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Review Article

Review of Analytical Techniques for the Analysis of Cephalosporins and Fluoroquinolones

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Abstract

This review surveys cephalosporins and fluoroquinolones analytical methodologies in biological and environmental samples. Since both humans and animals have been using antibiotics carelessly, the amount of antibiotics in wastewater and animal products has increased. The presence of cephalosporins and fluoroquinolones, the most commonly used antibiotics, in aqueous matrices can result in treatment failure. For the sake of both human health and environmental protection, these levels must be established. To improve stability and evaluate the possible risk of impurity products, more details regarding the drug's structure and degradation are required. A more detailed knowledge of degradation processes is necessary to ensure the stability of prescription medications. The current study provides an overview of the behaviors, features, and analytical techniques utilized to identify cephalosporins and fluoroquinolones. Data collection was done by searching scientific publications in the international literature. Reversed-phase high-performance liquid chromatography with UV detection and precipitation or extraction cleanup procedures are the mainstays of cephalosporins and fluoroquinolones techniques for biological and environmental samples. Although high-performance liquid chromatography is used in the majority of the methods, ultraviolet, infrared spectroscopy, and spectrometry techniques have also been used. There was a

discussion emphasizing the necessity of creating new ecological techniques that use less hazardous solvents, analyze data quickly, and reduce sample size.

Keywords: Analytical techniques, Antibiotics, Cephalosporins, Fluoroquinolones, Review

1. Introduction

Medical care wastewater, which is mostly generated by healthcare facilities, is a major source of dangerous materials that can have a serious negative impact on the environment and public health [1–5]. The most effective drugs are antibiotics, which have been used to either eradicate or stop the growth of bacteria [6]. One of the ways antibiotics function is by stopping the synthesis of nucleic acids and peptidoglycans, which stops cell division [7]. Antibiotics have been detected in drinking water, wastewater, surface and groundwater, and a variety of aquatic habitats [8–10]. Wastewater treatment plant releases are one of the most important sources of antibiotics reaching environmental waters, as they have a direct impact on the receiving water body [11]. The relationship between antibiotic use and human health begins with normal antibiotic use and then progresses to contamination of food and drinking water [12].

An overview of the characteristics, features, and analytical methods used to determine ceftriaxone sodium is given in the current study. Both official compendia and scientific publications in the international literature were searched to gather data. The significance of creating efficient and trustworthy analytical techniques for quality control. The majority of the techniques discovered make use of high-performance liquid chromatography, but there have also been approaches that employ ultraviolet, infrared, absorption spectroscopy, and spectrofluorimetry techniques. The necessity of creating new ecological techniques with less hazardous solvents, quick analysis, and sample miniaturization was discussed [13].

More information about the drug's breakdown structure is needed to increase stability and assess the potential risk of impurity products [14]. The ease of use and low cost of spectrophotometric techniques make them useful for natural sample identification [15–18]. LC combined with MS/MS is one of the most popular techniques in recent years because it provides excellent stability and specificity along with significant potential for determining identity and quantification [19,20].

2. Literature review and analytical methods

Remaining antibiotics in a range of matrices, such as food, agricultural products, animal products, and portable water, must be identified. Antibiotics can now be found in soil, surface water, and wastewater, using a variety of detection methods. The two categories of detection techniques used to identify antibiotics are quantitative or confirmatory assays and qualitative or rapid screening procedures.

According to a review of the literature, cephalosporins have been identified in a variety of matrices using capillary electrophoresis (CE), HPTLC, UPLC, HPLC, and UV spectrophotometry during the period 2004 to 2024. Furthermore, the four medications being investigated have been identified using official pharmacopeial chromatographic techniques. Analytical Quality by Design functions to create a thorough framework for method variables, such as flow rate, pH, column temperature, and mobile phase composition. The chromatographic method ensures efficient separation and quantification of analytes in pharmaceutical formulations [21].

The creation of analytical instruments and procedures that lessen or eliminate the production and use of hazardous materials is the sole focus of the "green analytical chemistry" (GAC) subfield of green chemistry. Maintaining or enhancing analytical processes while making them more ecologically friendly is the aim. This can be accomplished with smaller sample sizes and reagent volumes, less waste, less energy, safer chemicals and solvents, and fewer derivatization reactions. As a result, GAC and AQbD work together to develop a comprehensive strategy for producing analytical methods that are economical, environmentally friendly, and scientifically sound32. The importance of this cooperation has grown in the analytical labs of today. Another crucial factor to take into account is the developed method's analytical viability [22].

The investigation by Alqahtani and co-authors has developed an HPLC method for the identification of four cephalosporin pharmaceuticals in both their formulations and water samples. Three chromatographic parameters were optimized using a Box-Behnken experimental design: buffer pH, flow rate, and mobile phase composition. Additionally, the method's accuracy, precision, specificity, and robustness were fully validated by ICH guidelines. The Analytical GREEnness tool was also used to assess the greenness profile of the optimized HPLC method. With an AGREE score of 0.75, it was determined to be an environmentally friendly option for routine analysis and quality control of the study. Additionally, demonstrates its significant potential for routine analysis applications and high analytical practicality [22].

Three cephalosporins can be identified in pharmaceutical formulations using a straightforward, accurate, and precise spectrophotometric method. Under ideal circumstances, the study suggests a method for utilizing 1,2-naphthoquinone-4-sulfonic (NQS) to derive cephalosporins. The method has detection limits of 0.12, 0.168, and 0.0465 μg mL^{-1} and is based on Beer's law for cefi, ceph, and cefo. Quality control labs can use this method [23].

In the study by Roopa and Jayanna, a straightforward, precise, and sensitive spectrophotometric technique has been created to analyze four cephalosporins, ceftriaxone, cefatoxime, ceftazidime, and cefepime in bulk and pharmaceutical formulations. In the final measured solution, the calibration graphs are rectilinear in

the concentration ranges of 20–160 μg mL^{-1}, 20–140 μg mL^{-1}, and 24–168 μg mL^{-1}, respectively. Other analytical parameters are assessed, and all ideal conditions are determined. Excipients that are frequently used did not affect the results. Results from statistical analysis show that the approach is accurate and precise [24].

A simple and reliable method was used to determine the presence of eight cephalosporin antibiotics including. The process relies on each drug under study oxidizing using spectrophotometry, whose absorbance changes at 610 nm. Calibration graphs are constructed to ascertain the concentration of the drugs under study. Using the initial rate method, the calibration graphs are linear in the concentration ranges of 5–15 μg mL^{-1} and 5–25 μg mL^{-1}, respectively. Recovery studies are used to verify the findings statistically. The technique has been effectively used to identify the cephalosporins under study in commercial dosage forms [25].

Solid-phase microextraction was used to create a sensitive and efficient technique for identifying six cephalosporins in milk samples. Following extraction and desorption, the analytes were analyzed using HPLC-PDA. N, N-dimethyl formamide was used to ultrasonically disperse graphene oxide, which was then immobilized in hollow fiber pores. High extraction efficiency, good linear ranges, low limits of determination, and high recoveries were the outcomes of optimizing parameters such as sample solution pH, solvent type, and extraction time. The results demonstrated that adding cephalosporins to dairy products using the GO-HF-SPME approach would be feasible [26].

In a study by Sahebi and co-authors, in conjunction with LC-MS/MS, nine cephalosporins were extracted using Fe3O4@[DABCO-DHP][Cl] nanoparticles, a novel adsorbent. The univariate and multivariate optimization techniques were used to examine the experimental parameters affecting the extraction efficiency. The analysis method was developed under optimal conditions. Correlation coefficients of 0.9963-0.9998 and a linear range of 0.1-400 $\mu g.kg^{-1}$ were found. For all analytes and samples, the suggested method's detection limits fell between 0.02-1.18 $\mu g.kg^{-1}$. The suggested technique for identifying cephalosporins in milk samples was effective, sensitive, and useful [27].

An HPLC method was developed to separate seven cephalosporins from human plasma and amniotic fluid, with three stages of optimization after preliminary experiments. To determine the method's fundamental analytical requirements, preliminary experiments were conducted. A fractional factorial design was then employed in the screening experiment to reduce the number of parameters by removing those that had negligible effects on responses. A full factorial design was used to further optimize the parameters that had a significant impact. After examining two responses, the experimental conditions (XTerra C18 column with a pH of 3.2, 18% MeOH, 0.85 mL min^{-1} flow rate, and 32°C column temperature)

under which the system produced the desired results were determined. Using MeOH, gradient elution was used. Using methanol, gradient elution was used. Samples of plasma and amniotic fluid were prepared using a straightforward and effective solid-phase extraction method [28].

In the study by Yu and co-authors, an analysis of the distribution of cephalosporins in wastewater that produces them was conducted. SPE-UPLC-MS/MS were the foundations of a quick and accurate cephalosporin detection method. The recoveries for all of the analytes in the cephalosporin-producing wastewater effluent ranged from 73% to 102%. Even though the cephalosporins had high removal efficiencies (78.8–99.7%), the examined C-WWTP discharged up to 1.9 kg of cephalosporins daily. High temperatures and light accelerated the tested cephalosporins' rates of degradation [29].

Cephalosporin antibiotic traces in water samples can be found with sensitivity using UV-diode array detection. For offline preconcentration and clean-up, the solid-phase extraction (SPE) method is combined with large-volume sample stacking (LVSS). High sensitivity, accuracy, and satisfactory recoveries of these compounds in water samples are made possible by the SPE-LVSS-CZE-DAD process [30].

Wang and co-authors have created a quick and accurate technique for detecting cephalosporin antibiotics in environmental waters using capillary electrochromatography. In environmental water samples, the cephalosporin formulations cefapirin (CP), ceftiofur (EFT), and cefixime (CFM) were simultaneously identified using DAD detection and an 8 kV voltage in a pH 5.0 buffer. Typically, the limits of detection are 0.1 µg/mL. When the technique was used to analyze cephalosporins in Kunming Lake water samples that had been spiked, recoveries ranging from 88 to 106% were obtained [31].

An automated enantioselective method for determining the environmental significance of fluoroquinolones in water samples has been developed by Mejías and co-authors. Online SPE, chiral LC-MS/MS served as the foundation for the analytical approach. In just 14 minutes, the analysis was completed. The technique's suitability for use with influent wastewater, effluent, and surface water was confirmed. The range of accuracy values for surface water and wastewater was 73.4 to 119 percent and 61.4 to 122%, respectively. The technique showed enantioselective conversion of LEV and a precision of less than 13.6% for all compounds in surface water and wastewater, with quantification limits ranging from 0.2 to 50 ng L^{-1} [32].

A novel, straightforward, precise, and accurate extractive spectrophotometric method for identifying fluoroquinolones (FQs), including ciprofloxacin (CFX) in pharmaceutical formulations, was presented in the study by Nguyen and co-authors. CFX was found to have a very low LOD of 0.084 µg mL^{-1}. According to Job's method of continuous variation, the complexes formed between FQs and BTB had a

+e stoichiometry of 1:1. There was no evidence of common excipients interfering with pharmaceutical formulations. The FQs in a few pharmaceutical products have been successfully ascertained using the suggested method. The suggested approach is appropriate for quantifying FQs in pharmaceutical formulations [33].

A sensitive online SPE methodology using selective molecularly imprinted polymer and fluorescent detection (HPLC-FLD) was developed for low ng L^{-1} fluoroquinolone detection in water. Under ideal circumstances, 7 FQs showed good linearity, ranging from 0.7 to 666 ng L^{-1}, attaining excellent precision and low ng L^{-1} (LOD). For every Fluoroquinolone tested, recoveries varied from 54 to 118% (RSD < 17%). The technique was used to find the Fluoroquinolones in river water. These outcomes showed how sensitive and selective the developed method is [34].

A sensitive salting-out-assisted dispersive liquid-liquid microextraction method was developed to identify fluoroquinolones in milk, honey, and water samples. Sample pH, volume, and other factors influencing extraction efficiency were all examined. Fluoroquinolones showed good linearity in the range of 0.020-3.200 µg mL^{-1} and 0.030-4.800 µg mL^{-1}. The recoveries fell between 95.0 and 104.9%, 90.1 and 110.2%, and 87.8 and 114.1%, respectively. All of the reproducibility relative standard deviations were less than 7.6%. The enrichment factors for analytes were found to be between 531 and 858 times under optimal conditions. The suggested technique was effectively used to identify fluoroquinolones in samples of milk, honey, and water [35].

An analytical technique for the measurement of three fluoroquinolones in soil matrix: ofloxacin, norfloxacin, and ciprofloxacin was created. Microwave-assisted extraction (MAE) and SPE were used in the proposed method to purify the samples, and an HPLC detector was used to analyze the pre-concentrated samples. The test compounds were extracted in this study using a variety of organic solvents. For all test compounds, the method demonstrated good linearity over concentrations ranging from 1 to 300 ng g^{-1}, with correlation coefficients (r2 > 0.998). Additionally, good recoveries ranging from 89 to 99 percent were obtained for the test compounds. The LOD and LOQ limits varied from 0.9 to 2.7 ng g^{-1}, and the RSD was less than 7% [36].

The efficient in-syringe solid phase extraction was achieved by using economical and environmentally friendly carboxy-terminated plant fibers as adsorbents. Citric acid-modified cattail demonstrated superior adsorption capacity for fluoroquinolones when compared to carboxy-terminated corncob and cotton. After the extraction conditions were optimized, a good extraction efficiency of 71.3% to 80.9% was attained. Fluoroquinolones in environmental water samples were analyzed using IS-SPE in conjunction with UPLC and a photodiode array detector, which was based on carboxylated cattail. Good accuracy with recoveries of 83.8% to 111.7% and high sensitivity with a limit of detection of 0.08 to 0.25 mg L^{-1} were

attained. All things considered, the straightforward and environmentally benign modified waste PFs may find use in the efficient extraction and identification of fluoroquinolones in natural waters [37].

To identify the antibiotic residues of ciprofloxacin in environmental waters, a new LC-fluorescence detection technique based on the use of a monolithic column was created. Fluoroquinolones (FQs) were isocratically eluted through an RP-18e column (10064.6 mm) at a flow rate of 2.5 mL/min. An Oasis HLB cartridge was used to extract water samples following acidification and EDTA addition. Correlation coefficients of 0.9974 for ciprofloxacin were determined after linearity was assessed in the range of 0.05 to 1 μg mL^{-1}. The three FQs had a quantification limit of 25 ng L^{-1}. Water samples were successfully analyzed using this technique, and eight water samples contained ciprofloxacin and enrofloxacin residues [38].

The vibrational modes of fluoroquinolones have been measured using vibrational spectroscopy, such as FTIR, which also offers details on the structural variations among its constituent members. The presence of distinct substituents in their parent nucleus has allowed Norfloxacin, Ofloxacin, and Ciprofloxacin to be identified from the interpreted spectral data. Bragg's angle (2θ) was used to scan the drugs from 10˚ to 70˚. All of the fluoroquinolones under study had powder XRD patterns that were distinctive enough to allow for identification. The most straightforward and conclusive methods for identifying fluoroquinolones are FTIR and XRD analyses, which also give a way to qualitatively evaluate pure medications. The current preliminary research serves as the foundation for validating powder XRD and FTIR as reliable official monitoring techniques for fluoroquinolone identification [39].

A sensitive and specific confirmatory technique for LC-MS/MS milk residue analysis of eight cephalosporins and ten quinolones has been developed. Target analytes were separated chromatographically using a Perfectsil ODS-2 (250 × 4 mm, 5 μm) analytical column and gradient elution with a mobile phase consisting of 0.1% w/w TFA in water and 0.1% w/w TFA in ACN. The method was validated to meet European legislation. RSD values were less than 13.7%, and the recovery rates for all antibiotics ranged from 81.7 to 117.9%. All of the compounds under investigation had quantification limits between 2.4 and 15.0 μg kg^{-1} [40].

A novel UV spectrophotometric method was used to quantify three fluoroquinolone antibiotics and ciprofloxacin, using chemometric tools. The method demonstrated satisfactory performance with a mean recovery ranging between 98.18 and 101.83 with %RSD<2. The method also showed ultrasensitive levels for ciprofloxacin, and its greenness and blueness were assessed using the analytical GREEnness metric approach and Blue applicability grade index [41].

Conclusion

The current review offers a modern and innovative, thorough report that summarizes the best available research on the different analytical methods used to detect fluoroquinolones and cephalosporins. The antibiotic helps with research that needs to be quantified analytically and bioanalytically; nevertheless, it's important to support and validate new analytical techniques in green chemistry. Despite the widespread use of spectrometry, high-performance liquid chromatography, and ultraviolet and infrared spectroscopy, new green techniques are required for smaller sample sizes, faster data analysis, and less toxic solvents.

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