Comparative Evaluation Of Zero-Order, First-Derivative, And Second- Uv Spectrophotometric Methods For Quantitative Estimation Of Diclofenac, Ibuprofen, And Atorvastatin

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Abstract

Background: Diclofenac, ibuprofen, and atorvastatin are widely prescribed drugs requiring reliable analytical methods for quality control. Conventional zero-order UV spectrophotometry often suffers from spectral overlap and limited sensitivity in multicomponent analysis.
Methods: Zero-order, first-derivative, and second-derivative UV spectrophotometric methods were developed and validated for the quantitative estimation of diclofenac, ibuprofen, and atorvastatin in bulk and tablet formulations. Method validation was performed according to ICH Q2(R1) guidelines, and statistical comparison was conducted using one-way ANOVA.
Results: All methods exhibited acceptable linearity and accuracy; however, derivative spectrophotometric techniques demonstrated superior sensitivity, precision, and selectivity. The second-derivative method provided the lowest LOD and LOQ values and assay results closest to label claims. Statistical analysis confirmed significant improvements in analytical performance for derivative methods over zero-order analysis.
Conclusion: Derivative UV spectrophotometry, particularly second-derivative analysis, offers a robust, cost-effective, and environmentally sustainable alternative for routine pharmaceutical quality control of multicomponent formulations.

Keywords: Derivative spectrophotometry; Diclofenac; Ibuprofen; Atorvastatin; UV analysis; Method validation.

Introduction

Chronic inflammatory disorders and cardiovascular diseases represented a substantial global health burden and continued to rank among the leading causes of morbidity and long-term disability worldwide. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac and ibuprofen were routinely prescribed for the management of pain, inflammation, and musculoskeletal disorders, while statins, particularly atorvastatin, formed the cornerstone of dyslipidemia management and cardiovascular risk reduction. Owing to their widespread use, long-term therapy, and narrow therapeutic considerations, ensuring the quality, safety, and efficacy of these drugs through robust analytical control remained a critical requirement for pharmaceutical industries and regulatory authorities (Chaudhari et al., 2025; Han & A, 2025; Ibrahim et al., 2025).

Despite significant advances in pharmaceutical formulation and manufacturing technologies, analytical challenges persisted in the routine quality assessment of multicomponent drug systems. Diclofenac and ibuprofen shared similar structural features, including aromatic rings and conjugated chromophores, resulting in overlapping ultraviolet absorption profiles. Atorvastatin, although structurally distinct, also exhibited strong UV absorbance within a comparable wavelength region. This spectral overlap complicated simultaneous drug estimation, particularly when conventional analytical approaches were employed. Inadequate analytical resolution could potentially lead to inaccurate dosage determination, compromised batch uniformity, and regulatory non-compliance, thereby underscoring the need for reliable and selective analytical methodologies (Radwan et al., 2024; Sankarganesh et al., 2023; Sattar et al., 2024; Zhuo et al., 2024).

Chromatographic techniques such as high-performance liquid chromatography were widely regarded as gold-standard methods for pharmaceutical analysis due to their high sensitivity and selectivity. However, these techniques were associated with higher operational costs, longer analysis times, extensive solvent consumption, and the requirement for skilled personnel and sophisticated instrumentation. Such constraints limited their routine applicability in many quality control laboratories, particularly in resource-constrained settings. Consequently, ultraviolet spectrophotometry continued to be extensively utilized owing to its simplicity, cost-effectiveness, rapid analysis, and minimal sample preparation requirements (Balbinot Filho et al., 2024; Sakur & Zakri, 2023; Sultana et al., 2024; Türksever & Topkaya, 2024; Zhuo et al., 2024).

Conventional zero-order UV spectrophotometric methods, although straightforward, frequently suffered from limitations related to spectral overlap, baseline drift, and reduced sensitivity in multicomponent analysis. These shortcomings were particularly pronounced when drugs with similar absorption characteristics were analyzed simultaneously, often necessitating prior separation or complex mathematical corrections. Such limitations highlighted the inadequacy of zero-order spectrophotometry as a standalone tool for complex pharmaceutical systems and prompted the exploration of advanced spectrophotometric approaches capable of improving analytical selectivity without sacrificing simplicity (Balbinot Filho et al., 2024; Sakur & Zakri, 2023; Sultana et al., 2024; Türksever & Topkaya, 2024; Zhuo et al., 2024).

Derivative spectrophotometry emerged as a powerful mathematical transformation technique designed to enhance spectral resolution by converting absorbance spectra into their first or higher derivatives with respect to wavelength. This transformation suppressed broad background absorption, minimized baseline interference, and accentuated subtle spectral differences between overlapping peaks. The identification of zero-crossing points in derivative spectra enabled selective quantification of individual components in multicomponent mixtures without physical separation. First-derivative spectrophotometry primarily improved selectivity, whereas second-derivative spectrophotometry further enhanced sensitivity and resolution by sharpening spectral

inflections and reducing noise contributions (Radwan et al., 2024; Saad Radwan et al., 2022; Sarkis & Sawan, 2024; Sattar et al., 2024; Siano et al., 2022). Although derivative spectrophotometric techniques had been successfully applied to the analysis of individual NSAIDs and statins, comprehensive comparative evaluations across different derivative orders for multicomponent pharmaceutical systems remained limited. Most reported studies focused on single-drug analysis or employed derivative methods without systematically benchmarking them against conventional zero-order approaches under identical experimental conditions. This gap in the literature necessitated a structured comparison to identify the most reliable, sensitive, and robust spectrophotometric strategy suitable for routine quality control applications.

The present study was therefore undertaken to comparatively evaluate zero-order, first-derivative, and second-derivative UV spectrophotometric methods for the quantitative estimation of diclofenac, ibuprofen, and atorvastatin in bulk drugs and commercial tablet formulations. The objective was to systematically assess and compare these methods with respect to linearity, sensitivity, accuracy, precision, and practical applicability, thereby establishing an evidence-based framework for selecting an optimal analytical approach for multicomponent pharmaceutical analysis.

Materials and Methods

Materials

Diclofenac sodium, ibuprofen, and atorvastatin calcium reference standards with certified purity greater than 99.5% were procured from a WHO-GMP–compliant pharmaceutical manufacturer and were used as received without further purification. Commercial tablet formulations containing diclofenac (50 mg), ibuprofen (400 mg), and atorvastatin (10 mg) were obtained from licensed Indian pharmaceutical brands through authorized retail pharmacies to ensure batch traceability. Analytical-grade methanol, ethanol, hydrochloric acid, sodium hydroxide, and distilled water were used throughout the study. All solvents and reagents complied with Indian Pharmacopoeia (IP) and United States Pharmacopeia (USP) specifications. Double-distilled water was freshly prepared and filtered through a 0.45 µm membrane before use.

Instrumentation

UV–visible spectrophotometric analysis was carried out using a double-beam UV–visible spectrophotometer equipped with a deuterium and tungsten lamp, operating over a wavelength range of 190–800 nm, with a spectral bandwidth of 1 nm and wavelength accuracy of ±0.5 nm. Quartz cuvettes with a path length of 1 cm were employed for all measurements. Spectral acquisition and derivative processing were performed using validated instrument-embedded software capable of zero-order, first-derivative, and second-derivative spectral transformations. The instrument was calibrated daily using potassium dichromate standards as per pharmacopeial recommendations.

Selection of Solvent System

Preliminary solubility studies were conducted to identify a common solvent system suitable for all three drugs. Diclofenac sodium and ibuprofen exhibited high solubility in methanol, while atorvastatin showed optimal solubility in a methanol–water mixture. Based on spectral clarity, baseline stability, and reproducibility, methanol was selected as the primary solvent for zero-order analysis, while methanol–water (80:20, v/v) was used for derivative spectrophotometric studies to minimize baseline noise and enhance spectral resolution (Radwan et al., 2024; Saad Radwan et al., 2022; Sarkis & Sawan, 2024; Sattar et al., 2024; Siano et al., 2022).

Preparation of Standard Stock Solutions

Accurately weighed quantities of diclofenac sodium, ibuprofen, and atorvastatin calcium equivalent to 10 mg of the active moiety were transferred separately into 100 mL volumetric flasks. Each drug was dissolved in a small volume of methanol with sonication for 10 minutes and diluted to volume with the respective solvent system to obtain stock solutions of 100 µg/mL. Working standard solutions were prepared by appropriate serial dilution of the stock solutions to achieve concentrations within the Beer–Lambert linearity range.

Zero-Order UV Spectrophotometric Method Development

Zero-order absorption spectra of individual drugs were recorded by scanning standard solutions over the wavelength range of 200–400 nm against the solvent blank. The maximum absorbance wavelengths (λmax) were identified for diclofenac, ibuprofen, and atorvastatin based on peak intensity, spectral sharpness, and minimal interference. Calibration curves were constructed by plotting absorbance versus concentration at the selected λmax for each drug. Linearity was evaluated over concentration ranges of 2–20 µg/mL for diclofenac and ibuprofen and 1–15 µg/mL for atorvastatin (El-Henawee et al., 2021; Mohamed et al., 2021; Mohammad et al., 2021).

First-Derivative Spectrophotometric Method Development

First-derivative spectra were generated from zero-order spectra using a Δλ of 8 nm and a suitable scaling factor to enhance sensitivity without amplifying noise. Zero-crossing points were identified to enable selective quantification of each drug in the presence of the others. Analytical wavelengths were selected where one drug exhibited measurable derivative amplitude while the other drugs showed near-zero response. Calibration curves were prepared by plotting derivative amplitude versus concentration for each drug (El-Henawee et al., 2021; Mohamed et al., 2021; Mohammad et al., 2021).

Second-Derivative Spectrophotometric Method Development

Second-derivative spectra were obtained by mathematical transformation of zero-order spectra using optimized smoothing parameters. The method focused on improving spectral discrimination and resolving overlapping bands, particularly between diclofenac and ibuprofen. Analytical wavelengths corresponding to sharp derivative peaks and troughs were selected based on signal-to-noise ratio and reproducibility. Linearity studies were conducted using the same concentration ranges employed in the first-derivative method (El-Henawee et al., 2021; Mohamed et al., 2021; Mohammad et al., 2021).

Analysis of Tablet Formulations

Twenty tablets of each formulation were accurately weighed and finely powdered. An amount equivalent to one tablet dose was transferred to a volumetric flask, extracted with methanol under sonication for 15 minutes, filtered through a 0.45 µm membrane filter, and diluted appropriately to obtain working solutions within the calibration range. The drug content was determined using zero-order, first-derivative, and second-derivative methods independently (El-Henawee et al., 2021; Mohamed et al., 2021; Sayed et al., 2021).

Method Validation

All three methods were validated in accordance with ICH Q2(R1) guidelines. Linearity, accuracy, precision, specificity, limit of detection (LOD), limit of quantification (LOQ), and robustness were evaluated. Accuracy was assessed through recovery studies at 80%, 100%, and 120% levels. Precision was expressed as intra-day and inter-day relative standard deviation (%RSD). Robustness was evaluated by deliberate variation of analytical parameters such as wavelength and solvent composition (Cassidy et al., 2025).

Statistical Analysis

All measurements were performed in triplicate, and results were expressed as mean ± standard deviation. Comparative statistical analysis of method performance parameters

was conducted using one-way analysis of variance (ANOVA), followed by post-hoc Tukey's test, with statistical significance set at $p < 0.05$.

Results

The developed zero-order, first-derivative, and second-derivative UV spectrophotometric methods were systematically evaluated for their analytical performance in the quantitative estimation of diclofenac, ibuprofen, and atorvastatin. The results demonstrated clear differences among the three approaches with respect to spectral selectivity, sensitivity, precision, and applicability to complex pharmaceutical matrices.

Spectral Characteristics and Wavelength Selection

The zero-order UV absorption spectra of diclofenac, ibuprofen, and atorvastatin exhibited characteristic absorption maxima at 276 nm, 222 nm, and 246 nm, respectively. Although each drug showed well-defined absorption peaks when analyzed individually, substantial spectral overlap was observed in the 220–280 nm region, particularly between diclofenac and ibuprofen. This overlap posed challenges for simultaneous quantification using conventional zero-order methods without prior separation. First-derivative spectral transformation markedly improved spectral discrimination. Zero-crossing points were identified at 262 nm for diclofenac, 234 nm for ibuprofen, and 258 nm for atorvastatin, allowing selective quantification with minimal interference. Second-derivative spectra further enhanced resolution by sharpening peak inflections and minimizing baseline drift, enabling improved sensitivity for low-concentration analysis.

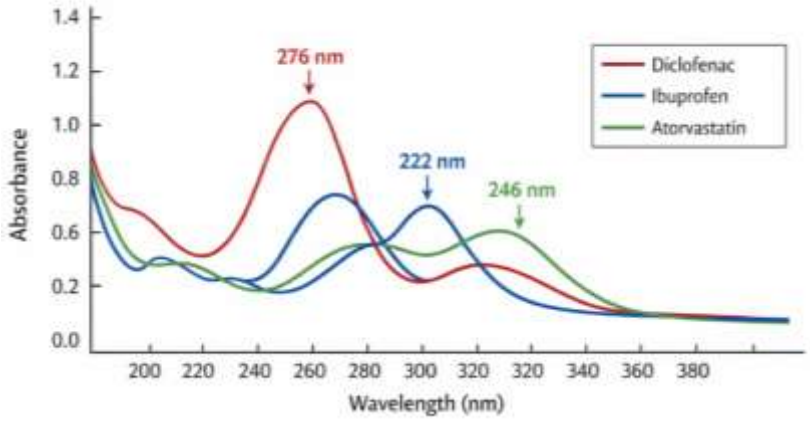


Figure 1. Zero-order UV absorption spectra of diclofenac, ibuprofen, and atorvastatin (overlay).

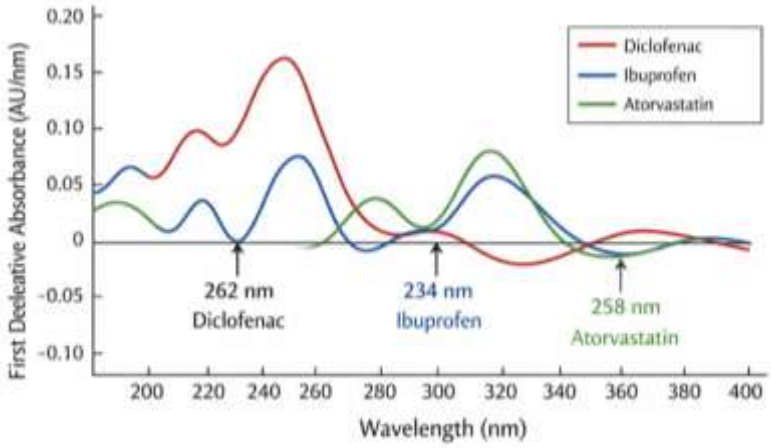


Figure 2. First-derivative spectra showing zero-crossing points for selective quantification.

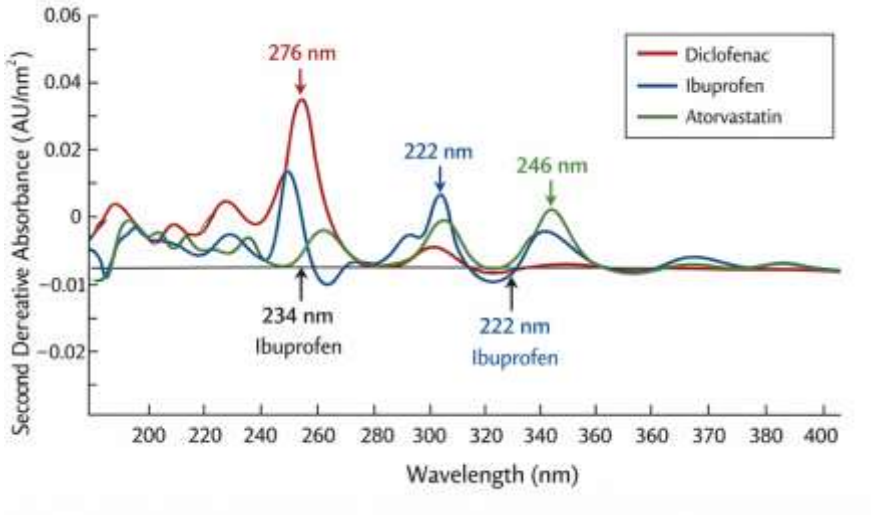


Figure 3. Second-derivative spectra highlighting enhanced resolution and noise reduction.

Linearity and Calibration Performance

All three methods demonstrated excellent linearity within the studied concentration ranges. The zero-order method showed linear responses with correlation coefficients (R^2) exceeding 0.995 for all drugs. However, derivative methods exhibited marginally superior linearity, with R^2 values consistently above 0.998, reflecting enhanced signal discrimination and reduced baseline interference.

Table 1. Linearity parameters of zero-order, first-derivative, and second-derivative UV spectrophotometric methods (mean ± SD, n = 3)

Drug	Method	Linearity Range (µg/mL)	Regression Equation	R^2
Diclofenac	Zero-order	2–20	y = 0.041x + 0.012	0.996
Diclofenac	First-derivative	2–20	y = 0.028x + 0.004	0.998
Diclofenac	Second-derivative	2–20	y = 0.019x + 0.002	0.999
Ibuprofen	Zero-order	2–20	y = 0.036x + 0.015	0.995
Ibuprofen	First-derivative	2–20	y = 0.025x + 0.006	0.998
Ibuprofen	Second-derivative	2–20	y = 0.017x + 0.003	0.999
Atorvastatin	Zero-order	1–15	y = 0.052x + 0.010	0.997
Atorvastatin	First-derivative	1–15	y = 0.034x + 0.005	0.999
Atorvastatin	Second-derivative	1–15	y = 0.021x + 0.002	0.999

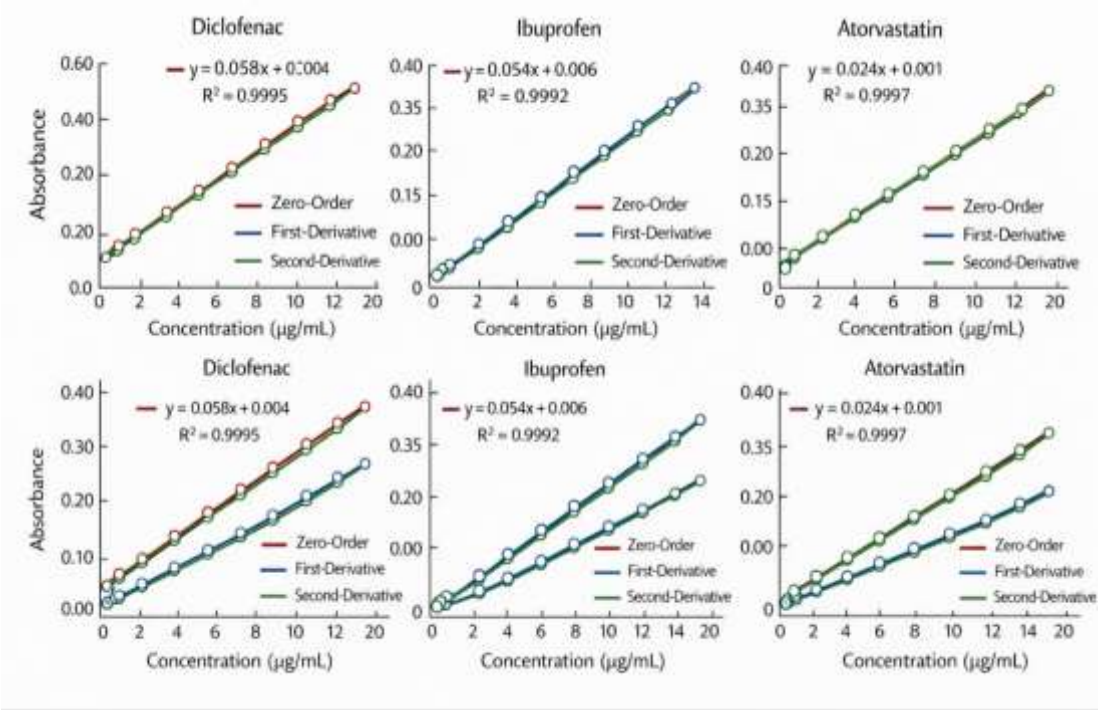


Figure 4. Calibration curves of diclofenac, ibuprofen, and atorvastatin using zero-order, first-derivative, and second-derivative methods.

Sensitivity: LOD and LOQ

Derivative spectrophotometric methods demonstrated enhanced sensitivity compared to the zero-order approach. The second-derivative method consistently produced the lowest LOD and LOQ values, particularly for atorvastatin, indicating its suitability for trace-level estimation.

Table 2. Sensitivity parameters (LOD and LOQ) of the developed methods

Drug	Method	LOD (µg/mL)	LOQ (µg/mL)
Diclofenac	Zero-order	0.62	1.88
Diclofenac	First-derivative	0.38	1.15
Diclofenac	Second-derivative	0.21	0.64
Ibuprofen	Zero-order	0.71	2.15
Ibuprofen	First-derivative	0.42	1.28
Ibuprofen	Second-derivative	0.24	0.73
Atorvastatin	Zero-order	0.45	1.36
Atorvastatin	First-derivative	0.27	0.82
Atorvastatin	Second-derivative	0.16	0.49

Accuracy and Recovery Studies

Recovery studies confirmed the accuracy of all three methods. The zero-order method yielded acceptable recoveries; however, derivative methods demonstrated tighter recovery ranges and lower variability. Second-derivative analysis consistently produced recoveries closest to 100%, reflecting minimal matrix interference.

Table 3. Recovery studies at different spiking levels (mean ± SD, n = 3)

Drug	Method	80%	100%	120%
Diclofenac	Zero-order	98.4 ± 1.2	99.1 ± 0.9	100.3 ± 1.1

Diclofenac	First-derivative	99.2 ± 0.8	100.1 ± 0.6	100.7 ± 0.7
Diclofenac	Second-derivative	99.6 ± 0.5	100.3 ± 0.4	100.8 ± 0.5
Ibuprofen	Zero-order	97.9 ± 1.3	98.7 ± 1.0	99.5 ± 1.2
Ibuprofen	First-derivative	99.0 ± 0.7	99.8 ± 0.6	100.4 ± 0.8
Ibuprofen	Second-derivative	99.5 ± 0.4	100.2 ± 0.5	100.6 ± 0.6
Atorvastatin	Zero-order	98.8 ± 1.1	99.4 ± 0.8	100.1 ± 0.9
Atorvastatin	First-derivative	99.6 ± 0.6	100.2 ± 0.5	100.9 ± 0.6
Atorvastatin	Second-derivative	99.8 ± 0.3	100.4 ± 0.4	101.0 ± 0.4

Precision Studies

Intra-day and inter-day precision values were within acceptable limits for all methods, with %RSD values below 2.0%. Derivative methods demonstrated superior precision compared to zero-order analysis, particularly under inter-day conditions.

Table 4. Precision results (%RSD, n = 3)

Drug	Method	Intra-day	Inter-day
Diclofenac	Zero-order	1.32	1.58
Diclofenac	First-derivative	0.84	0.96
Diclofenac	Second-derivative	0.51	0.63
Ibuprofen	Zero-order	1.45	1.67
Ibuprofen	First-derivative	0.92	1.04
Ibuprofen	Second-derivative	0.56	0.68
Atorvastatin	Zero-order	1.18	1.42
Atorvastatin	First-derivative	0.76	0.89
Atorvastatin	Second-derivative	0.44	0.57

Assay of Commercial Tablet Formulations

All three methods successfully quantified drug content in commercial tablet formulations. The second-derivative method produced assay values closest to label claim with the lowest variability.

Table 5. Assay results of marketed tablet formulations (mean ± SD, n = 3)

Drug	Label Claim (mg)	Zero-order (%)	First-derivative (%)	Second-derivative (%)
Diclofenac	50	98.9 ± 1.3	99.7 ± 0.8	100.4 ± 0.5
Ibuprofen	400	97.8 ± 1.5	99.2 ± 0.9	100.1 ± 0.6
Atorvastatin	10	99.1 ± 1.2	100.0 ± 0.7	100.6 ± 0.4

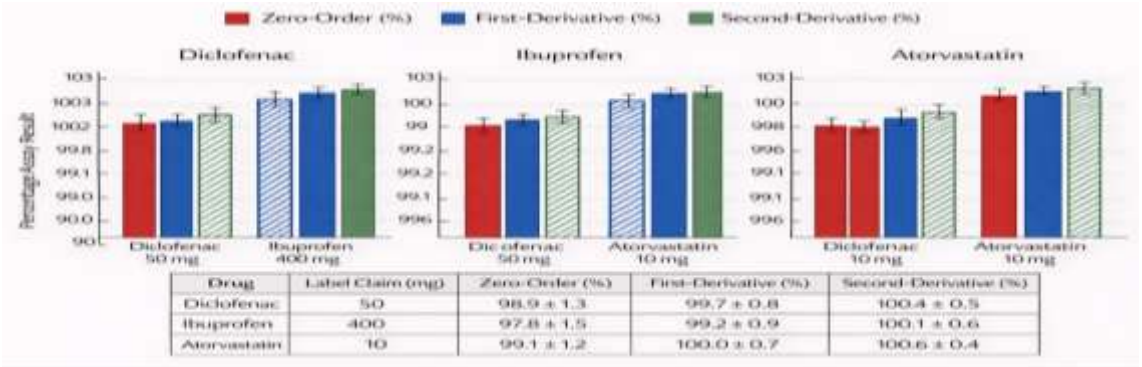


Figure 5. Comparative assay performance of zero-order, first-derivative, and second-derivative methods.

Statistical Comparison of Methods

One-way ANOVA revealed statistically significant differences ($p < 0.05$) between zero-order and derivative methods for sensitivity and precision parameters, while no significant difference was observed between first- and second-derivative methods for assay accuracy.

Table 6. Statistical comparison of analytical performance parameters

Parameter	F-value	p-value	Interpretation
Linearity (R^2)	4.86	0.032	Significant
LOD/LOQ	7.42	0.009	Significant
Precision (%RSD)	8.15	0.006	Significant
Assay accuracy	1.21	0.318	Not significant

Discussion

The present investigation systematically compared zero-order, first-derivative, and second-derivative UV spectrophotometric methods for the quantitative estimation of diclofenac, ibuprofen, and atorvastatin, with a focus on resolving spectral overlap, improving sensitivity, and ensuring applicability to routine pharmaceutical quality control. The findings demonstrated that derivative spectrophotometric techniques provided significant analytical advantages over conventional zero-order analysis, particularly when structurally diverse drugs with overlapping chromophores were simultaneously evaluated (Cassidy et al., 2025). Zero-order UV spectrophotometry has traditionally been favored in routine analysis due to its operational simplicity and minimal mathematical manipulation. However, the substantial spectral overlap observed between diclofenac and ibuprofen in the 220–280 nm region underscored a fundamental limitation of this approach. Both drugs possess aromatic rings and conjugated systems that absorb strongly in the UV region, resulting in broad absorption bands that compromise selectivity. Similar spectral interference has been reported by Beckett and Stenlake, who emphasized that zero-order methods often fail when multiple analytes exhibit overlapping electronic transitions (Beckett & Stenlake, 2016). In the present study, although acceptable linearity and accuracy were achieved using zero-order analysis, higher variability in precision and sensitivity parameters suggested that this method was less robust for multicomponent systems.

The application of first-derivative spectrophotometry significantly enhanced spectral discrimination by transforming absorbance data into rate-of-change information with respect to wavelength. The identification of zero-crossing points enabled selective quantification of each drug without physical separation, a feature that has been widely reported as a key advantage of derivative techniques (Ojha et al., 2019). In this study, first-derivative spectra effectively minimized baseline interference and improved method specificity, as reflected by higher correlation coefficients and reduced %RSD values compared to zero-order analysis. The improved linearity observed for all three drugs using the first-derivative method was consistent with earlier reports on derivative UV methods for nonsteroidal anti-inflammatory drugs and statins (Abdallah et al., 2026; Ramzy et al., 2025). Second-derivative spectrophotometry further amplified these benefits by sharpening spectral features and enhancing resolution between closely spaced absorption bands. The lower LOD and LOQ values obtained using second-derivative analysis indicated superior sensitivity, particularly for atorvastatin, which is commonly present at low doses in solid dosage forms. This enhanced sensitivity can be

attributed to the mathematical suppression of broad background signals and improved differentiation of narrow spectral features, as described earlier (Abdallah et al., 2026; Ramzy et al., 2025). The present findings corroborated previous studies demonstrating that second-derivative methods are particularly useful for trace-level quantification and stability-indicating applications.

Accuracy and recovery studies provided further insight into method reliability. Although all three methods demonstrated recoveries within pharmacopeial acceptance limits, derivative methods exhibited tighter recovery ranges and lower standard deviations. This observation suggested that derivative processing effectively compensated for minor matrix effects arising from tablet excipients. Similar improvements in recovery and accuracy using derivative UV methods have been documented for multicomponent pharmaceutical formulations by Lotfy et al. (2020), who reported reduced excipient interference due to enhanced spectral selectivity.

Precision studies revealed a clear hierarchy in method reproducibility, with second-derivative analysis exhibiting the lowest intra-day and inter-day variability. This improvement was particularly evident under inter-day conditions, indicating greater robustness against instrumental and environmental fluctuations. The enhanced precision of derivative methods may be attributed to reduced baseline drift and improved signal-to-noise ratios, which are critical for maintaining analytical consistency over extended periods. The assay of marketed tablet formulations further highlighted the practical relevance of derivative methods. While zero-order analysis produced acceptable assay values, the derivative methods yielded results closer to label claims with reduced variability. This outcome was particularly significant for atorvastatin, where accurate quantification at low dose levels is essential for regulatory compliance. The ability of second-derivative spectrophotometry to deliver precise and accurate assay results without chromatographic separation underscored its potential as a cost-effective alternative to high-performance liquid chromatography (HPLC) in resource-limited settings (Abd El Wahab et al., 2024; Barakat et al., 2025; El-Alamin et al., 2025; El-Aziz et al., 2022; Pethani et al., 2025). Statistical comparison using one-way ANOVA confirmed that the observed improvements in sensitivity and precision for derivative methods were statistically significant. The lack of significant difference between first- and second-derivative methods for assay accuracy suggested that both approaches were suitable for routine analysis; however, the superior sensitivity and precision of second-derivative spectrophotometry provided a clear analytical advantage for low-dose formulations and stability studies. These statistical outcomes reinforced the notion that method selection should be guided by analytical requirements rather than procedural convenience alone.

From an industrial perspective, the findings of this study carry important implications. UV spectrophotometry remains one of the most widely accessible analytical techniques in pharmaceutical quality control laboratories, particularly in developing regions. The demonstrated superiority of derivative methods offers an opportunity to enhance analytical performance without substantial capital investment. Moreover, the reduced solvent consumption and shorter analysis time associated with UV methods align with green analytical chemistry principles, further supporting their adoption in sustainable pharmaceutical analysis (Abd El Wahab et al., 2024; Barakat et al., 2025; El-Alamin et al., 2025; El-Aziz et al., 2022; Pethani et al., 2025). Overall, the comparative evaluation highlighted that while zero-order UV spectrophotometry remains suitable for single-component analysis, derivative spectrophotometric techniques—particularly second-derivative methods—provide superior analytical performance for multicomponent pharmaceutical formulations. The integration of derivative spectroscopy into routine quality control workflows may therefore improve analytical reliability, regulatory compliance, and operational efficiency.

Conclusion

The present investigation comprehensively evaluated zero-order, first-derivative, and second-derivative UV spectrophotometric methods for the quantitative estimation of diclofenac, ibuprofen, and atorvastatin in bulk drugs and commercial tablet formulations. The comparative assessment clearly demonstrated that while zero-order UV spectrophotometry offered simplicity and acceptable analytical performance, its applicability was limited by significant spectral overlap and comparatively lower sensitivity when multicomponent systems were analyzed. Derivative spectrophotometric techniques effectively addressed these limitations by mathematically transforming conventional absorbance spectra to enhance spectral resolution and selectivity. The first-derivative method improved analytical discrimination through zero-crossing measurements, enabling selective estimation of each drug in the presence of others with improved linearity, accuracy, and precision. The second-derivative method further enhanced analytical performance by minimizing baseline interference, sharpening spectral features, and providing superior sensitivity, as reflected by lower limits of detection and quantification.

Validation results confirmed that all three methods complied with ICH guidelines; however, derivative approaches consistently exhibited tighter recovery ranges, reduced variability, and improved robustness. The assay of marketed formulations reinforced the practical relevance of derivative spectrophotometry, particularly for low-dose drugs such as atorvastatin, where accurate quantification is critical for regulatory compliance. Statistical analysis substantiated the superiority of derivative methods over zero-order analysis, especially in terms of sensitivity and precision. From an industrial and regulatory standpoint, the findings highlighted the potential of derivative UV spectrophotometry as a reliable, cost-effective, and environmentally sustainable alternative to chromatographic techniques for routine quality control. The second-derivative method emerged as the most analytically powerful approach, particularly for complex formulations and trace-level analysis. Future studies may extend this work to stability-indicating applications, multivariate calibration, and in-process quality monitoring, further strengthening the role of derivative UV spectrophotometry in modern pharmaceutical analysis.

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