A Robust Visible Spectrophotometric Method for The Determination of Selected Pharmaceutical Formulations Based on Cerium (Iv)-Mediated Oxidation and Methylene Blue Bleaching

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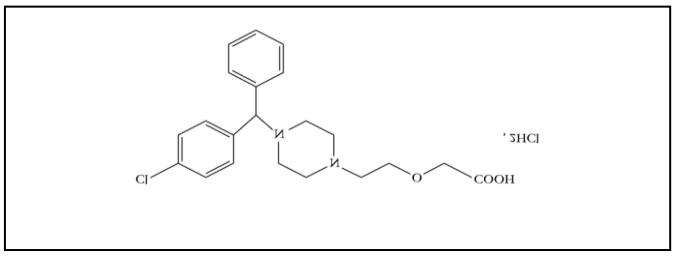
Abstract:
A simple, sensitive, and reproducible spectrophotometric method was developed for the quantitative estimation of Cetirizine Dihydrochloride (CDC), Imatinib Mesylate (INM), and Voriconazole (VNZ) in both pure drug substances and pharmaceutical dosage forms. The analytical procedure is based on the oxidation of the selected drugs by a measured excess of Cerium(IV) in an acidic medium. The residual Cerium(IV) was subsequently determined through its reaction with Methylene Blue, resulting in a measurable decrease in dye absorbance.
The proposed method was systematically validated according to established analytical guidelines. Key performance characteristics, including linearity, accuracy, precision, sensitivity, robustness, and ruggedness, were evaluated. The method demonstrated excellent analytical performance, providing percentage recoveries in the range of 97–100% with relative standard deviation values below 2%, indicating satisfactory accuracy and precision. Detection and quantification limits confirmed the high sensitivity of the procedure. Furthermore, statistical comparison of the obtained results with those of established reference methods using Student's *t*-test and *F*-test revealed no significant differences in accuracy or precision.
Owing to its simplicity, cost-effectiveness, and reliable analytical performance, the developed method is well suited for routine quality-control analysis of these pharmaceutical compounds in bulk and tablet formulations.

Keywords: Cetirizine Dihydrochloride, Imatinib Mesylate, Voriconazole, Spectrophotometric Analysis, Cerium(IV), Methylene Blue, Pharmaceutical Quality Control, Method Validation.

INTRODUCTION

1. Cetirizinedihydrochloride (CDC):



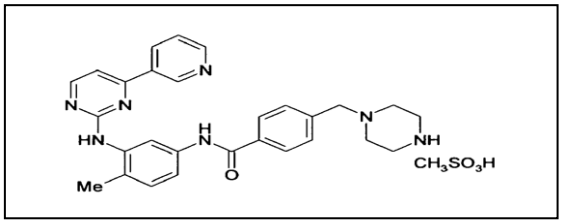
Structure of Cetirizinedihydrochloride (fig:1)

Cetirizine Dihydrochloride (CDC) is a widely prescribed second-generation antihistamine used for the treatment of various allergic conditions, including seasonal and perennial allergic rhinitis, chronic idiopathic urticaria, and other hypersensitivity disorders. Chemically, it is designated as (RS)-2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl ethoxy acetic acid dihydrochloride (Fig. 1). Unlike first-generation antihistamines, cetirizine exhibits minimal sedative effects owing to its limited ability to cross the blood–brain barrier, thereby offering improved patient compliance and safety.

Several analytical methods have been reported for the determination of CDC in pharmaceutical formulations and biological samples. These include spectrophotometric techniques [1], high-performance liquid chromatography (HPLC) [1], spectrofluorimetric methods [2, 20-22], titrimetric procedures [3], and liquid chromatography coupled with mass spectrometry (LC–MS) [4]. Although these methods provide satisfactory analytical performance, some require sophisticated instrumentation, extensive sample preparation, or higher operational costs, which may limit their routine application in quality-control laboratories.

In the present investigation, a simple, sensitive, and cost-effective spectrophotometric method has been developed for the quantitative determination of Cetirizine Dihydrochloride. The proposed approach is based on the oxidation of the drug by Cerium(IV) in an acidic medium, followed by the spectrophotometric measurement of the residual oxidant using Methylene Blue as a chromogenic reagent. A thorough review of the available literature revealed no reports describing the use of Cerium(IV) and Methylene Blue in combination for the spectrophotometric determination of CDC. Therefore, the proposed method represents a convenient and reliable approach for routine pharmaceutical quality-control analysis.

2. Imatinib Mesylate:

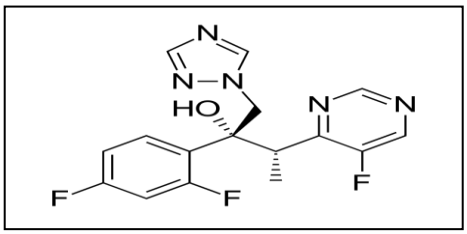


Structure of Imatinib Mesylate (fig:2)

Imatinib Mesylate (INM) is the mesylate salt of imatinib, chemically known as 4-[(4-methylpiperazin-1-yl)methyl]-N-[4-methyl-3-[(4-pyridin-3-ylpyrimidin-2-yl)amino]phenyl]benzamide methanesulfonate (Fig. 2). It is a targeted anticancer agent that selectively inhibits specific tyrosine kinases involved in the growth and proliferation of cancer cells. INM is widely used in the treatment of Philadelphia chromosome-positive (Ph^+) chronic myeloid leukemia (CML), acute lymphoblastic leukemia, and gastrointestinal stromal tumors (GISTs) [5].

Several analytical methods have been reported for the determination of INM in pharmaceutical formulations and biological samples, including spectrophotometry [6,24], high-performance liquid chromatography (HPLC) [7,23], high-performance thin-layer chromatography (HPTLC) [8], and spectrofluorimetry [9]. Despite their reliability, many of these methods require sophisticated instrumentation and higher operational costs. In the present study, a simple, sensitive, and cost-effective spectrophotometric method based on Cerium(IV) oxidation and Methylene Blue determination has been developed for the quantitative estimation of INM. To the best of our knowledge, this method has not been reported previously.

3. Voriconazole:



Structure of Voriconazole (fig:3)

Voriconazole (VNZ) is a second-generation triazole antifungal drug widely used for the treatment of serious fungal infections, particularly invasive aspergillosis and esophageal candidiasis. Its antifungal activity is attributed to the inhibition of fungal cytochrome P450-dependent 14α-demethylase, an enzyme essential for ergosterol biosynthesis and fungal cell membrane formation. Chemically, VNZ is designated as (αR,βS)-(2,4-difluorophenyl)-5-fluoro-β-methyl-α-(1H-1,2,4-triazol-1-ylmethyl)-4-pyrimidineethanol (Fig. 3) [10].
Several analytical methods have been reported for the determination of VNZ, including spectrophotometry [1,26], reversed-phase ultra-performance liquid chromatography (RP-UPLC) [12], high-performance thin-layer chromatography (HPTLC) [13,25,27,28], and colorimetric methods [14]. Although these techniques provide reliable results, many require specialized instrumentation and complex procedures. In the present work, a simple, sensitive, and economical spectrophotometric method based on Cerium(IV) oxidation and Methylene Blue determination has been developed for the quantitative determination of VNZ. To the best of our knowledge, this method has not been previously reported.

2.ABOUT THE METHOD:

Cerium(IV) is a powerful oxidizing agent widely employed in analytical chemistry because of its high oxidation potential, stability in acidic media, and ability to react with a wide range of organic compounds. These properties make it particularly suitable for the quantitative analysis of pharmaceutical substances through oxidation-based reactions.
The analytical procedure involves the reaction of the drug with a known excess of Cerium(IV) in an acidic medium, whereby the drug undergoes oxidation and the residual oxidant is subsequently determined spectrophotometrically. The residual, unreacted Cerium(IV) is subsequently determined indirectly by its reaction with a suitable chromogenic dye. Various dyes, including Rhodamine B, Indigo Carmine, Safranin O, Malachite Green, and Methylene Blue, were evaluated for this purpose. Among these, Methylene Blue was found to be the most effective, offering superior sensitivity and reproducibility. The decrease in dye absorbance, measured at 665 nm, is proportional to the amount of residual Cerium(IV), thereby enabling the accurate quantification of the drug.

3. EXPERIMENTAL

3.1 Instrumentation

Absorbance measurements were carried out using ELICO SL-210 double-beam and ELICO SL-159 single-beam UV–Visible spectrophotometers equipped with 10 mm matched quartz cells. A Thermo Nicolet 1000 spectrophotometer was used for spectral studies. All weighing operations were performed on a Dhona 200 electronic analytical balance.

3.2 Chemicals and Reagents

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

3.2.1 Cerium(IV) Solution

A stock Cerium(IV) solution was prepared by dissolving 750 mg of cerium(IV) sulfate dihydrate ($Ce(SO_4)_2 \cdot 2H_2O$, Merck, Mumbai, India) in 2 M sulfuric acid with gentle heating. The solution was filtered through glass wool, diluted to 250 mL with the same acid, and standardized against ferrous ammonium sulfate using ferroin indicator. A working solution of 4.0×10^{-3} M was prepared by suitable dilution.

3.2.2 Methylene Blue Solution

A stock solution of Methylene Blue (0.002 M) was prepared by dissolving 0.0639 g of the dye in distilled water and diluting to 100 mL. After filtration through glass wool, a working solution of 1.8×10^{-4} M was obtained by appropriate dilution with distilled water.

3.2.3 Sulfuric Acid

A 2 M sulfuric acid solution was prepared by diluting concentrated sulfuric acid (98%, Merck, Mumbai, India) with distilled water.

3.2.4 Standard Drug Solutions

Stock solutions (200 μg mL^{-1}) of Cetirizine Dihydrochloride (CDC), Imatinib Mesylate (INM), and Voriconazole (VNZ) were prepared separately by dissolving 20 mg of each drug in a suitable solvent and diluting to 100 mL in volumetric flasks. Working solutions were prepared by further dilution with the same solvent.

4. PROCEDURE

Aliquots of drug solution containing concentrations within the Beer's law range were transferred into a series of 10 mL volumetric flasks. To each flask, 1 mL of Cerium(IV) solution and 1 mL of 2 M sulfuric acid were added. The mixtures were shaken and allowed to stand for 15 min to ensure complete oxidation of the drug. Subsequently, 1 mL of 1.8×10^{-4} M Methylene Blue solution was added, and the contents were mixed thoroughly. The volume was then adjusted to the mark with distilled water, and the absorbance was measured at 665 nm against a reagent blank.

5. ASSAY OF PURE DRUG SAMPLE

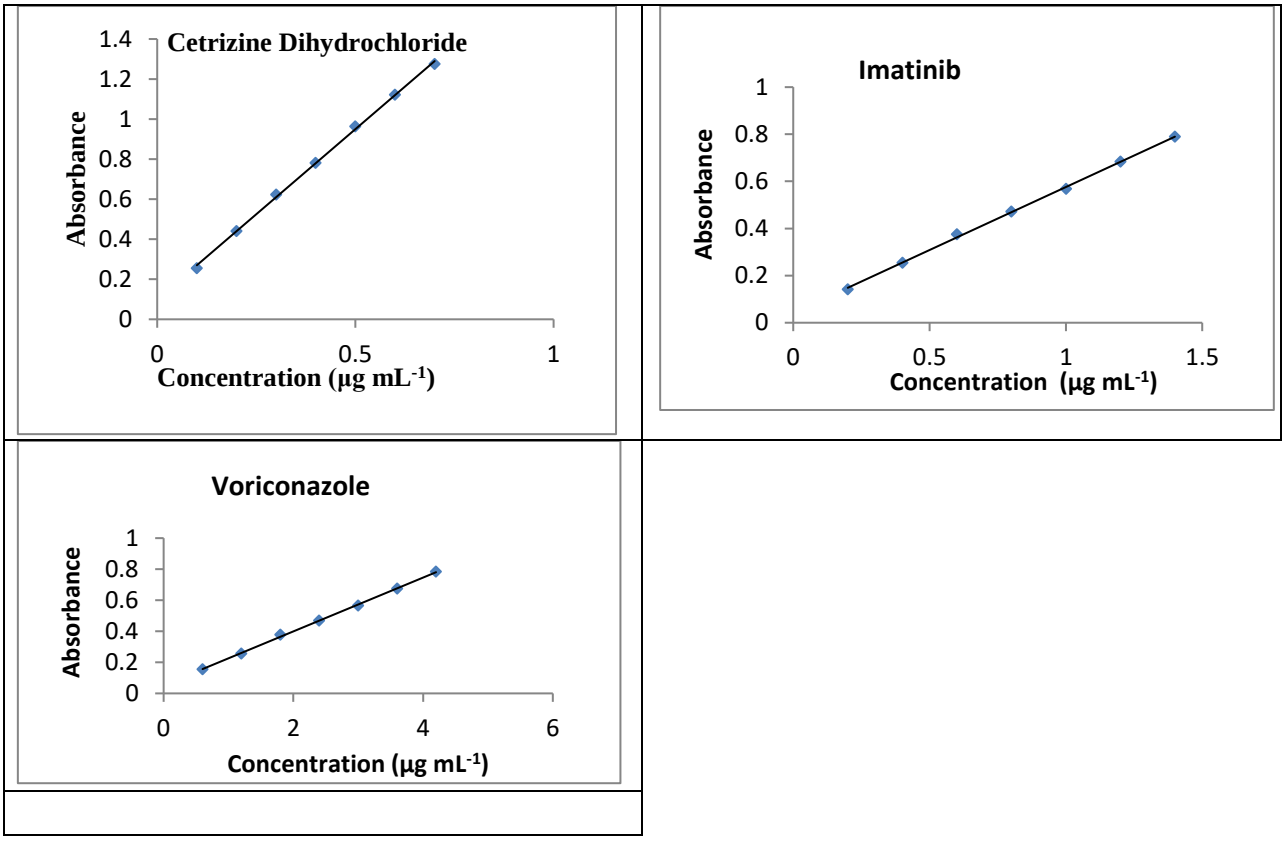
The proposed method was evaluated using standard drug solutions prepared within the respective Beer's law ranges: 2–14 μg mL^{-1} for CDC, 0.2–1.4 μg mL^{-1} for INM, and 0.8–4.87 μg mL^{-1} for VNZ. The assay was performed according to the general procedure. Calibration graphs were constructed by plotting absorbance against drug concentration.

Each determination was carried out in six replicates. Method accuracy was assessed through recovery studies, while precision was evaluated from the relative standard deviation (%RSD) values. The obtained recoveries ranged from 97–100%, and %RSD values were below 2%, demonstrating the excellent accuracy and precision of the proposed method. The analytical results are presented in Table 2.

5.1 Procedure For Assay Of Pure Drug

The accuracy and precision of the proposed method were evaluated by analyzing pure drug samples at selected concentrations within their respective Beer's law ranges. Recovery studies were performed to assess method accuracy, while precision was determined from the calculated relative standard deviation (%RSD) values. Each determination was carried out in six replicates following the recommended procedure. The recovery results and statistical parameters are presented in Table 2. The satisfactory recoveries (97–100%) and low %RSD values (< 2%) demonstrate the reliability, accuracy, and precision of the proposed method for the quantitative estimation of CDC, INM, and VNZ.

Calibration curves of drugs (Fig. 4)



6. PROCEDURE FOR ANALYSIS OF TABLETS

6.1 Cetirizine Dihydrochloride (CDC)

Twenty tablets of Cetcip® (10 mg CDC per tablet) were weighed, finely powdered, and mixed thoroughly. An amount of powder equivalent to 20 mg of CDC was accurately weighed, transferred to a 100 mL volumetric flask, dissolved in double-distilled water, and shaken for 10 min. The solution was filtered, and the residue was washed with the same solvent. The combined filtrate and washings were diluted to volume with double-distilled water to obtain the stock solution. Appropriate dilutions were prepared for analysis according to the proposed procedure.

6.2 Imatinib Mesylate (INM)

Twenty tablets of Imatib® (100 mg INM per tablet) were powdered and mixed uniformly. A portion equivalent to 20 mg of INM was accurately weighed and transferred into a 100 mL volumetric flask. The drug was dissolved in double-distilled water with sonication and diluted to volume with the same solvent. Suitable aliquots of the stock solution were further diluted to obtain working concentrations within the Beer's law range.

6.3 Voriconazole (VNZ)

Twenty tablets of Voritek® (200 mg VNZ per tablet) were finely powdered and homogenized. An accurately weighed quantity equivalent to 20 mg of VNZ was transferred to a 100 mL volumetric flask, dissolved in double-distilled water, and diluted to the mark. The resulting solution was filtered, and suitable dilutions were prepared from the filtrate to obtain working solutions within the required concentration range for analysis.

The prepared sample solutions were analyzed according to the general procedure, and the drug contents were determined from the corresponding calibration graphs. The assay results are summarized in Table 3.

7. METHOD OF VALIDATION

The proposed spectrophotometric methods were validated in accordance with standard analytical guidelines by evaluating parameters such as linearity, accuracy, precision, selectivity, limit of detection (LOD), limit of quantification (LOQ), and ruggedness. Calibration curves were constructed by plotting absorbance against drug concentration within the respective Beer's law ranges.

Method precision was assessed through six replicate determinations at selected concentration levels, while accuracy was evaluated by recovery studies and expressed as percentage recovery and relative standard deviation (%RSD). The high recovery values (97–100%) and low %RSD values (< 2%) demonstrated the excellent accuracy and precision of the proposed methods (Table 2).

The limit of detection (LOD) was calculated using the formula:

$$\text{LOD} = \frac{3.3\, s_a}{S}$$

where s_a is the standard deviation of the intercept (n = 6) and S is the slope of the calibration curve.

The limit of quantification (LOQ), which represents the lowest concentration that can be reliably quantified, was determined using the formula:

$$\text{LOQ} = \frac{10\, s_a}{S}$$

The linearity of the proposed methods was established over the respective Beer's law concentration ranges, and the corresponding calibration plots are shown in Figure 4.

Method selectivity was evaluated through recovery studies by analyzing drug samples in the presence of commonly used pharmaceutical excipients. The satisfactory recovery values obtained indicated the absence of interference from excipient materials, confirming the selectivity of the methods.

Ruggedness was assessed by performing the analysis using different analysts and instruments under identical experimental conditions. The results showed no significant variations in absorbance or recovery values, demonstrating that the proposed methods are reliable and reproducible for routine pharmaceutical analysis.

8. FACTORS EFFECTING ABSORBANCE

8.1 Effect of Acid Type

The influence of the acidic medium on the oxidation reaction was investigated using Hydrochloric acid, Sulfuric acid, Phosphoric acid, and Acetic acid. Among the acids examined, Sulfuric acid provided the highest and most consistent absorbance values, indicating its suitability for the Cerium(IV)-mediated oxidation reaction. Therefore, sulfuric acid was selected for subsequent studies.

8.2 Effect of Acid Concentration

The effect of sulfuric acid concentration was evaluated by varying both the concentration (0.5–2.5 M) and volume (0.5–2.5 mL) of H_2SO_4 while maintaining all other experimental parameters constant. Maximum absorbance was obtained with 1 mL of 2 M H_2SO_4. Further increases in acid concentration or volume resulted in a decrease in absorbance. Accordingly, 1 mL of 2 M H_2SO_4 was chosen as the optimum condition for all analyses.

8.3 Effect of Reaction Time

The influence of reaction time on the oxidation process was investigated over the range of 2.5–20 min. Absorbance increased gradually with time and reached a maximum at 15 min, after which no significant change was observed. Therefore, a reaction time of 15 min was considered sufficient for complete oxidation and was adopted throughout the study.

8.4 Effect of Sequence of Addition

The order of reagent addition was found to have a significant effect on the analytical response. Several sequences were examined, and the highest absorbance values were obtained when the reagents were added in the order: drug → sulfuric acid → Cerium (IV) → Methylene Blue. This sequence was therefore employed in all subsequent measurements.

9. ANALYSIS OF PHARMACEUTICALS

The applicability of the proposed methods was evaluated by analyzing commercial tablet formulations containing CDC, INM, and VNZ. Sample solutions were prepared and analyzed according to the recommended procedure using concentrations within the respective Beer's law ranges.

The precision of the methods was assessed by performing six replicate determinations for each formulation, while accuracy was evaluated through percentage recovery studies and relative standard deviation (%RSD) values. The assay results showed excellent recoveries with %RSD values below 2%, indicating good accuracy and precision (Table 3).

The absence of interference from common tablet excipients and the satisfactory statistical results demonstrate that the proposed methods are reliable and suitable for the routine quality-control analysis of pharmaceutical formulations.

10. RESULTS AND DISCUSSION

The proposed indirect spectrophotometric method is based on the oxidation of the selected drugs by a known excess of Cerium (IV) in an acidic medium. After completion of the oxidation reaction, the residual Cerium (IV) is determined by its ability to oxidize Methylene Blue dye. The absorbance of the unreacted dye is then measured at 665 nm (Scheme 1).

As the concentration of the drug increases, a greater amount of Cerium (IV) is consumed during oxidation, leaving less residual oxidant available to react with Methylene Blue. Consequently, a larger amount of the dye remains unoxidized, resulting in an increase in absorbance. Thus, the absorbance at 665 nm is directly proportional to the drug concentration within the Beer's law range.

Experimental studies showed that 1 mL of 2 M sulfuric acid provided the optimum acidic medium for the reaction, ensuring complete oxidation and maximum analytical sensitivity.

Reaction Scheme:

Scheme 1. Proposed Reaction Pathway

The proposed indirect spectrophotometric method involves two sequential reactions. In the first step, the drug undergoes oxidation by a known excess of Cerium(IV) in an acidic medium. In the second step, the residual Cerium(IV) reacts with a fixed amount of Methylene Blue dye.

Step 1: Oxidation of the Drug

$$\text{Drug} + \text{Excess Cerium(IV)} \rightarrow \text{Oxidized drug product} + \text{Unreacted Cerium(IV)}$$

Step 2: Reaction of Residual Cerium(IV) with Methylene Blue

$$\text{Unreacted Cerium(IV)} + \text{Fixed amount of Methylene Blue} \rightarrow \text{Oxidized Methylene Blue} + \text{Unreacted Methylene Blue}$$

The concentration of unreacted Methylene Blue was determined spectrophotometrically by measuring its absorbance at 665 nm. Since the amount of residual Cerium(IV) decreases with increasing drug concentration, a greater proportion of the dye remains unoxidized, resulting in higher absorbance values. Thus, the absorbance measured at 665 nm is directly proportional to the concentration of the drug present in the sample.

Scheme 1. Schematic representation of the proposed Cerium(IV)-Methylene Blue based indirect spectrophotometric method for the determination of CDC, INM, and VNZ.

11. ANALYTICAL DATA

A linear relationship was observed between absorbance at 665 nm and drug concentration over the respective Beer's law ranges. The analytical performance of the proposed methods was evaluated by determining important sensitivity parameters, including Sandell's sensitivity, limit of detection (LOD), and limit of quantification (LOQ), in accordance with ICH guidelines [15]. The obtained values, presented in Table 1, demonstrate the high sensitivity of the developed methods.

Linear regression analysis of the calibration data was performed using the least-squares method to obtain the regression equation, slope (b), intercept (a), and correlation coefficient (r). The excellent correlation coefficients obtained indicate good linearity and confirm the suitability of the methods for quantitative analysis over the studied concentration ranges. The corresponding analytical and regression characteristics are summarized in Table 1.

Table 1: Analytical and Regression parameters of Spectrophotometric Method

Name of drug Property	**CDC**	**INM**	**VNZ**
λ_{max}, nm	665	665	665
Beer's law limits (µg mL^{-1})	2-15	0.3-1.5	0.9-5.8
Molar absorptivity	$3.5920X10^4$	$3.4835X10^5$	$4.6057X10^4$
Sandell's sensitivity(µg cm^{-2})	0.019239	0.0018629	0.00650
Variance $(S_a)^2$	0.0000228	0.002249	0.0001268
Limit of detection µg mL^{-1}	0.1313041	0.303988	0.234746.
Limit of quantification µg mL^{-1}	0.950621	0.900833	0.69148
Regression equation, Y**	Y=0.0529x+0.057	Y=0.5238x+0.042	Y=0.1601x + 0.013
Intercept, (a)	0.0569	0.0418	0.0129
Slope, (b)	0.0528	0.5337	0.1569
Correlation coefficient, (r)	0.996404	0.09795	0.996504
Standard deviation of intercept (S_a)	0.011248	0.0475591	0.011339
Standard deviation of slope (S_b)	0.0141539	0.0661899	0.0141537

*The limit of determination is defined as the concentration of the drug in µg/mL that produces an absorbance of 0.001 in a cuvette with a 1 cm² cross-sectional area and a 1 cm path length. The calibration relationship is expressed as Y** = a + bX, where Y represents the measured absorbance and X denotes the drug concentration in µg/mL.*

12. ACCURACY AND PRECISION

The accuracy and precision of the proposed methods were evaluated by analyzing pure drug samples at six different concentration levels within the respective Beer's law ranges. Accuracy was assessed in terms of percentage recovery and relative error (%), whereas precision was expressed as the percentage relative

standard deviation (%RSD). The results, presented in Table 2, demonstrated satisfactory recoveries, low relative errors, and %RSD values below 2%, confirming the excellent accuracy and precision of the developed methods.

13. ROBUSTNESS AND RUGGEDNESS

The robustness of the proposed methods was evaluated by introducing small deliberate variations in experimental parameters, including the volume of sulfuric acid and the reaction time (15 ± 2 min) allowed for oxidation by Cerium(IV). The effects of these changes on the analytical response were found to be negligible, indicating that the methods are robust.

Ruggedness was assessed by performing the analysis using three different analysts and three independent spectrophotometers under similar experimental conditions. No significant differences were observed in the obtained results, demonstrating the reproducibility and reliability of the developed methods for routine analytical applications.

Table 2 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
CDC	2 4 6	1.89 3.96 6.08	0.50 1.00 1.33	99.50 99.00 100.33	0.68	99.61 ± 0.68
INM	2 4 6	1.99 3.95 5.94	2.50 1.25 1.00	97.50 98.75 99.00	0.81	98.42 ± 0.80
VNZ	0.8 1.6 2.4	0.82 1.6 2.38	2.50 1.00 0.83	102.50 100.00 99.17	1.71	100.56 ± 1.72

14. APPLICATION TO FORMULATIONS

The proposed methods were successfully applied to the determination of CDC, INM, and VNZ in commercial tablet formulations. The assay results (Table 3) were in close agreement with the labeled drug contents, indicating the accuracy of the methods and the absence of interference from commonly used tablet excipients. The obtained results were statistically compared with those reported by established reference methods [16–19]. Evaluation using Student's *t*-test and *F*-test revealed no significant differences in accuracy or precision at the 95% confidence level, confirming the reliability of the proposed methods.

The validity of the methods was further verified by recovery studies employing the standard addition technique. Known quantities of pure drug equivalent to 50%, 100%, and 150% of the tablet drug content were added to pre-analyzed tablet samples and subsequently determined using the proposed procedure. Each experiment was performed in six replicates. The satisfactory recovery values obtained (Table 3) demonstrate the accuracy of the methods and confirm that tablet excipients do not interfere with the assay.

Table 3 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 Mean± SD
Cetcip (CDC)	0.50	2.0	2.47	1.20	98.80	0.95	99.93 ±0.657	99.83 ± 0.95
	0.50	4.0	4.48	0.67	100.67			
	0.50	6.0	6.49	0.15	99.85			
	2.0	0.0	2.02	1.00	101.0			
	4.0	0.0	4.00	0.00	100.00			
	6.0	0.0	5.92	1.33	98.67			
Imatib (INM)	0.50	0.2	0.68	2.86	97.14	1.99	98.70 ±3.80	99.05 ± 1.97
	0.50	0.4	0.92	2.22	102.22			
	0.50	0.6	1.09	0.91	99.09			
	0.2	0.0	0.20	0.00	100.0			
	0.4	0.0	0.39	2.50	97.50			
	0.6	0.0	0.59	1.67	98.33			
Voritek (VNZ)	0.50	0.8	1.32	1.54	101.54	0.90	99.72 ±1.254	100.33 ±0.90
	0.50	1.6	2.09	0.48	99.52			
	0.50	2.4	2.89	0.34	99.66			
	0.8	0.0	0.80	0.00	100.0			
	1.6	0.0	1.59	1.25	101.25			
	2.4	0.0	2.40	0.00	100.00			

Table 4: F-test and t-test values

	Cetcip (CDC)	Imatib (INM)	Voritek (VNZ)
F-test*	0.212067 (5.0503)	3.720270 (5.050329)	1.941378 (5.050329)
t-test**	2.090855 (2.228)	0.200295 (2.228139)	0.968029 (2.28139)

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

15. CONCLUSION

A simple, rapid, sensitive, and economical spectrophotometric method was developed and validated for the quantitative determination of Cetirizine Dihydrochloride, Imatinib Mesylate, and Voriconazole in bulk drug samples and pharmaceutical formulations. The method is based on the oxidation of the drugs by Cerium(IV) in an acidic medium, followed by the determination of residual oxidant using Methylene Blue dye.

The proposed method exhibited excellent linearity, accuracy, precision, selectivity, and sensitivity, with satisfactory recovery values and low %RSD. Common pharmaceutical excipients did not interfere with the analysis, demonstrating the specificity of the method. Statistical comparison with reported reference methods showed no significant differences in analytical performance.

Owing to its simplicity, reliability, cost-effectiveness, and use of readily available reagents, the developed method is well suited for routine quality-control analysis of these drugs in pharmaceutical laboratories and offers a practical alternative to more sophisticated instrumental techniques.

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