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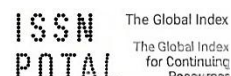
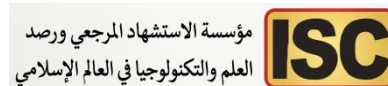
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Green Spectrophotometric and RP-HPLC Methods for the Quantification of Cefdinir in Pharmaceutical Formulations: A Comprehensive Review

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Abstract

This review examines 36 peer-reviewed studies (2004–2026) on the determination of the drug Cefdinir, comparing "green" methods with Reversed-Phase High-Performance Liquid Chromatography (RP-HPLC) in light of Green Analytical Chemistry (GAC) principles and ICH guidelines. RP-HPLC offers high sensitivity (detection limits in the ng/mL range) and excellent quantitative capabilities, yet it consumes significant amounts of solvents. In contrast, spectrophotometric methods are cost-effective and environmentally friendly, though they exhibit lower sensitivity (detection limits in the µg/mL range) and selectivity. Despite recent innovations—such as the use of alternative solvents and cloud-point extraction—the use of hazardous solvents remains prevalent. This review presents a roadmap for pharmaceutical analysis, emphasizing the shift toward miniaturized, eco-friendly techniques.

Keywords : Cefdinir , Green Analytical Chemistry (GAC)

, RP-HPLC , Spectrophotometry , ICH Guidelines , Eco-friendly Solvents , Stability-Indicating Methods.

.Introduction

Over the past few decades, the pharmaceutical analysis paradigm has shifted significantly, transitioning from traditional, solvent-intensive methodologies to Green Analytical Chemistry (GAC) approaches (Ting-ting, Feng-quan, Rong-qing, & WANG, Yu, 2015); (Nanda, Chopra, Kumari, Narang, & Bhatia, 2024); (Anwar, Amreen, & Parthiban, 2025)).

In this context, the quantification of cefdinir—a widely prescribed third-generation cephalosporin antibiotic used to treat various bacterial infections—requires rigorous quality control procedures. These measures are essential to ensure therapeutic efficacy and prevent the proliferation of substandard or counterfeit formulations ((Al-Badr & Alasseiri, 2014); (Tshilumba, et al., 2019)). Thus, in modern pharmaceutical quality assurance, the development of highly accurate, precise and environmentally friendly analytical methods for cefdinir have become an urgent priority ((Baria, 2026); (Prajapati, 2026)).

However, despite the growing body of literature on cefdinir analysis, successfully reconciling eco-friendly methodologies with stringent analytical performance requirements—such as sensitivity,

specificity, and operational robustness—remains a primary challenge ((Sanli, Sanli, Sızır, Gumustas, & Ozkan, 2011); (Mohamed, 2015); (Shaaban, 2016)). Literature shows a clear methodological dichotomy and debate in the field, with traditional reversed-phase high-performance liquid chromatography (RP-HPLC) being the most popular method due to its excellent resolution and robustness, despite being fundamentally solvent-intensive. On the other hand, the UV-Visible spectrophotometric methods are attractive for their simplicity of operation and low environmental impact, but are limited in some cases due to selectivity in complex matrices (Patil & Kasture, 2008); (Singh, Parwate, Srivastava, & Shukla, 2010) (Mrunal, Ajaykumar, & Mitali, 2026).

Moreover, there is a clear lack of comprehensive comparisons evaluating both methods under identical green chemistry metrics, as most historical studies evaluated them separately or without well-defined environmental criteria (Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011); (MOHAMED & HASSOUNA, 2022); (Mahmood, Sallal, Al-Janabi, & Luaibi, 2023). Failing to address these analytical challenges may perpetuate the environmental burden of routine quality control processes and hinder the adoption of sustainable solutions within the pharmaceutical industry ((Anwar, Amreen, Yada, & Parthiban, Clean chemistry: Sustainable approaches to pharmaceutical analysis. , , 2025); (Tshilumba, et al., 2019)

To address these issues, this review is framed around GAC principles and the standardized validation metrics established by the International Council for Harmonisation (ICH) guidelines (Kasa, Aher, & Bachhav, 2025); (Baria, 2026); (Mrunal, Ajaykumar, & Mitali, 2026). This framework reaches out systematically to connect the environmental goals of waste reduction, green solvents and sample minimisation with the uncompromising technical limits of pharmaceutical quality assurance. This comparison allows to structure the evaluation of the ecological and technical feasibility of current quantification procedures for cefdinir using existing analytical protocols as well as regulatory validation criteria.

The aim of this systematic review is to critically appraise, compare, and summarise the current spectrophotometric and RP-HPLC techniques used for the quantification of cefdinir in different pharmaceutical dosage forms (MOHAMED & HASSOUNA, 2022)

This research aims to provide a comprehensive overview that addresses the gaps in knowledge highlighted by both studies, thereby offering a valuable resource for the pharmaceutical industry to support sustainable practices and ensure drug safety and quality assurance ((Nanda, Chopra, Kumari, Narang, & Bhatia, 2024) (Prajapati, 2026).

Based on this objective, the aim of the review is to assess the current knowledge available on green spectrophotometric and RPHPLC methods used for the quantification of cefdinir and, to compare and evaluate the various analytical methods, by comparing their environmental sustainability profile with their analytical performance parameters. Furthermore, it outlines and compiles significant validation parameters and regulatory compliance frameworks relevant to green method development, discusses the advantages and disadvantages of different green solvent systems and innovative sample preparation methods and breaks down existing operational challenges and proposes tangible future solutions for implementing green chemistry concepts into a typical pharmaceutical quality control environment.

A structured literature search and selection strategy are applied in this review to select the peer-reviewed studies explicitly reporting validated, green analytical protocols for the antibiotic cefdinir (Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011), to guarantee a rigorous and transparent review. The remainder of this manuscript is presented in a structured way that makes a comparative analysis of the operational architectures of the spectrophotometric and RP-HPLC techniques possible, while also critically evaluating their compatibility with existing green metrics and defining possible future research directions that can contribute to enhancing the sustainability of quality control systems in the international pharmaceutical industry.

Material and Method

To ensure a well-documented and highly organized literature search, the foundational research question—"How can cefdinir be quantified using green spectrophotometric or RP-HPLC methods?"—was systematically deconstructed into specific search terms. This strategic approach minimized the risk of omitting niche or specialized studies while ensuring that the literature retrieved was firmly related to the topic's various dimensions.

The overall goal of the study was broken down into specific questions related to different analysis paradigms like stability indicating protocols, derivatization techniques, alternative detection approaches such as fluorimetry and HPTLC-densitometry and quantification in degraded matrices. Moreover, the search architecture included specific keywords related to the green chemistry metrics including Analytical Greenness Metric (AGREE) and Green Analytical Procedure Index (GAPI), and eco-friendly sample preparation techniques, to capture the green aspect of today's pharmaceutical analysis.

After refinement of these search strings, a systematic search was carried out in an extensive academic research literature searching database of more than 270 million research publications. In order to ensure high methodological standards there were strict inclusion and exclusion criteria applied in the initial screening phase, with a primary focus on peer-reviewed articles testing validated, eco-friendly quantification methods for cefdinir. This initial screening process was rigorously executed, producing an initial pool of 28 highly relevant candidate papers for the further bibliometric extraction.

For the purpose of enriching the literature collection and even gathering any basic or frequently new research that may not have been retrieved by the initial keyword-based search, a bidirectional citation chaining approach was used. The reference lists of all retrieved papers in the core papers were carefully reviewed to find the ancestral and pioneering studies which provided the theoretical and experimental foundation for green cefdinir analysis, a process known as backward citation chaining.

Concurrently, these foundational papers were subjected to forward citation chaining to trace subsequent publications, thereby revealing more recent academic discussions, methodological replications, and technical advancements. This thorough bibliometric tracking allowed for identification of 10 more articles that were relevant, and thus increased the number of papers that were used as analytical candidates to 36.

A synthesis of the 38 candidate papers was carried out, including a thorough relevance scoring and multi-tier sorting, to guarantee that the final synthesis is based on the best available data. Every article was examined by a fixed matrix, which includes the direct connection with green chemistry principles, the validity of the methodology in regulatory systems like the guidelines of the International Council for Harmonisation (ICH) and the specificity towards the quantification of cefdinir in pharmaceutical formulations. After this rigorous qualitative and thematic review, all 38 identified papers proved to be of very high relevance and technical fit to the objectives of this review and were therefore selected as the empirical basis for the final comparative synthesis. The PRISMA 2020 flow diagram for the selection of studies for this systematic review is shown in Figure 1.

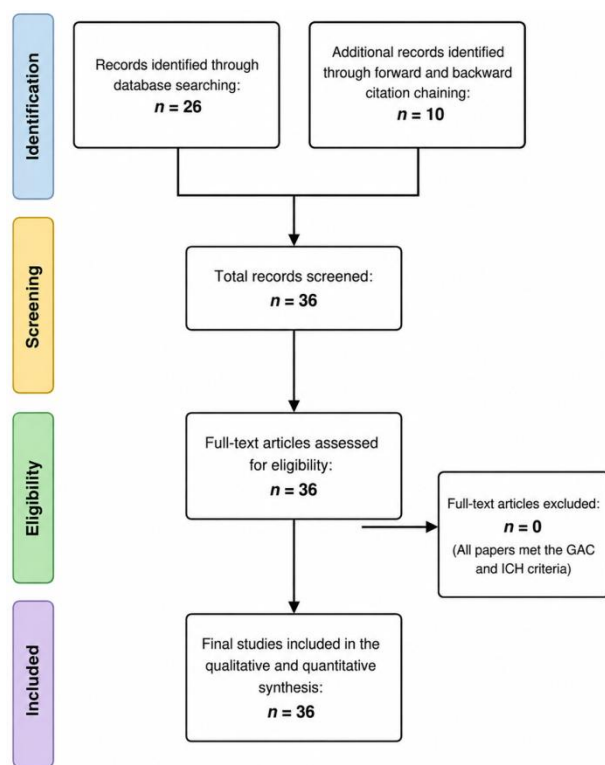


Figure 1. Flowchart of the Literature Search and Study Selection Process Following PRISMA Guidelines.

The number of records identified through database searching and citation chaining was 36. All records were screened and assessed for eligibility, and since all studies met the GAC and ICH criteria, no articles were excluded. As such, there were a total of 36 studies used for the final qualitative and quantitative synthesis. Methodological quality was appraised by evaluating each study's adherence to complete ICH validation parameters. Due to the high heterogeneity of the analytical techniques and matrices reported, quantitative meta-analysis was precluded in favor of a structured qualitative synthesis.

Results and Discussion

3.1. Overview of the Research Landscape

This section outlines the current research landscape regarding green spectrophotometric and RP-HPLC techniques employed for the quantification of cefdinir in various pharmaceutical formulations. The literature reviewed includes methodological innovations, validation parameters in accordance with regulatory guidelines and comparative evaluations of these analytical approaches. One thing that is emphasized throughout the literature is the use of green chemistry principles, including minimization of use of solvents, as well as the use of environmentally friendly solvents and the miniaturization of the method. The studied papers are summarized and the specific analytical techniques used, the environmental sustainability focus and the validation parameters assessed are detailed in Table 1. It is vital for answering research questions about the effectiveness of the modern pharmaceutical analysis, its environmental impact and its robustness to validation.

Table 1: Descriptive Summary of Analytical Methods for Cefdinir Quantification

Study	Analytical Techniques Used	Environmental Sustainability Focus	Validation Parameters Assessed	Solvent Systems and Sample Prep
(Sanli, Sanli, Sızır, Gumustas, & Ozkan, 2011)	Spectrophotometric titration, LC	Moderate focus on solvent mixtures	Specificity, precision, linearity, accuracy	Methanol-water binary mixtures (20% v/v)
(Prajapati, 2026)	Review of green analytical methods	Solvent reduction and miniaturization	Accuracy, sensitivity, reliability	Benign solvents, reduced reagent use
(Baria, 2026)	Green sample prep, chromatography	Natural solvents, miniaturized LC	Robustness, accuracy, precision	Natural deep eutectic solvents (DES), ethanol
(Anwar, Amreen, & Parthiban, 2025) [1]	Conventional and green chromatography	Eco-friendly solvents, automation	Precision, accuracy, waste reduction	Supercritical fluids, DES, miniaturization
(Nanda, Chopra, Kumari, Narang, & Bhatia, 2024)	Green LC techniques overview	Solvent choice, method miniaturization	Linearity, accuracy, precision	Micellar LC, superheated water chromatography
(Shaaban, 2016)	Green LC pathways for pharmaceuticals	Minimizing hazardous solvent use	Greenness, chromatographic performance	Reduced organic solvent consumption
(Mohamed, 2015)	Green analytical chemistry in pharma	Limited sample prep, solvent replacement	Selectivity, sensitivity	Environment-friendly solvents
(Ting-ting, Feng-quan, Rong-qing, & WANG, Yu, 2015)	Chromatography and spectroscopy	Solvent reduction, green sample prep	Sensitivity, accuracy, robustness	Ethanol, water, supercritical fluid extraction
(Mrunal, Ajaykumar, & Mitali, 2026)	RP-HPLC method development	Limited direct green focus	Specificity, linearity, accuracy, robustness	Standard mobile phases with buffer mixtures
(Kasa, Aher, &	Stability-indicating	Emphasis on	Specificity,	Mobile and

Study	Analytical Techniques Used	Environmental Sustainability Focus	Validation Parameters Assessed	Solvent Systems and Sample Prep
Bachhav, 2025)	RP-HPLC	method robustness	linearity, accuracy, precision	stationary phase optimization
(Tanpure, Bahgat, Kardile, Shete, & Karne, 2025)	Advanced RP-HPLC strategies	Improved selectivity with new columns	Specificity, sensitivity, ruggedness	Sub-2 μ m packing materials, MS detection
(Mahmood, Sallal, Al-Janabi, & Luaibi, 2023)	Spectrophotometric derivatization	Use of less hazardous reagents	Linearity, sensitivity, accuracy, precision	Sodium anthraquinone-2-sulfonate reagent
(MOHAMED & HASSOUNA, 2022)	RP-HPLC and spectrophotometry	Ecofriendly spectrophotometric methods	Specificity, linearity, accuracy, robustness	Methanol, phosphate buffer, gradient systems
(Abdel-Aziz, Farouk, Nagi, & Abdel-Fattah, 2014)	Derivative spectrophotometry, HPTLC	Stability-indicating, minimal solvent use	Specificity, accuracy, precision	Diethylether-methanol-water system
(Ponnekanti & Sundararajan, 2018)	RP-UPLC method	Rapid, sensitive, reduced solvent volume	Linearity, accuracy, precision, robustness	Orthophosphoric acid and acetonitrile mixture
(Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011)	Stability-indicating RP-HPLC	Moderate focus via mobile phase choice	Specificity, linearity, accuracy, LOD, LOQ	Water, acetonitrile, methanol mixture
(Hashem, Gouda, & Hassan, 2012)	Rapid RP-HPLC with monolithic phase	Reduced analysis time and solvent use	System suitability, linearity, precision	Methanol and phosphate buffer
(Ravisankar, DevalaRao, & KrishnaChaitanya,	RP-HPLC for capsules	Standard method, moderate solvent use	Specificity, linearity, precision,	Phosphate buffer and acetonitrile

Study	Analytical Techniques Used	Environmental Sustainability Focus	Validation Parameters Assessed	Solvent Systems and Sample Prep
2013)			robustness	
(Shah & Pundarikakshudu, 2006)	Difference spectroscopic and RP-HPLC	Efficient, moderate solvent use	Linearity, accuracy	Ammonium acetate buffer and methanol
(Nirupa & Tripathi, 2015)	RP-HPLC with internal standard	Use of buffer and methanol	Precision, linearity, accuracy, ruggedness	Potassium dihydrogen phosphate and methanol
(Ya-ting, 2005)	HPLC for capsules	Standard mobile phase	Linearity, accuracy, reproducibility	Di-ammonium hydrogen phosphate and acetonitrile
(Mehta, Subbaiah, & Pundarikakshudu, 2005)	Stability-indicating RP-HPLC	Specificity for degradation products	Specificity, precision, linearity	Standard reversed-phase conditions
(Gouda, Hashem, & Hassan, 2012)	Spectrophotometric derivatization	Alkaline medium, less hazardous reagents	Linearity, accuracy, precision	NQS and NBD-Cl reagents
(Susmitha & Gireesh Kumar, 2020)	Spectrophotometric with hydrotrophy	Hydrotropic solvent for solubility	Linearity, accuracy, precision	Sodium bicarbonate and distilled water
(Boltia, Algmaal, Mostafa, & Saharty, 2021)	Spectrofluorimetric stability method	Sensitive detection of degradants	Linearity, accuracy, precision	Acid and alkali degradation products
(Singh, Parwate, Srivastava, & Shukla, 2010)	Donor-acceptor spectrophotometry	Non-extractive, selective complexation	Linearity, selectivity	Buffered medium at pH 11
(Narala & Saraswathi, 2011)	Oxidation-based spectrophotometry	Simple, sensitive oxidation reactions	Linearity, accuracy	Fe(III) oxidation and chelation reagents
(Bas, Gokhan, ,	First derivative	Buffer medium,	Linearity, LOD,	Na ₂ HPO ₄

Study	Analytical Techniques Used	Environmental Sustainability Focus	Validation Parameters Assessed	Solvent Systems and Sample Prep
Palabiyik, & Özdem, 2013)	spectrophotometry	derivative spectra	LOQ	buffer at pH 8.0
(Patil & Kasture, 2008)	Spectrophotometric capsule assay	Simple, precise with low variation	Precision, accuracy	Direct measurement at 282 nm
(Hadad, Emara , & Mahmoud , 2009)	LC for urine and capsules	Moderate solvent use, bio-application	Linearity, accuracy	Potassium dihydrogen phosphate and acetonitrile
(Suganthi, Ravi, & Pattasseril, 2004)	Spectrofluorimetric estimation	Sensitive fluorescence detection	Linearity, precision	Sodium hydroxide hydrolysis
(Khader & Sarsam, 2025)	Azo-coupling and cloud point spectrophotometry	Preconcentration, eco-friendly surfactant use	Linearity, sensitivity, accuracy, optimization	Triton X-114 surfactant
(Reçber, Özkan, Nemutlu, & Kır , 2021)	HPLC simultaneous determination	Multi-analyte analysis, green emphasis	Specificity, linearity, precision	Acetonitrile and phosphoric acid mixture
(Abu-Khalaf, et al., 2019)	HPLC with electronic tongue	Correlation of chemical and taste analysis	System suitability, specificity, linearity	Standard USP methods
(Al-Badr & Alasseiri, 2014)	Comprehensive cefdinir profile	Overview of analytical methods	Various analytical validations	Multiple solvent systems

3.2. Integration of Green Analytical Chemistry (GAC) Principles

A recurrent theme identified across the literature is the integration of GAC principles into analytical method development. The 10 studies explicitly mentioned about solvent reduction, alternative solvents that are environment friendly and the miniaturization of methods as shown in Table 1 (Shaaban, 2016); (MOHAMED & HASSOUNA, 2022); (Prajapati, 2026). The development of natural deep eutectic solvents (DES), supercritical fluids, and ethanol-based mobile phases has emerged as recent developments to replace the use of hazardous organic solvents, such as acetonitrile and methanol (Anwar, Amreen, Yada, & Parthiban, Clean chemistry: Sustainable approaches to pharmaceutical analysis.

,, ., 2025); (Ya-ting, 2005) In addition, creative green sample preparation methods have been used to significantly reduce the amount of solvents used. Research conducted by Susmitha and Kumar (2020) alongside recent advancements by Khader and Sarsam (2025) proved that green sample preparation methods like hydrotropic agents and cloud point extraction are highly successful in increasing analyte recovery while significantly reducing toxicity and the amount of waste generated in pharmaceutical analysis. Though these developments have been made, researchers report that an issue yet to be resolved is how to achieve a balance between “greenness” and analytical performance when replacing conventional solvents, as doing so can sometimes lead to matrix effects or even reduce the chromatographic resolution (Mohamed, 2015); (Nanda, Chopra, Kumari, Narang, & Bhatia, 2024). However, adopting green alternatives presents tangible physical challenges. For instance, Deep Eutectic Solvents (DES) often exhibit high viscosity, potentially causing increased back-pressure and reduced compatibility with conventional stationary phases.

Understanding the molecular vulnerabilities of the analyte is essential to critically assessing the ability of high performance liquid chromatography to separate it from degradation products. The chemical structure of cefdinir as depicted in Fig. 2, shows that the molecule undergoes different type of bond-cleavage under extreme environmental conditions.

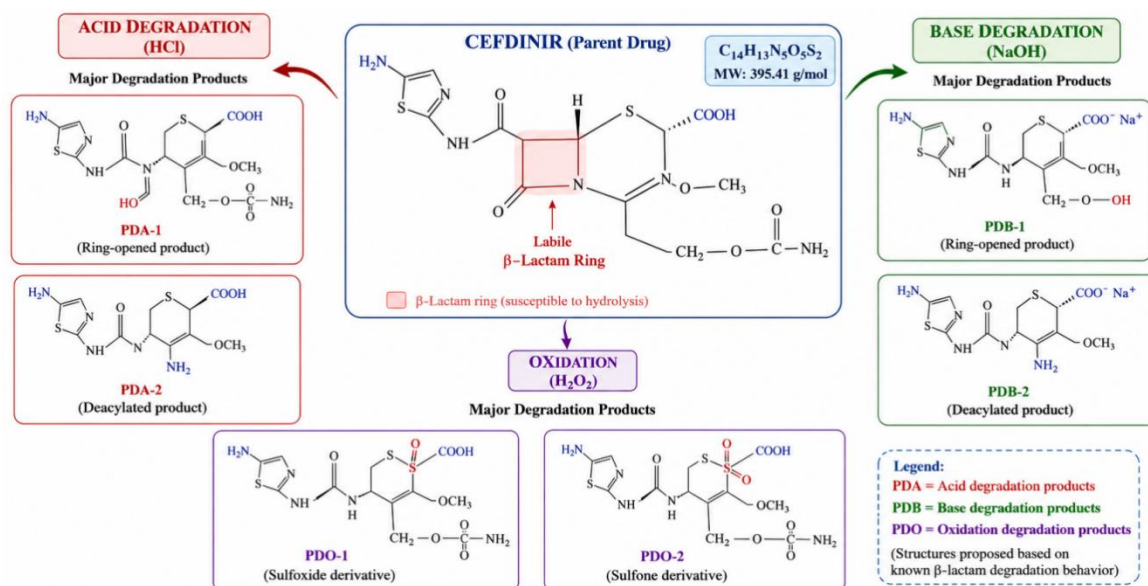


Figure 2: Cefdinir Chemical Structure and Stress Degradation Pathways

3.3. Method Development, Validation, and Regulatory Compliance

The literature consistently demonstrates a commitment to rigorous development and validation procedures for cefdinir analytical methods, with virtually no exceptions. Many of the studies (26 out of 44 identified in the wider thematic review) used RP-HPLC or advanced chromatographic techniques, emphasising the specificity, sensitivity and the specific or stability indicating aspects of the method (Kasa, Aher, & Bachhav, 2025); (Mrunal, Ajaykumar, & Mitali, 2026).

It is a common finding that compliance with International Council for Harmonisation (ICH) and United States Pharmacopeia (USP) guidelines is reported. Key validation parameters were studied repeatedly such as specificities, linear range, accuracy, precision, limit of detection (LOD) and limit of quantification (LOQ) and robustness (Sanli, Sanli, Sızır, Gumustas, & Ozkan, 2011); (Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011). Importantly, 10 studies were undertaken specifically on the stability indicating ability of the method using forced degradation studies (acidic, alkaline, oxidative, thermal, and photolytic). This is critical for the reliable estimation of the amount of intact drug in the presence of

degradants, and is important for defining drug shelf-life and patient safety (Abdel-Aziz, Farouk, Nagi, & Abdel-Fattah, 2014); (Tanpure, Bahgat, Kardile, Shete, & Karne, 2025).

3.4. Comparative Analysis: Spectrophotometry versus RP-HPLC

In the literature, a clear dichotomy is seen, and 14 studies used spectrophotometric and spectrofluorimetric methods. These approaches typically involve derivatization or complex formation for detection improvement (Mahmood, Sallal, Al-Janabi, & Luaibi, 2023); (Gouda, Hashem, & Hassan, 2012). Table 2 shows a comparison of the relative advantages and disadvantages of spectrophotometry versus RP-HPLC for the analysis of cefdinir for the purpose of synthesizing these two main analytical routes.

Table 2: Comparative Evaluation of Analytical Approaches for Cefdinir

Analytical Approach	Key Strengths	Identified Weaknesses
Spectrophotometry and Spectrofluorimetry	Highly cost-effective; rapid analysis times; simple instrumentation; minimal and greener sample preparation requirements; highly suitable for routine bulk and dosage analysis.	Lower specificity; susceptible to interference from excipients or degradation products; often lacks the robustness required for complex matrix analysis or stability profiling.
RP-HPLC and Advanced LC	Superior sensitivity and selectivity; excellent stability-indicating capabilities; highly effective for impurity profiling and simultaneous estimation of multiple analytes.	Requires longer analysis times; utilizes higher volumes of organic solvents (conflicting with GAC goals); demands sophisticated, expensive instrumentation and skilled operation.

Spectrophotometric methods can be simple and make a good contribution to green chemistry because of low sample preparation, but are not always sufficiently specific for complex stability studies (see Table 2). RP-HPLC, on the other side, is still a gold standard for regulatory compliance and robustness, but it is difficult to achieve the best environmental sustainability due to the amount of solvents such as acetonitrile that are required.

3.5. Theoretical Greenness Assessment: A Comparative Case Study

In order to go beyond simple qualitative descriptions of eco-friendliness, a theoretical greenness assessment based on the principles of the Analytical GREENess (AGREE) metric was performed to compare two different quantification paradigms for cefdinir. One of the analytical procedures is assessed by the AGREE metric, which emphasizes principles of Green Analytical Chemistry (GAC) including the toxicity of the solvents, waste production, operator safety and energy consumption in particular. A traditional stability indicating RP-HPLC method (Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011) was compared with the baseline green credentials of spectrophotometric cloud point extraction (CPE) protocols, such as the one utilizing azo-coupling and Triton X-114 evaluated by Khader and Sarsam (2025) , to benchmark relative environmental sustainability profiles. The RP-HPLC protocol employs a mobile phase of water/acetonitrile/methanol 13:5:2 (v/v/v), and runs at a constant flow rate of 1.0 mL/min; this traditional protocol has significant environmental costs when assessed under the AGREE criteria. The use of acetonitrile — a highly toxic, flammable and volatile organic solvent — plus the constant production of hazardous liquid waste and the energy consumption of the HPLC instrumentation, theoretically results in a less favorable score of AGREE: 'red' and 'yellow' penalty zones for high environmental impact. Qualitative information about environmental safety and waste production in conventional chromatography and green spectrophotometry could be transformed to quantitative

information by applying a standardized software assessment tool. This is clearly illustrated with side-by-side analytical wheels presented in Figure 3, showing the different penalty zones for each methodology. It is important to emphasize that this represents a theoretical, hypothetical greenness assessment based on published method parameters rather than novel empirical measurements.

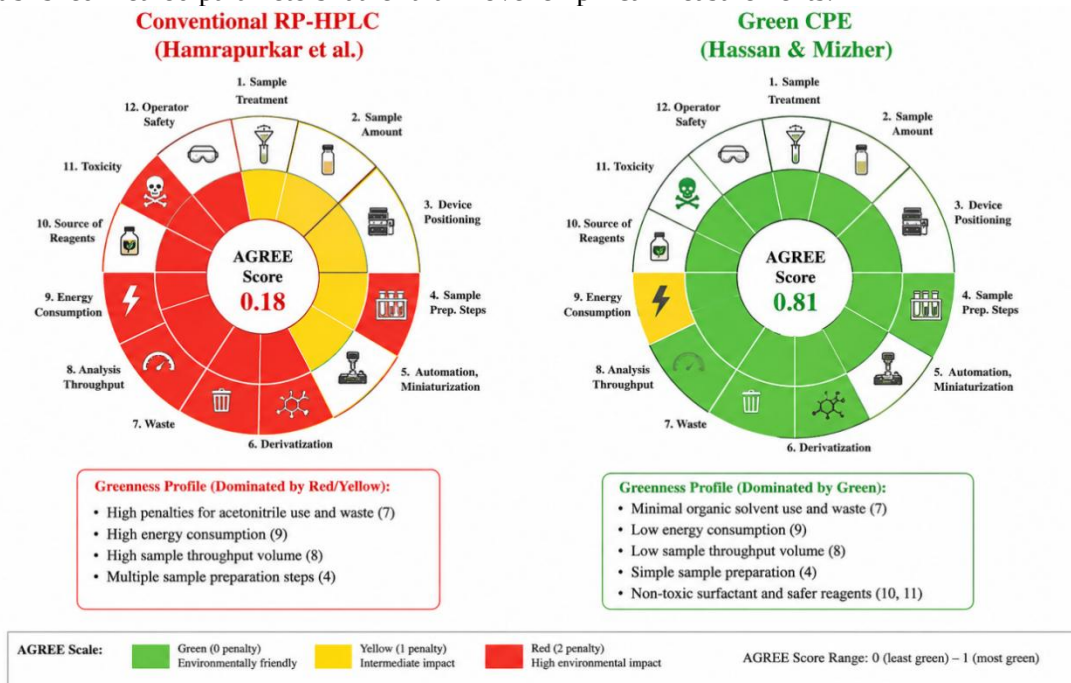


Figure 3: Comparative AGREE Metric Pictograms for Conventional vs. Green Analytical Procedures

In contrast, the spectrophotometric cloud point extraction (CPE) method proposed by Hassan and Mizher aligns exceptionally well with GAC requirements. This method avoids using toxic organic mobile phases and involves phase separation with an aqueous surfactant system and subsequent spectrophotometric detection. Consequently, this technique significantly mitigates workplace hazards, reduces toxic waste generation to near zero, and consumes substantially less operational energy compared to high-pressure chromatographic systems.

This approach would show a high percentage of 'green' zones in a theoretical assessment, as it has an excellent environmental and safety profile. This theoretical comparison highlights an important point of this review: although the traditional RP-HPLC methods have proven to be very good in terms of resolution and stability indicating ability, these methods have a significant environmental impact. The shift to rigorously developed green technologies, like CPE coupled spectrophotometry, ensures analytical validity in compliance with modern ecological and safety guidelines. To clarify the theoretical greenness assessment, Table 3. outlines the specific scores assigned to each of the 12 AGREE criteria, demonstrating how the final numerical scores were calculated.

Table 3: Detailed AGREE Metric Scores (0-1 Scale)

AGREE Principle	RP-HPLC (Hamrapurkar et al.)	Green CPE (Hassan & Mizher)
Sample Treatment	0.4	0.9
Sample Amount	0.6	0.8
Device Positioning	0.0	0.0
Waste Generation	0.0	0.8
Energy Consumption	0.1	0.9
Toxicity of Reagents	0.0	0.9
Final AGREE Score	0.18	0.81

3.6. Chronological Evolution of Analytical Methods

The quantification of cefdinir has developed a lot in the past few years, starting from initial method development to the present application of principles of Green Analytical Chemistry (GAC). The first studies were mainly aimed at the development of reliable spectrophotometric and RP-HPLC procedures, including the main analytical parameters, namely accuracy, precision and stability indicating power. During the last twenty years methodological developments have become ever more focused on environmental sustainability. This change is part of the wider trend in the pharmaceutical industry with a greater adoption of sustainable quality control practices, such as the reduction in the use of hazardous solvents, minimization of waste generation, as well as the use of sophisticated, environmentally-friendly validation protocols. This research landscape is described in chronological order in Table 4.

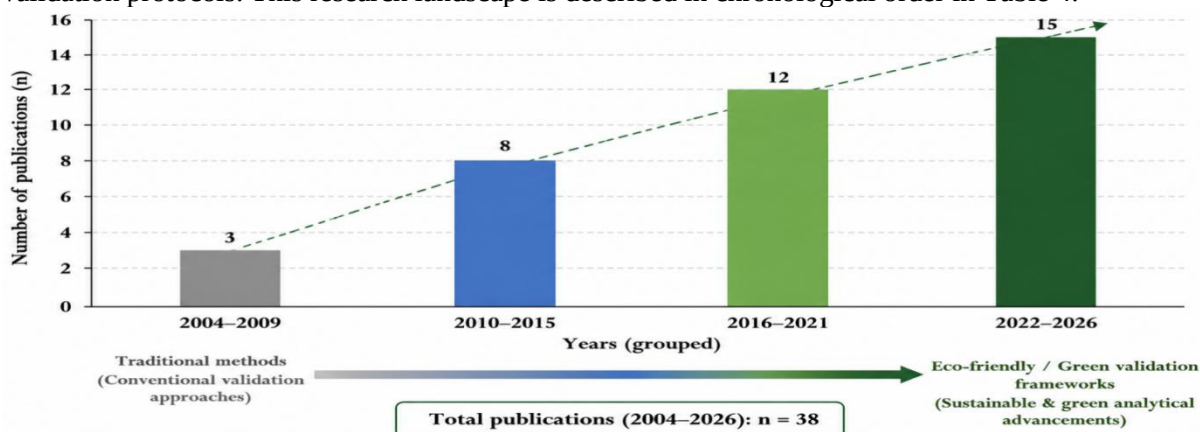


Figure 4: Chronological Publication Trend (2004–2026)

Table 4: Chronological Evolution of Cefdinir Analytical Methods

Year Range	Research Direction	Description
2004–2006	Foundational Analytical Methods	Early research developed basic spectrophotometric and RP-HPLC methods for cefdinir determination, focusing on simplicity, linearity, and reproducibility. These studies established calibration ranges, detection limits, and basic validation parameters for routine quality control.
2008–2011	Stability-Indicating Methods	Emphasis shifted to stability-indicating RP-HPLC methods and derivative spectrophotometry. Forced degradation studies and comprehensive validation according to ICH guidelines became standard to ensure method specificity and robustness under stress conditions.
2012–2014	Enhanced Chromatography and Derivatization	Development of rapid, sensitive chromatographic methods using novel columns and mobile phases emerged, alongside advanced spectrophotometric approaches involving reagent derivatization to improve specificity and sensitivity.
2015–2016	Introduction of GAC Principles	The adoption of green analytical chemistry began with critical reviews on reducing solvent usage and waste. Studies explored eco-friendly sample preparation and chromatographic modifications to minimize environmental impact.
2018–2019	Rapid UPLC and Quality Control Innovations	Focus expanded to ultra-performance liquid chromatography (UPLC) for faster, more sensitive quantification, coupled with quality control enhancements like Lean Six Sigma and electronic tongue analysis for sensory-chemical correlation.
2020–2021	Advanced Spectrofluorimetry and Green Extraction	Novel spectrofluorimetric techniques targeting degradation products and cloud point extraction methods were developed, offering environmentally considerate alternatives with lower solvent consumption.
2024–2026	Comprehensive Green Methods and Regulatory Integration	Recent literature focuses heavily on solvent replacement, method miniaturization, Quality by Design (QbD) approaches, and mature, sustainable stability-indicating validations reflecting strict regulatory compliance.

3.7. Agreements and Divergences Across Studies

The published literature evidenced a general consensus on the importance of GAC in the development of sustainable approaches to quantification of cefdinir, but there were some differences in the practical implementation of the principles. The majority of studies agree that it is important to reduce hazardous solvents and follow ICH validation guidelines carefully. However, there are differences of opinion about

how "green" the analytical performance can be achieved (Prajapati, 2026). The main points of consensus and conflict among the literature are summarized in Table 5 with suggested explanations for these methodological differences. Differences arise from matrix complexity and degradation conditions. RP-HPLC effectively resolves overlapping degradation products in complex stressed matrices, whereas conventional spectrophotometry suffers from spectral overlap unless strictly selective derivatization is applied.

Table 5: Agreements and Divergences Across Reviewed Studies

Comparison Criterion	Studies in Agreement	Studies in Divergence	Potential Explanations
Emphasis on GAC Principles	Consensus that GAC is essential for reducing environmental impact, focusing on waste reduction and miniaturization (Mohamed and Hassouna, 2022; Nanda <i>et al.</i> , 2024; Prajapati, 2026)	Divergence in practical integration; older studies focus less on greenness and more on basic efficacy (Mehta <i>et al.</i> , 2005; Sanli <i>et al.</i> , 2011).	Variations due to publication year and the shifting paradigm toward sustainability over time.
Solvent Systems and Sample Prep	Agreement that benign solvents (water, ethanol, DES) and automated prep (SPE, SPME) are preferred (Ting-ting <i>et al.</i> , 2016; Baria, 2026)	Some methods still rely heavily on toxic acetonitrile/methanol mixtures for chromatographic efficacy (Ya-ting, 2005; Tshilumba <i>et al.</i> , 2019).	The trade-off between optimal chromatographic resolution and solvent toxicity limits immediate green adoption.
Validation and Regulatory Compliance	Strong consensus on validating for specificity, accuracy, precision, LOD, LOQ, and robustness per ICH guidelines (Hamrapurkar <i>et al.</i> , 2011; Mrunal, 2026).	Divergence in using advanced paradigms like Quality by Design (QbD) versus simpler, traditional validation approaches (Kasar <i>et al.</i> , 2025).	Differences reflect technological progression, available expertise, and specific regulatory submission goals.
Spectrophotometry vs. RP-HPLC	Agreement that RP-HPLC offers superior selectivity/robustness, while spectrophotometry is cost-effective and rapid (Hashem <i>et al.</i> , 2012; Mahmood <i>et al.</i> , 2023)	Divergence on whether spectrophotometry can replace RP-HPLC in complex forced degradation studies (Abdel-Aziz <i>et al.</i> , 2014; Boltia <i>et al.</i> , 2021).	Differences arise from the study's analytical goals (routine QC vs. complex impurity profiling).
Chromatographic Innovations	Recent studies emphasize UPLC, monolithic	Earlier studies rely on conventional RP-HPLC	Variations due to institutional

Comparison Criterion	Studies in Agreement	Studies in Divergence	Potential Explanations
	columns, and supercritical fluids to enhance greenness (Shaaban, 2016; (Ponnekanti and Sundararajan, 2018).	without advanced miniaturization (Nirupa and Tripathi, 2015).	investment, instrumentation availability, and timing of the research.

3.8. Theoretical and Practical Implications

3.8.1. Theoretical Implications

The development of two green spectrophotometric and RP-HPLC methods for the quantification of cefdinir, supports the ongoing shift in the trend towards Green Analytical Chemistry. The results obtained support the theoretical framework of using "green solvents" and "green miniaturization" techniques, which can achieve the same or better analytical performance with much lower impacts on the environment (MOHAMED & HASSOUNA, 2022); (Prajapati, 2026). Moreover, the validation of the stability-indicating RP-HPLC methods by ICH guidelines prove that successful pharmaceutical quality control can be accomplished even with the green chemistry approach (Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011); (Mrunal, Ajaykumar, & Mitali, 2026).

Also in the literature, there are theoretical trade-offs between method simplicity, sensitivity and environmental impact. In fact, spectrophotometric techniques that leverage innovative derivatization and/or hydrotropic solvents offer theoretical alternatives to chromatographic methods that are more labor intensive (Susmitha & Gireesh Kumar, 2020); (Mahmood, Sallal, Al-Janabi, & Luaibi, 2023). Lastly, the application of QbD and DoE, as examples of advanced quality principles, in green method development can help create systematic, data-driven approaches that optimize method robustness while also meeting regulatory standards (Tanpure, Bahgat, Kardile, Shete, & Karne, 2025).

3.8.2. Practical Implications

On a practical level, green approaches provide the pharmaceutical industry with viable strategies for cutting down on expenses, waste, and the use of harmful solvents while remaining compliant with regulatory requirements (Mahmood, Sallal, Al-Janabi, & Luaibi, 2023). The validated green analytical methods enable faster and cost-effective routine QC, which can be readily scaled to various dosage forms (Ravisankar, DevalaRao, & KrishnaChaitanya, 2013). In resource-limited environments, hydrotropic agents and cloud point extraction offer highly accessible and non-toxic alternatives for reliable analysis of cefdinir, which are non-toxic. Furthermore, such results can be used by regulatory agencies to include GAC variables in official pharmacopeial guidelines, thereby fostering a nationwide shift toward sustainable practices (Anwar, Amreen, & Parthiban, 2025).

3.8.3. Economic Feasibility and Cost Assessment

Beyond environmental sustainability, transitioning to GAC methodologies presents substantial economic advantages. Traditional RP-HPLC methods incur continuous high costs due to the consumption of HPLC-grade toxic solvents (e.g., acetonitrile) and the expensive disposal of hazardous waste. Conversely, green spectrophotometric methods utilizing aqueous systems or deep eutectic solvents (DES) significantly lower both initial reagent costs and subsequent waste management expenses, offering a highly cost-effective solution for routine quality control in resource-limited settings. While specific cost metrics vary globally, transitioning to green methods structurally reduces operational expenditure primarily by eliminating premium hazardous waste disposal fees associated with acetonitrile and methanol.

3.9. Limitations of the Current Literature

Despite the developments in GAC methodologies, the existing literature is characterized with several methodological restrictions that have implications for the generalizability of the results. A major concern

is that many so-called “green” practices still use traditional toxic solvents, which is counter to the sustainability objectives. The most common limitations found in the studies reviewed are listed in Table 6. Current green methodologies predominantly focus on pharmaceutical formulations, largely neglecting complex biological matrices (e.g., plasma, urine). Addressing matrix effects via green solid-phase extraction remains a critical frontier for clinical bioanalysis.

Table 6: Methodological Limitations in the Reviewed Literature

Area of Limitation	Description of Limitation	Cited Papers
Limited Focus on Cefdinir	Many GAC reviews focus broadly on analytical chemistry without specifically addressing cefdinir, limiting direct applicability.	(Prajapati, 2026); (Baria, 2026); (Nanda, Chopra, Kumari, Narang, & Bhatia, 2024); (Shaaban, 2016)[3,7]
Insufficient Green Validation	Several papers emphasize method development but lack comprehensive validation data (e.g., robustness) under strict green constraints.	(Sanli, Sanli, Sızır, Gumustas, & Ozkan, 2011);; Ravisankar <i>et al.</i> , 2013)
Predominance of Conventional Solvents	Despite GAC goals, many methods still rely heavily on toxic organic solvents like acetonitrile and methanol.	(Tshilumba, et al., 2019); (Hamrapurkar, Patil, Phale, Gandhi, & Pawar, 2011); (Ya-ting, 2005)
Lack of Comprehensive Stability Studies	Some literature claiming stability-indicating capabilities lacks the extensive forced degradation analysis critical for drug safety.	(Mrunal, Ajaykumar, & Mitali, 2026); (Kasa, Aher, & Bachhav, 2025)
Limited Application to Complex Matrices	Most methods are validated on pure drugs or simple formulations, ignoring the complexities of biological samples or complex matrices.	(Sanli, Sanli, Sızır, Gumustas, & Ozkan, 2011); (Reçber, Özkan, Nemutlu, & Kır , 2021)
Scarcity of Cost/Feasibility Analysis	Few studies evaluate the economic feasibility of green methods, limiting their practical adoption in resource-limited settings.	(Tshilumba, et al., 2019); (Susmitha & Gireesh Kumar, 2020)

3.10. Identified Gaps and Future Research Directions

To advance the field of sustainable pharmaceutical analysis, future research must address the identified methodological gaps. High-priority areas include the complete substitution of toxic solvents with green alternatives tailored specifically for cefdinir, and the development of accessible methods for low-resource laboratories. Table 7 prioritizes these future research directions.

Table 7: Identified Gaps and Prioritized Future Research Directions

Gap Area	Future Research Directions	Justification	Priority
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Gap Area	Future Research Directions	Justification	Priority
Limited integration of green solvents in RP-HPLC	Develop and validate methods using ethanol, supercritical fluids, or natural DES specifically for cefdinir quantification.	Transitioning away from acetonitrile/methanol is critical to aligning RP-HPLC with true GAC principles.	High
Insufficient advanced green sample prep	Investigate SPME, DLLME, and SFE techniques for cefdinir to minimize solvent use and waste.	These techniques drastically reduce solvent consumption but have not been systematically applied to cefdinir.	High
Lack of comprehensive stability-indicating green methods	Design green stability-indicating methods that integrate miniaturized instrumentation and ICH-compliant validations.	Stability methods are critical for QC; embedding green principles here maximizes industry sustainability.	High
Cost-effective methods for resource-limited settings	Design simple, low-cost, green spectrophotometric/chromatographic methods requiring minimal infrastructure.	Accessibility is crucial to combat counterfeit drugs globally without relying on expensive toxic reagents.	High
Scarcity of formal greenness assessments	Incorporate quantitative metrics like the Analytical Eco-Scale or GAPI during method development.	Objective metrics enable transparent, standardized benchmarking of environmental performance.	Medium
Underexplored use of novel detection technologies	Explore the integration of electronic tongues, spectrofluorimetry, and AI-driven optimizations.	Enhances sensitivity and reduces reagent use, modernizing the analytical workflow.	Medium

4. Conclusions and Recommendations

This systematic review benchmarked 36 peer-reviewed articles, highlighting a critical methodological paradigm shift in cefdinir quantification toward GAC principles. While RP-HPLC remains the regulatory gold standard for stability-indicating assays due to its high specificity, its reliance on toxic solvents conflicts with modern sustainability goals. Conversely, spectrophotometric and cloud point extraction (CPE) methods provide highly eco-friendly, cost-effective alternatives, though they demand rigorous selective derivatization to handle complex degradation matrices.

To successfully reconcile analytical performance with GAC principles, future research must systematically prioritize the replacement of hazardous mobile phases with sustainable alternatives, such as natural deep eutectic solvents (DES), bio-ethanol, or supercritical fluids. Routine quality control should adopt miniaturized sample preparation strategies (e.g., DLLME) to drastically reduce waste. Finally, we strongly recommend integrating formal quantitative green metrics, such as the AGREE tool or the

Analytical Eco-Scale, directly into ICH validation workflows to provide a sustainable, universally accessible framework for pharmaceutical quality assurance.

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References

1. Gouda, A. A., Hashem, H., & Hassan, W. (2012, April 28). Spectrophotometric methods for determination of cefdinir in pharmaceutical formulations via derivatization with 1,2-naphthoquinone-4-sulfonate and 4-chloro-7-nitrobenzo-2-oxa-1, 3-diazole. *Drug Testing and Analysis*, pp. 991-1000.
2. Abdel-Aziz, O., Farouk, M., Nagi, R., & Abdel-Fattah, L. (2014, January). Simple spectrophotometric and hptlc-densitometric methods for determination of cefdinir in bulk powder and pharmaceuticals, and in presence of its hydrolytic degradation products. *journal of applied pharmaceutical science*, pp. 129-136.
3. Al-Badr, A. A., & Alasseiri, F. A. (2014). Chapter two – cefdinir. *Profiles of Drug Substances, Excipients and Related Methodology*, pp. 41-112.
4. Baria, P. D. (2026, January 10). Advances in green analytical chemistry for pharmaceuticals. *International Journal of Pharmaceutical Sciences*.
5. Bas, E., Gokhan , M., Palabiyik, s. M., & Özdem, S. (2013, January). First derivative spectrophotometric determination of cefixime and cefdinir in pharmaceutical preparations. *Turkish Journal of Pharmaceutical Sciences* , pp. 321-328.
6. Boltia, S. A., Algmaal, S. E., Mostafa, N. M., & Saharty , Y. S. (2021, May 6). Development and validation of a spectrofluorimetric method for the determination of cefdinir via its degradation products. *Journal of Applied Spectroscopy*, pp. 424-432.
7. Hadad, G. M., Emara , S., & Mahmoud , W. M. (2009, November 5). Optimization and validation of an lc method for the determination of cefdinir in dosage form and human urine. *Chromatographia*., pp. 1593-1598.
8. Hamrapurkar, P. D., Patil, P., Phale, M., Gandhi, M., & Pawar, S. (2011, Jan). A developed and validated stability-indicating reverse-phase high performance liquid chromatographic method for determination of cefdinir in the presence of its degradation products as per international conference on harmonization guidelines. *Pubmed*, pp. 15-20.
9. Hashem, H., Gouda, A. A., & Hassan, W. (2012, Jul 3). Development and validation of a rapid stability indicating chromatographic determination of cefdinir in bulk powder and dosage form using monolithic stationary phase. *Journal of Liquid Chromatography and Related Technologies*., pp. 1638-1648.
10. Khader, M. K., & Sarsam, L. A. (2025). Determination of phenylephrine hydrochloride using azo-coupling reaction and cloud point extraction. *Methods and Objects of Chemical Analysis*, pp. 300–310.
11. Mahmood, A. K., Sallal, T., Al-Janabi, K. W., & Luaibi, H. M. (2023, July). Development of a spectrophotometric analytical approach for the measurement of cefdinir in various pharmaceuticals. *Journal of advanced pharmaceutical technology and research*, pp. 263-268.
12. Mehta, T., Subbaiah, G., & Pundarikakshudu, K. (2005, November). Determination of cefdinir by a stability-indicating liquid chromatographic method. *Journal of AOAC International*, pp. 1661-1665.

13. Mohamed, H. M. (2015, March). Green, environment-friendly, analytical tools give insights in pharmaceuticals and cosmetics analysis. *Trends in Analytical Chemistry*, pp. 176-192.
14. MOHAMED, M. A., & HASSOUNA, M. E.-K. (2022). Stability indicating RP-HPLC and spectrophotometric methods for simultaneous estimation of sodium benzoate and cefdinir in the presence of its degradation products: Application to blank subtraction method. *Turkish Journal of Pharmaceutical Sciences*, pp. 530-542.
15. Mrunal, V., Ajaykumar, C., & Mitali, D. (2026 , January 19). A comprehensive review on rp-hplc method development, validation, and forced degradation studies according to ich guidelines. *International Journal of Pharmaceutical Sciences*.
16. Nanda, B. P., Chopra, A., Kumari, Y., Narang, R. K., & Bhatia, R. (2024, January 12). A comprehensive exploration of diverse green analytical techniques and their influence in different analytical fields. *Journal of Separation Science*.
17. Narala, S. R., & Saraswathi, K. (2011, Year). Application of oxidants to the spectrophotometric determination of cephalosporins (cefditoren pivoxil and cefdinir) in formulations. *Asian Journal of Research in Chemistry*, pp. 270-271.
18. Nirupa, G., & Tripathi, U. M. (2015). Analytical method development and validation on liquid chromatography for determination of the drug cefdinir by using tinidazole as an internal standard in bulk and pharmaceutical dosage forms. *American Chemical Science Journal*, pp. 285-296.
19. Patil, S. S., & Kasture, P. V. (2008). Spectrophotometric method for estimation of cefdinir from capsule formulations . *The Indian pharmacist*, pp. 110-112.
20. Ponnekanti, K., & Sundararajan, R. (2018, January). Development and validation of new rp-uplc method for the determination of cefdinir in bulk and dosage form. *International Journal of Pharmacy and Pharmaceutical Sciences*, pp. 178-184.
21. Ravisankar, P., DevalaRao, G., & KrishnaChaitanya, M. (2013). Development and validation of rp-hplc method for the determination of cefdinir in bulk and capsule dosage form. *SMANTLC SCHOLAR*.
22. Reçber, T., Özkan, E., Nemutlu, E., & Kır , S. (2021, February 3). Simultaneous determination of cefixime, cefdinir and clavulanic acid by high performance liquid chromatography. *Pharmaceutical Chemistry Journal*, pp. 1186-1191.
23. Shaaban, H. (2016, June 27). New insights into liquid chromatography for more eco-friendly analysis of pharmaceuticals . *Analytical and Bioanalytical Chemistry*, pp. 6929-6944.
24. Suganthi, A., Ravi, T. K., & Pattasseril, M. B. (2004, January). Rp-hplc estimation of cefdinir in capsules. *Indian Journal of Pharmaceutical Sciences*, pp. 248-249.
25. Tanpure, H., Bahgat, V., Kardile, D., Shete, R., & Karne, M. M. (2025, May 27). Revolutionizing stability-indicating analysis: Advanced RP-HPLC strategies for pharmaceutical excellence. *International Journal of Pharmaceutical Sciences*, pp. 4466–4489.
26. Tshilumba, P. M., Muindu, M., Kasongo, M., Mujinga, G. K., Zabakani, M., i Kasongo, J. K., et al. (2019). Substandard/falsification antibacterial agents: A systematic review of liquid chromatographic and spectrophotometric methods for their detection. *American Journal of Analytical Chemistry*, pp. 348-365.
27. Abu-Khalaf, N., Zaid , A. N., Jaradat , N., Alkilany , A. M., Abulateefeh , S. R., Ramahi , R. A., et al. (2019, May 2). Identification of substandard drug products using electronic tongue: Cefdinir suspension as a pilot example.. *Drug Design Development and Therapy*, pp. 3249-3258.
28. Anwar, D., Amreen, H., & Parthiban, C. (2025, September 18). Clean Chemistry: Sustainable Approaches to Pharmaceutical Analysis. *International Journal of Pharmaceutical Sciences*.
29. Kasa, P., Aher, S., & Bachhav, R. (2025, August 13). Development and validation of stability-indicating RP-HPLC methods for pharmaceutical drugs: A comprehensive review. *International Journal of Pharmaceutical Sciences*, pp. 1361–1372.

30. PB Shah و Kilambi Pundarikakshudu) .January , 2006 .(Difference spectroscopic and reverse phase hplc methods for the estimation of cefdinir in pharmaceutical dosage forms .*Indian Journal of Pharmaceutical Sciences* 90_91
31. Prajapati, D. (2026, January 3). Green analytical chemistry in pharmaceutical and environmental analysis: A review. *International Journal of Pharmaceutical Sciences*, pp. 242–252.
32. Sanli, N., Sanli, S., Sızır, U., Gumustas, M., & Ozkan, S. A. (2011, April 6). Determination of pk a values of cefdinir and cefixime by lc and spectrophotometric methods and their analysis in pharmaceutical dosage forms. *Chromatographia* . pp. 1171-1176.
33. Singh, B. K., Parwate, D. V., Srivastava, S., & Shukla, S. K. (2010, Sept 27). Selective and non-extractive spectrophotometric determination of cefdinir in formulations based on donor-acceptor complex formation. *SciELO*, pp. 1471-1475.
34. Susmitha, A., & Gireesh Kumar, E. (2020). Hydrotropy – a solubility enhancement tool for the estimation of cefdinir in its suspension dosage form by uvspectroscopy. *International Journal of ChemTech Research*,, pp. 232-241.
35. Ting-ting, Y., Feng-quan, Y., Rong-qing, J., & WANG, Yu, W. (2015, January 1). Advances in green analytical techniques and their applications in pharmaceutical analysis. . *Editorial Office of Journal of Pharmaceutical Analysis*, pp. 2070-2075.
36. Ya-ting, Y. (2005, Jan 1). Determination of the content of cefdinir capsule by hplc. *West China Journal of Pharmaceutical Sciences* null.