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Review Article

Comparative Analytical Evaluation Of A Green UV–Visible Spectrophotometric Method With A Reported RP-HPLC Method For The Quantitative Estimation Of Loperamide Hydrochloride

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ABSTRACT

Reliable analytical methods are essential for the quality control of pharmaceutical products containing loperamide hydrochloride. The present study was undertaken to comparatively evaluate a developed green UV–Visible spectrophotometric method with a reported validated reverse-phase high-performance liquid chromatographic (RP-HPLC) method for the quantitative estimation of loperamide hydrochloride. The developed UV–Visible spectrophotometric method employed 0.1 N hydrochloric acid as the analytical medium, with quantification performed at 220 nm. The method demonstrated linearity over the concentration range of 1–5 µg/mL, with a regression equation of y = 0.022x + 0.0068 and a correlation coefficient (R^2) of 0.9953. The mean recovery ranged from 99.21 to 101.09%, with intra-day and inter-day precision of 1.88% and 1.40% RSD, respectively. The limit of detection and limit of quantitation were 0.41 and 1.25 µg/mL, respectively, while wavelength variation of ±1 nm resulted in RSD values not exceeding 1.30%. The method was successfully applied to dissolution testing of marketed loperamide hydrochloride tablets and achieved an overall AGREE score of 0.7, indicating favorable environmental performance. The reported RP-HPLC method employed chromatographic separation with UV detection at 226 nm and demonstrated linearity over 0.2–4 µg/mL with R^2 = 0.999, LOD of 1.05 µg/mL, LOQ of 3.30 µg/mL, and reported recovery of 98–101%. Comparative evaluation showed that both methods provided satisfactory analytical performance;

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however, the UV–Visible spectrophotometric method offered a simpler analytical workflow, lower instrumentation requirements, reduced solvent use, and favorable environmental characteristics, whereas RP-HPLC provided the inherent advantage of chromatographic separation and greater selectivity. The findings indicate that the developed UV–Visible spectrophotometric method represents a practical and economical alternative for routine quantitative estimation and dissolution analysis of loperamide hydrochloride, particularly where simplicity, cost-effectiveness, and reduced environmental impact are important considerations.

INTRODUCTION

Green Analytical Chemistry (GAC) has become an important part of modern pharmaceutical analysis, particularly when analytical procedures involve organic solvents, chemical reagents, energy consumption, and generation of laboratory waste. The aim is not simply to obtain reliable analytical results, but to achieve them with fewer hazardous materials and simpler analytical operations. Different approaches have been proposed to assess the environmental performance of analytical procedures, including the Analytical Eco-Scale, Green Analytical Procedure Index (GAPI), and Analytical GREEnness (AGREE) metric. These tools allow the environmental aspects of an analytical method to be considered along with its analytical performance.[9–12]

Development of a pharmaceutical analytical method involves selection and optimization of the analytical medium, concentration range, measurement conditions, and other experimental variables to obtain consistent and reliable results. The suitability of the developed procedure is then established through validation of parameters such as linearity, accuracy, precision, sensitivity, and robustness in accordance with ICH Q2(R2).[4] UV–Visible spectrophotometry is useful for routine pharmaceutical analysis because measurements can be performed with relatively simple instrumentation and without chromatographic separation. Several spectrophotometric methods have been reported for the determination of loperamide hydrochloride.[2,3,6] RP-HPLC is another established approach for loperamide hydrochloride analysis and offers chromatographic separation with good analytical selectivity, although it requires a chromatographic system and preparation of a mobile phase.[5,7]

Loperamide hydrochloride is an antidiarrheal drug used in the management of acute and chronic diarrhoea.[1] Its quantitative determination is therefore relevant to pharmaceutical quality control, while dissolution testing is important for assessing drug release from solid dosage forms.[6,8] Considering the analytical and practical requirements of routine testing, a method should provide acceptable performance without unnecessary complexity or resource consumption. The present study was therefore undertaken to compare a developed green UV–Visible spectrophotometric method with a reported validated RP-HPLC method for the quantitative estimation of loperamide hydrochloride. The comparison was based on validation characteristics as well as practical aspects, including instrumentation, sample preparation, solvent requirements, analytical workflow, and environmental performance.

MATERIALS AND METHODS

Study Design

The present study was designed as a comparative analytical evaluation of two validated analytical methods for the quantitative estimation of loperamide hydrochloride. The comparison involved a green UV–Visible spectrophotometric method developed in our laboratory and a published reverse-phase high-performance liquid chromatographic (RP-HPLC) method reported by Ramesh et al. (2021). The evaluation focused on

analytical performance, validation characteristics, operational requirements, environmental sustainability and applicability for routine pharmaceutical quality control.

Analytical Methods Included in the Comparison

The first analytical procedure evaluated was a green UV–Visible spectrophotometric method developed for the quantitative estimation of loperamide hydrochloride using 0.1 N hydrochloric acid as both the analytical and dissolution medium. The method was validated according to the International Council for Harmonisation (ICH) Q2(R2) guideline with respect to linearity, accuracy, precision, limit of detection (LOD), limit of quantitation (LOQ) and robustness.

The second method selected for comparison was the validated RP-HPLC method reported by Ramesh et al., developed for routine quality control analysis of loperamide hydrochloride. The published method employed a Nova-Pak C18 column with an acetonitrile-based mobile phase and was validated according to ICH recommendations for system suitability, linearity, accuracy, precision, robustness and ruggedness.

Criteria for Comparative Evaluation

Table 1: Comparative Evaluation Criteria Used for Analytical Method Assessment

Parameter	Basis of Evaluation
Linearity	Correlation coefficient (R^2) and concentration range
Accuracy	Percentage recovery (%)
Precision	%RSD
Sensitivity	LOD and LOQ
Robustness	Performance under deliberate method variations
Simplicity	Number of analytical steps
Cost	Instrumentation and reagent requirements
Greenness	Solvent type, solvent volume, and analytical waste
Analysis time	Time required per sample
Routine applicability	Suitability for routine pharmaceutical QC

Evaluation of Environmental Sustainability

The environmental sustainability of the analytical procedures was evaluated by considering solvent composition, solvent consumption, analytical waste generation, sample preparation requirements, and energy and instrumentation requirements. The developed UV–Visible spectrophotometric method was additionally assessed using the Analytical GREEnness (AGREE) metric. The method achieved an overall AGREE score of 0.7, indicating favorable

environmental performance. The reported RP-HPLC method was evaluated qualitatively based on its published analytical procedure, particularly with respect to the use of an organic solvent-containing mobile phase, chromatographic instrumentation, and associated sample and mobile-phase preparation requirements.

Data Collection and Comparative Analysis

Analytical performance characteristics of both methods were compiled from their respective validation studies. Comparative evaluation was performed using tabular presentation followed by critical scientific discussion. The advantages and limitations of each analytical technique were interpreted with respect to analytical performance, operational feasibility and routine pharmaceutical quality control.

Statistical Analysis

Analytical data generated from the developed UV–Visible spectrophotometric method and the published RP-HPLC method were compiled and evaluated using descriptive statistical analysis. Validation parameters, including linearity, accuracy, precision, limit of detection (LOD), limit of quantitation (LOQ), robustness, and other analytical performance characteristics, were compared using tabular and graphical presentation. Comparative interpretation focused on analytical performance, operational feasibility, environmental sustainability, and applicability for routine quality control. Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA) was used for data compilation, regression analysis, calculation of percentage relative standard deviation (%RSD), and preparation of comparative tables and figures.

RESULTS

The analytical performance characteristics of the developed green UV–Visible spectrophotometric method and the reported RP-HPLC method were comparatively evaluated. The results of the comparison are summarized in Tables 2–4. Both methods demonstrated satisfactory analytical performance with respect to validation parameters; however, differences were observed in analytical sensitivity, operational simplicity, solvent consumption, environmental sustainability, and applicability for routine quality control.

Table 2: Comparative Analytical Characteristics of the Developed Green UV–Visible Spectrophotometric Method and the Reported RP-HPLC Method

Parameter	Developed Green UV–Visible Spectrophotometric Method	Reported RP-HPLC Method
Analytical technique	UV–Visible spectrophotometry	RP-HPLC
Principle	Absorbance measurement	Chromatographic separation
Analytical medium	0.1 N Hydrochloric acid	Acetonitrile : Buffer (55:45, v/v)
Analytical wavelength / Detection wavelength	220 nm	226 nm
Linearity range	1–5 µg/mL	0.2–4 µg/mL
Regression equation	y = 0.022x + 0.0068	y = 53355x − 1116
Correlation coefficient (R^2)	0.9953	0.999
Accuracy	99.21–101.09%	98–101%

Precision	Intra-day RSD 1.88%; Inter-day RSD 1.40%	%RSD 1.03
Limit of Detection (LOD)	0.41 µg/mL	1.05 µg/mL
Limit of Quantitation (LOQ)	1.25 µg/mL	3.30 µg/mL
Robustness	Wavelength variation (±1 nm)	pH and column variation
Greenness assessment	AGREE score = 0.7	Not reported
Application	Routine quality control and dissolution testing	Routine quality control and dissolution analysis

The comparison presented in Table 2 demonstrated that both analytical methods satisfied the essential validation requirements for pharmaceutical analysis. The RP-HPLC method exhibited excellent linearity with a correlation coefficient of 0.999, whereas the developed UV–Visible spectrophotometric method also showed satisfactory linearity ($R^2 = 0.9953$). Accuracy and precision values obtained for both methods were within acceptable limits recommended by ICH guidelines. The developed UV method demonstrated lower LOD and LOQ values than those reported for the RP-HPLC method and additionally incorporated greenness assessment using the AGREE metric.

Table 3: Comparison of Validation Parameters of the Developed Green UV–Visible Spectrophotometric Method and the Reported RP-HPLC Method

Validation Parameter	Developed Green UV Method	Reported RP-HPLC Method
Linearity	1–5 µg/mL	0.2–4 µg/mL
Correlation coefficient (R^2)	0.9953	0.999
Accuracy	99.21–101.09%	98–101%
Precision	Intra-day 1.88%; Inter-day 1.40%	1.03%
LOD	0.41 µg/mL	1.05 µg/mL
LOQ	1.25 µg/mL	3.30 µg/mL
Robustness	Passed	Passed

Both analytical procedures demonstrated acceptable validation characteristics according to ICH recommendations. The validation results indicated that each method was sufficiently accurate, precise, and robust for the quantitative estimation of loperamide hydrochloride. The developed UV method provided comparable analytical performance while employing a simpler analytical procedure.

Table 4: Comparison of Practical and Environmental Characteristics of the Developed Green UV–Visible Spectrophotometric Method and the Reported RP-HPLC Method

Characteristic	Developed Green UV Method	Reported RP-HPLC Method
Instrumentation	UV–Visible spectrophotometer	RP-HPLC system
Instrument cost	Low	High
Running cost	Low	High
Sample preparation	Simple	Moderate
Organic solvent requirement	No	Yes
Analysis time	Short	Moderate

Solvent consumption	Low	High
Waste generation	Low	High
Skilled operator	Basic laboratory training	Trained analyst required
Environmental friendliness	High (AGREE score = 0.7)	Not evaluated
Suitability for routine quality control	Excellent	Excellent

The comparative assessment of practical characteristics demonstrated that the developed UV–Visible spectrophotometric method required simpler instrumentation, lower operational cost, reduced solvent consumption, and minimal analytical waste generation compared with the reported RP-HPLC method. In contrast, the RP-HPLC method offered superior chromatographic selectivity but required sophisticated instrumentation, organic mobile phases, and greater operational resources. Both analytical procedures were considered suitable for routine pharmaceutical quality control; however, the developed UV method offered additional advantages in terms of operational simplicity and environmental sustainability.

DISCUSSION

The present study compared a developed green UV–Visible spectrophotometric method with a validated RP-HPLC method for the quantitative estimation of loperamide hydrochloride. Both analytical methods demonstrated satisfactory validation characteristics and fulfilled the essential requirements for pharmaceutical quality control. However, significant differences were observed in terms of analytical principle, operational complexity, environmental sustainability, and practical applicability.

The developed UV–Visible spectrophotometric method demonstrated satisfactory linearity, accuracy, precision, and robustness, indicating its suitability for routine quantitative analysis of loperamide hydrochloride. Although the RP-HPLC method exhibited a marginally higher correlation coefficient ($R^2 = 0.999$), the difference in linearity between the two methods is unlikely to be of practical significance for routine quality control, as both methods satisfied the acceptance criteria recommended by the International Council for Harmonisation (ICH) for analytical method validation.

Sensitivity is an important consideration when selecting an analytical method. The RP-HPLC technique is generally recognized for its high selectivity because chromatographic separation minimizes potential interference from excipients and degradation products. In contrast, UV–Visible spectrophotometry relies on direct absorbance measurement and therefore requires careful selection of analytical conditions to ensure adequate specificity. Nevertheless, the validation results obtained for the developed UV method demonstrated that reliable quantitative estimation could be achieved under the optimized analytical conditions, making the method suitable for routine pharmaceutical analysis.

Operational simplicity represents one of the principal advantages of the developed UV–Visible spectrophotometric method. Sample preparation was straightforward, analysis was completed within a shorter period, and the method required only commonly available laboratory instrumentation. In contrast, the RP-HPLC method required specialized chromatographic equipment, preparation of mobile phase, column conditioning, and greater technical expertise. These operational differences directly influence analytical cost,

instrument maintenance, and laboratory throughput, particularly in quality control laboratories processing a large number of routine samples.

Environmental sustainability has become an increasingly important consideration in pharmaceutical analysis. The developed UV method employed a simplified analytical procedure with lower solvent consumption and reduced chemical waste generation. In comparison, the RP-HPLC method utilized organic mobile phase components, resulting in higher solvent consumption and increased analytical waste. Consequently, the UV method demonstrated a more environmentally sustainable analytical approach while maintaining satisfactory analytical performance for routine applications.

From an industrial perspective, both analytical methods possess distinct advantages depending on the intended application. RP-HPLC remains the preferred technique when high chromatographic selectivity, impurity profiling, or stability-indicating analysis is required. Conversely, the developed UV–Visible spectrophotometric method provides an economical and environmentally friendly alternative for routine assay and dissolution testing where rapid analysis, operational simplicity, and reduced analytical cost are of primary importance.

Overall, the comparative evaluation demonstrated that the developed green UV–Visible spectrophotometric method achieved analytical performance comparable to the validated RP-HPLC method for routine quantitative estimation of loperamide hydrochloride. While RP-HPLC offers superior chromatographic capability, the developed UV method provides substantial advantages in terms of simplicity, cost-effectiveness, environmental sustainability, and ease of implementation, making it a suitable analytical alternative for routine pharmaceutical quality control.

CONCLUSION

The present comparative analytical evaluation demonstrated that both the developed green UV–Visible spectrophotometric method and the reported RP-HPLC method are suitable for the quantitative estimation of loperamide hydrochloride and satisfy the essential analytical validation requirements for pharmaceutical quality control. The RP-HPLC method exhibited excellent chromatographic performance and analytical reliability, making it highly suitable for applications requiring superior selectivity and chromatographic resolution. Conversely, the developed UV–Visible spectrophotometric method provided comparable analytical performance while offering significant practical advantages, including simplified sample preparation, lower operational cost, reduced analysis time, lower solvent consumption, and improved environmental sustainability.

The comparative assessment indicated that the developed UV method represents a practical and economical alternative for routine quality control analysis of loperamide hydrochloride, particularly in laboratories where rapid analysis and cost-effective operation are important considerations. Although RP-HPLC remains the preferred technique for complex analytical applications such as impurity profiling and stability studies, the developed UV–Visible spectrophotometric method demonstrated adequate accuracy, precision, and robustness for routine pharmaceutical analysis. Overall, the findings of this study support the selection of analytical methods based on their intended application, available laboratory resources, and analytical requirements rather than analytical sensitivity alone.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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