simultaneous Determination Of Rosuvastatin And Fenofibrtae In Bulk And Pharmaceutical Formulation, , International Journal Of Pharmacy And Pharmaceutical Sciences, Vol 6issue 7, 2014.
50. Sacide Altınöz*[a] and Banu Uyar[a] Electrochemical behaviour and voltammetric determination of rosuvastatin calcium in pharmaceutical preparations using a square-wave voltammetric method Analytical Methods, issue 20, 2013,**5**, 5709-5716.
51. International Conference on Hormonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonised Tripartite Guideline, Validation of Analytical procedures.

52. Khushbu B. Patel*, Krupa C. Thula and Dilip G Maheshwari, Stability indicating HPLC method for simultaneous estimation of Ciprofloxacin and phenylephrine in pharmaceutical dosage form, , Pharmacophore 2014, Vol. 5 (2), 262-272 USA CODEN: PHARM7 ISSN 2229-5402.
53. Kampati Anil Kumar*, Sree.V. Janadharanan, Yarasi Surendranath Reddy, Vanam Naveen Kumar , Method development and validation for simultaneous estimation of Pantoprazole sodium and Itopride Hydrochloride in its bulk dosage forms by RP-HPLC by, International Journal of Pharmacy and Pharmaceutical Sciences ISSN- 0975-1491, Vol 5, Suppl 1, 2013.
54. M Lakshmi Surekha 1*, G Kumara Swamy1 and D Vinay Kumar2, Development and Validation of RP-HPLC Method for the Estimation of Atorvastatin in Bulk and Tablet Dosage Form, Austin Chromatography 09/2014; 1(1):1-4.
55. Mohammed Ishaq Beludari[a], Karanam Vanitha Prakash[b], RP-HPLC method for simultaneous estimation of Rosuvastatin and Ezetimibe from their combination tablet dosage form, International Journal of Chemical and AnalyticalScience12/2013.
56. Rajendrakumar , Development and Validation of Stability-Indicating Assay Method by RP-HPLC for Simultaneous Estimation of Rosuvastatin Calcium and Fenofibrate in Pharmaceutical Dosage Form, Journal of Drug Delivery and Therapeutics, Volume 10, Issue 4, July-august 2020.