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Comprehensive review of chromatographic, hyphenated, and spectrophotometric methods for the determination of loxoprofen sodium

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Loxoprofen sodium, a propionic acid derivative and non-steroidal anti-inflammatory drug (NSAID), is widely prescribed for the management of pain, inflammation, and musculoskeletal disorders. As its therapeutic application expands, robust and precise analytical methods are essential to ensure the quality, safety, and efficacy of loxoprofen sodium in bulk drug substances, pharmaceutical formulations, and biological matrices. In recent years, significant progress has been made in the development and validation of analytical approaches, including UV spectrophotometry, RP-HPLC, HPTLC, and advanced UHPLC techniques. Optimization of chromatographic parameters, such as mobile phase composition, column selection, and detection wavelength, has enhanced sensitivity, resolution, and reproducibility. Method validation, in line with ICH guidelines, routinely evaluates accuracy, precision, linearity, specificity, and robustness to confirm reliability. Stability-indicating methods are particularly important for assessing degradation under stress conditions, providing insight into drug stability and shelf-life. Current analytical trends emphasize green and quality-by-design (QbD) approaches, supporting eco-friendly and efficient method development. Collectively, these analytical advancements establish a comprehensive framework for the routine quality control and research of loxoprofen sodium, reinforcing its clinical relevance and regulatory compliance.

Keywords: Loxoprofen sodium; Chromatographic methods; UV spectrophotometry; Method development; Stability-indicating analysis; RP-HPLC; HPTLC; UHPLC.

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Introduction

Inflammation is a fundamental biological response of the body to harmful stimuli such as infections, tissue injury, or chemical irritants. It serves as a protective mechanism aimed at eliminating the initial cause of damage, removing necrotic cells, and initiating tissue repair. The process involves a complex interplay of immune cells, chemical mediators, and vascular changes that collectively restore homeostasis. While acute inflammation is beneficial and self-limiting, chronic or uncontrolled inflammation is implicated in the progression of many disorders, including arthritis, cardiovascular disease, and certain cancers (1).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely prescribed medications for the management of pain, fever, and inflammatory conditions. Their therapeutic action is primarily achieved through the inhibition of cyclooxygenase (COX) enzymes, which regulate the synthesis of prostaglandins involved in inflammation and pain signaling. Owing to their analgesic, antipyretic, and anti-inflammatory properties, NSAIDs play a central role in both acute and chronic disease management. However, long-term or high-dose use is often associated with gastrointestinal, renal, and cardiovascular adverse effects, underscoring the need for careful patient monitoring and tailored therapy (2).

Chemical structure of Loxoprofen sodium (Figure. 1), which is a propionic acid derivative of the NSAID class, is widely used for managing pain, inflammation, and musculoskeletal disorders (3). Acting as a prodrug, it is rapidly converted in vivo to an active trans-alcohol metabolite that inhibits cyclooxygenase enzymes, thereby reducing prostaglandin synthesis with comparatively lower gastrointestinal irritation than conventional NSAIDs (4).

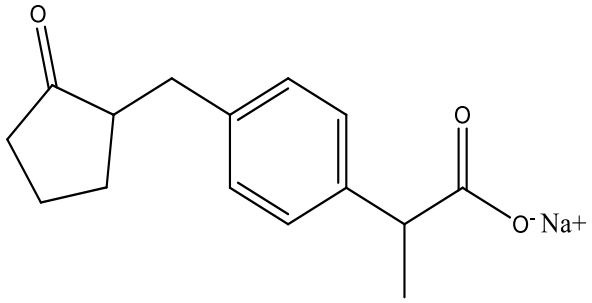

Figure 1. Chemical Structure of Loxoprofen sodium

Analytical methods are vital in current pharmaceutical trends as they ensure accurate drug quality, safety, and regulatory compliance, while also supporting innovation through systematic, risk-based approaches like AQbD (5). To guarantee the quality, therapeutic effectiveness, and safety of Loxoprofen Sodium across different

pharmaceutical formulations, active ingredient, and biological samples, the development of precise and robust analytical methods is indispensable. Method development and validation are ongoing, interlinked processes that involve research and development, quality control, and quality assurance activities. These approaches are fundamental in defining product-specific acceptance limits and in maintaining the consistency and reliability of results (6). Several analytical techniques have been applied for the estimation of Loxoprofen Sodium, such as UV spectroscopy (7, 11), reverse-phase high-performance liquid chromatography (RP-HPLC)(12, 20), high-performance thin-layer chromatography (HPTLC)(21, 33), and some hyphenated techniques like LC-MS (24, 25), each offering distinct benefits and limitations with respect to sensitivity, specificity, rapidity, and cost-efficiency.

Stability-indicating studies on loxoprofen sodium have been reported using UV (7), HPLC (21), HPTLC (21), and LC–MS (25) techniques, demonstrating the ability to quantify the drug in the presence of degradation products and impurities. These methods evaluate its stability under stress conditions, including hydrolytic, oxidative, thermal, and photolytic degradation, ensuring reliable assessment of drug quality and safety.

In spite of the clinical importance and growing number of analytical reports regarding the determination of loxoprofen sodium, there appears to be no specific and exhaustive review consolidating and critically comparing all the published analytical methods for loxoprofen sodium. Although some review articles on analytical methods of similar NSAIDs such as ibuprofen, naproxen, ketoprofen have been published, they either do not address the analysis of loxoprofen sodium or present it partially and focus on only specific techniques. The closest relevant review is a database of retention indices for propionic acid class NSAIDs by Suzuki and Watanabe (2005), which is purely a collection of preliminary screening data without any aspect of systematic review of the method, benchmarking of validation procedures or critical comparison of suitability of different techniques. This paper aims at a comprehensive and dedicated, method-class-wise review and critical comparison covering all possible UV spectrophotometric, RP-HPLC, HPTLC and hyphenated (LC-MS/MS) methods for determination of loxoprofen sodium in a wide variety of matrices.

The main objectives of the present review article are to:

(i) collate and consolidate all the published analytical methods for determination of loxoprofen sodium in bulk drug, drug formulations and biological samples.

(ii) critically and comparatively analyze the performance of the reported methods, i.e., the chromatographic (RP-HPLC, HPTLC), hyphenated (LC-MS/MS) and spectrophotometric (UV direct and indirect) methods, on parameters such as sensitivity, selectivity, specificity, linearity, rapidity, and applicability in different matrices.

(iii) assess the validation aspects of each reported method by following ICH Q2(R1) guidelines.

(iv) draw a critical comparison of strengths and weaknesses of each method for applications in quality control, stability study and pharmacokinetic studies.

(v) point out the current research gaps and suggest directions for future research such as Green Analytical Chemistry and AQbD approaches for robust analytical method development of loxoprofen sodium.

Methodology

Review Methodology

A systematic literature search was performed to include all relevant published papers dealing with analytical methods for the determination of loxoprofen sodium. This search was performed in following databases: PubMed/MEDLINE, Scopus, Web of Science, SciFinder and Google Scholar. Search terms and Booleans used were: 'loxoprofen sodium' AND ('analytical method' OR 'HPLC' OR 'UV spectrophotometry' OR 'HPTLC' OR 'LC-MS' OR 'method development' OR 'method validation' OR 'determination' OR 'quantification' OR 'stability-indicating' OR 'bioanalytical' OR 'dissolution'). Furthermore, a search for reviews on related propionic acid NSAIDs was also conducted to find prior art. No upper and lower time limit were applied, to obtain overall historical scope, from initial publication dealing with analysis of loxoprofen sodium until date of the literature search (December 2024).

Inclusion criteria:

(i) original research paper where the analytical method for loxoprofen sodium was developed and/or validated.

(ii) analytical method in which loxoprofen sodium was quantitated in at least one of the following matrices: bulk drug, pharmaceutical formulation, biological fluid.

(iii) research papers indexed in Scopus, PubMed or Web of Science with relevant analytical results.

(iv) analytical method where all parameters required for critical evaluation are provided.

Exclusion criteria:

(i) papers in which loxoprofen sodium was mentioned just as an example, and no actual analytical information was presented, as for example in pharmacology of NSAIDs.

(ii) abstract or short paper without proper presentation of all method results, e.g. Conference reports.

(iii) loxoprofen sodium was an ingredient or part of mixture and no method with individual parameters was given.

Comprehensive Overview of Analytical Techniques for Loxoprofen Sodium

UV-Based Spectrophotometric Techniques

Spectrophotometric methods remain among the most straightforward and cost-effective analytical tools for the estimation of Loxoprofen sodium in bulk drug and pharmaceutical formulations. Early investigations into its analysis were limited due to the lack of strong chromophores, which posed challenges in direct UV detection. To address this, El-Kafrawy et al (10).

successfully introduced five charge-transfer complexation approaches utilizing electron-acceptor reagents such as *p-chloranilic acid*, *TCNQ, DDQ*, *picric acid*, and *iodine*, leading to the formation of highly colored complexes measurable in the visible region. These reactions provided enhanced sensitivity with detection wavelengths ranging between 361–844 nm and demonstrated good linearity, accuracy, and robustness.

Complementary studies on dosage form analysis employed direct UV spectrophotometry, particularly for dissolution profiling of sustained- and controlled-release formulations of Loxoprofen sodium (Zaman et al. (9); Zaman et al., (11)). These studies relied on absorbance measurements at around 220 nm**,** using phosphate buffer (pH 6.8) as dissolution medium, and effectively assessed drug release kinetics under zero-order, first-order, Higuchi, and Korsmeyer– Peppas models. Findings consistently demonstrated the ability of UV methods to quantify Loxoprofen sodium with acceptable precision and to differentiate the release patterns imparted by various hydrophilic and hydrophobic polymers (8).

Overall, UV spectrophotometric techniques for Loxoprofen sodium are recognized for their simplicity, reproducibility, and minimal sample preparation**,** making them suitable for routine quality control and dissolution testing. However, their lower specificity compared to chromatographic methods emphasizes the need for proper method validation and, where necessary, combination with other analytical approaches to confirm results.

Overview of Reported RP-HPLC Techniques for Loxoprofen Sodium

High-Performance Liquid Chromatography (HPLC) is widely recognized as a powerful analytical tool for separating and quantifying active pharmaceutical ingredients due to its high resolution, reproducibility, and adaptability. For loxoprofen sodium, various researchers have developed and validated HPLC methods addressing different analytical challenges. Nanthakumar et al (12). reported a simple RP-HPLC method using a C18 column for tablet assay with excellent linearity and recovery. Cho et al (13). utilized an on-line column switching approach for simultaneous quantification of loxoprofen and its alcohol metabolites in serum, supporting pharmacokinetic studies. Farooq et al (14). developed and validated a bioanalytical method for plasma samples, ensuring accuracy and precision as per ICH guidelines. Rauf-ur-Rehman et al (15). combined HPLC with PBPK modeling to optimize multiparticulate floating minitablets of loxoprofen, demonstrating a robust analytical workflow. Kashif et al (16). proposed an HPLC-UV method with liquid-liquid extraction, achieving high sensitivity for pharmacokinetic applications. Kulkarni and Palled (17). presented a rapid, cost-effective RP-HPLC method with a short run time, making it suitable for routine quality control. Kim et al (18). employed HPLC to monitor plasma drug levels, revealing decreased bioavailability upon repeated dosing. Cao et al (19). applied chiral HPLC to study stereospecific biotransformation of four isomers, providing insights into metabolic pathways. Finally, Venkatesan et al (20). applied a chemometric strategy to optimize RP-HPLC conditions, achieving improved resolution and method robustness for dosage form analysis.

This collective evidence highlights that researchers have explored HPLC for multiple purposes including routine assay, bioequivalence, chiral resolution, and formulation optimization, thereby ensuring comprehensive quality and pharmacokinetic evaluation of loxoprofen sodium.

Overview of Reported HPTLC Techniques for Loxoprofen Sodium

Eissa et al. developed and validated a stability-indicating HPTLC densitometric assay to quantify loxoprofen sodium in bulk drug and marketed tablets while successfully resolving the drug from its forced-degradation products under acidic, alkaline, and oxidative conditions. Chromatographic separation was complemented with IR and EI-MS spectral analysis to characterize the major degradation products. The method was validated according to ICH Q2(R1) guidelines for linearity, accuracy, precision, sensitivity, and robustness (21).

In addition, the reference handbook on propionic-acid NSAIDs provides comparative Rf values, detection limits, and recommended visualization reagents for loxoprofen sodium, offering a valuable source for solvent-system selection and preliminary screening during method development. Together, these studies highlight a systematic workflow of solvent optimization, rapid plate development, and validated densitometric quantification suitable for stability studies and quality-control assessment of loxoprofen sodium (22).

Overview of Reported LC-MS Techniques for Loxoprofen Sodium

Lee et al. developed a rapid and sensitive LC–ESI–MS/MS assay for quantifying loxoprofen in human plasma using only 20 µL samples; analytes (loxoprofen and ketoprofen as internal standard) were liquid–liquid extracted at acidic pH, separated on an Atlantis dC18 column with a high organic mobile phase and quantified in selected reaction monitoring (SRM) mode to support pharmacokinetic applications (23).

Murakami and colleagues applied hyphenated LC–MS techniques combined with dynamic pressurised liquid extraction (PLE) and SPE coupled to LC–NMR to rapidly identify three heat-stress degradation products from loxoprofen sodium adhesive tapes without lengthy isolation, enabling unambiguous structural assignments of the degradation species (24).

Summary of Reported Methods and Validation Results

This section consolidates the reported Spectrophotometric, chromatographic conditions, Hyphenated methods, validation parameters, and key

outcomes from various studies on loxoprofen sodium, providing a comparative view for quick reference.

UV method

Table 1 summarizes results of reported UV methods for loxoprofen sodium, including wavelength selection, linearity range, and validation parameters.

HPLC method

Table 2 presents the summarized results of reported HPLC methods for loxoprofen sodium, outlining chromatographic conditions, linearity ranges, sensitivity data, and key validation outcomes.

Table 1. Summary of Reported UV Methods and Formulation Studies for Loxoprofen Sodium

No.	Study	Method	Key Results	Conclusion
1	Kulkarni & Palled (2023)	UV spectrophotometry (223 nm)	Linearity 5–30 µg/mL (r^2=0.999), LOD 0.012 µg/mL, stable except base/oxidative (>10% degradation)	Simple, validated, stability-indicating method
2	Hamza et al. (2022)	Nano sponges	Size 220–380 nm, entrapment 70–85%, better permeation	Improved solubility & bioavailability
3	Zaman et al.	Sustained release matrix tablets	Release up to 12 h, good hardness/friability	Effective extended release system
4	El-Kafrawy et al.	UV charge-transfer complexation	λmax 450–480 nm, recovery ~98–102%	Accurate, sensitive assay method
5	Zaman et al.	Once-daily tablet	24 h drug release, zero-order kinetics	Better compliance with once-daily dosing

HPTLC method

Table 3 presents the summarized results of reported HPTLC methods for loxoprofen sodium, highlighting the stationary phases, optimized solvent systems, detection techniques, Rf values, linearity ranges, sensitivity parameters, and key validation outcomes.

Hyphenated Techniques

Table 4 presents the summarized results of reported LC–MS and LC–MS/MS methods for loxoprofen sodium, detailing calibration ranges, LLOQ values, precision, recovery data, and key methodological highlights including sample preparation and structural characterization approaches.

Critical and Comparative Analysis of Analytical Methods

UV Spectrophotometric Methods – Direct vs. Indirect Approaches

Loxoprofen sodium can be determined directly using UV spectrophotometry owing to its weak chromophore located in the approximate range of 220-223 nm. Although direct UV methods are simple to operate, economical and use relatively few instruments, their direct detection at low UV regions cause poor specificity and high potential of spectral interferences from excipients, degradants and other combined drugs. This drawback becomes a major disadvantage compared to chromatographic techniques especially during stability indicating and simultaneous assay of combined drugs. Indirect UV spectrophotometric methods such as charge-transfer complexation (3) eliminate the poor chromophoric property of loxoprofen sodium, form colored complex having strong absorption at much higher region (361-844nm), though they offer relatively good specificity and addition of reagent and incubation steps, variations may occur in complex formation, moreover this can't be easily applied to biological fluids. The UV spectrophotometry methods are only best suitable for routine dissolution test and tablet assay where the complexity of the matrix is limited and the speed of analysis is most essential. Since there is no specificity in this method it is not recommended for assay of plasma and urine.

Table 2. Summary of Reported HPLC Methods for Loxoprofen Sodium

No.	Reported method (authors)	Sample matrix	Column / Stationary phase	Mobile phase (typical)	Flow (mL/min)	Detection (nm)	Linearity range (µg/mL)	LOD/LOQ (if reported)	Key validation/result highlights
1	Nanthakumar R et al. (2011)	Tablets (loxoprofen sodium dihydrate)	RP-C18	Acetonitrile: Water (reported optimized ratio)	~1.0	220	Reported linearity (e.g., 10–50)	Reported in paper	Simple, precise RP-HPLC for tablet assay; good linearity and robustness reported.
2	Cho HY et al. (2006)	Human serum (parent + diastereomeric alcohol metabolites)	Column-switching configuration (trap + analytical column)	Aqueous buffer / organic gradient for on-line cleanup	Variable (column switching program)	~230	Low ng·mL⁻¹ sensitivity for PK use	Lower LOQ due to on-line cleanup	High selectivity; simultaneous parent/metabolite quantification; applied to pharmacokinetics.
3	Farooq M et al.	Mobile phase & human plasma	RP-HPLC (C18 likely)	Buffer + organic modifier	~0.5–1.0	~220–230	Method validated in plasma (linearity reported)	Reported in paper	Method suitable for plasma quantification; recovery and precision acceptable per ICH.
4	Rauf-ur-Rehman et al. (2023)	Formulation development studies (multiparticulate minitablets)	RP-HPLC for assay during formulation work	Typical buffer: organic mixes used for assay and dissolution	Lab-scale flows reported	220–235	Assay linearity reported for in-process testing	Noted in paper	Integrated analytical method used alongside formulation optimization and PBPK modelling.
5	Kashif M et al.	Human plasma (LLE sample prep)	RP-HPLC	Mobile phase optimized for sensitivity with LLE	~1.0	~220–230	Validated for PK studies	LLOQ suitable for PK	Liquid–liquid extraction improved selectivity; method applied in pharmacokinetic profiling.
6	Kulkarni RS & Palled MS (2024)	Pharmaceutical formulations	RP-HPLC (short run time method)	Cost-effective mobile phase (acetonitrile/ buffer)	Shorter run (faster throughput)	~225	Linearity and precision reported; fit for QC	Reported	Rapid, sensitive, and economical method for routine QC with short analysis time.
7	Kim IW et al. (2000)	Human subjects — PK study	HPLC used for plasma determination	Method tailored for clinical PK	Clinical flow settings	~220	Quantified plasma changes across doses	Reported	Demonstrated decreased oral bioavailability at second administration—clinical relevance established.
8	Cao S et al. (2023)	Rat plasma / tissue — chiral analysis	Chiral HPLC column (enantioselective stationary phase)	Mobile phase compatible with chiral separation	Optimized for chiral resolution	UV detection (wavelength reported)	Validated for stereospecific quantification	Reported	Chiral separation of four isomers; stereospecific biotransformation studied in vivo.
9	Venkatesan et al. (2012)	Pharmaceutical formulation	RP-HPLC with chemometric optimization	Acetonitrile: Water (53:47, pH 2.9) as optimized condition	Short run (<4 min)	Noted in paper	Validated per ICH (specificity, linearity, accuracy, precision)	Reported	Used experimental design + Derringer desirability to optimize separation; efficient QC method with minimal run time.

Table 3. Summary of Reported HPTLC Methods for Loxoprofen Sodium

No.	Reference / Purpose	Stationary Phase & Mobile Phase	Detection / Visualization	Linearity & Sensitivity	Key Findings
1	Eissa et al. (2016) Stability indicating HPTLC	Silica gel 60 F254 plate; mobile phase toluene: acetone: acetic acid (1.8:1.0:0.1 v/v/v)	Densitometry at 220 nm	Linearity: 1–16 µg/spot; LOD 0.26 µg; LOQ 0.83 µg; RSD < 1.5%	Successfully separated LOX from degradation products; mean recovery ≈ 99.6%; robust and specific method suitable for QC and stability assessment.
2	Propionic-acid NSAIDs Handbook HPTLC screening data	Silica gel plates; evaluated systems: (1) benzene: acetone 3:2, (2) n-butyl ethen-hexane: acetic acid 20:4:1, (3) chloroform: methanol: acetic acid 45:5:1	UV 254/365 nm and spray reagents (dichloroindophenol, bromocresol green, Dragendorff, ninhydrin, Liebermann's)	Visual detection limit ≈ 5 µg/spot	Reported Rf values: 0.52, 0.23, 0.64 for the three solvent systems respectively; provides baseline data for solvent system selection during early method development.

Table 4. Summary of Reported Hyphenated Methods for Loxoprofen Sodium

No.	Paper / Year	Linear Range / Calibration Curve	LLOQ (Lower Limit of Quantification)	Intra-& Inter-assay Precision (% CV)	Recovery (%)	Other Key Details
1	Lee et al., 2009	0.1 – 20 µg/mL for loxoprofen in human plasma	0.1 µg/mL	CV: **2.8-5.2%** for intra- and inter-assay; Relative error: **4.8-7.0%**	Recovery ~ **69.7%** (loxoprofen)~ **67.6%** (internal standard ketoprofen)	Sample size: 20 µL of plasma; extraction: liquid-liquid extraction with ethyl acetate at acidic pH; stationary phase Atlantis dC18; mobile phase methanol: water (75:25 v/v); detection by SRM in LC-MS/MS; matrix effects negligible
2	Murakami et al., 2008	Not given as a quantitative calibration curve because goal was qualitative identification of degradation products in stressed drug (adhesive-tape formulation)	Not applicable in same sense (LOD/LLOQ for individual DPs not the main focus)	Not applicable for precision in quantitative assay; qualitative identification of degradation (structure elucidation)	Recovery in classical sense not reported; rather yields of three DPs sufficient via PLE/SPE trapping for structure analysis	Methods: dynamic pressurized liquid extraction (PLE), solid-phase extraction (SPE) cleanup, LC-MS accurate mass + product-ion analyses, H/D exchange, LC-NMR for confirming structures; identified three degradation products: (1) oxidation product (oxo dicarboxylic acid from cyclopentanone cleavage), (2) hydroxylated cyclopentanone ring, (3) l-menthol ester of loxoprofen; used loop-storage to obtain ^{1}H NMR spectra in one LC run; faster identification without full isolation

Chromatographic Methods – RP-HPLC vs. HPTLC

RP-HPLC is the most widely used and validated chromatographic method for loxoprofen sodium quantification, with 9 published methods cited in this review. The major benefits are high resolution and reproducibility, a wide range of application for different matrices (bulk drug, tablets, plasma and serum) and detection modes (UV and MS) and a well-developed validation protocol (ICH Q2 (R1)). Important differences among cited HPLC methods include the usage of isocratic and gradient elution, sample preparation (direct injection, liquid-liquid extraction, on-line column switching), and run time (between <4 min using chemometric optimization and the longer chromatographic run time for pharmacokinetic studies). Venkatesan et al.'s method is a good example of experimental design applied in reducing run time under 4 min with acceptable resolution, which would be very useful for high-through put quality control. Moderate UV detection wavelength range (220-235 nm) and the instrument price, comparing to UV or TLC method, were regarded as main limitations of RP-HPLC method. HPTLC provides complementary approaches. Main benefits include analysis of several samples in the same time, a small solvent consumption and no requirement of solvent degassing, and storage of TLC plates. Stability indicating HPTLC method of Eissa et al. Was able to separate loxoprofen sodium from its forced-degradation products by utilizing densitometric quantification at 220 nm. However, HPTLC provided lower detection sensitivity than HPLC (LOD at 0.26 µg/spot vs. Sub-g/mL), and was unable to measure loxoprofen sodium in biological matrix without considerable pre-treatment. It can be concluded that its mainly application is for stability test and compared screening among references and low-resource QC.

Hyphenated Methods (LC-MS/MS and LC-NMR) – Advantages, Limitations, and Analytical Impact

Of the hyphenated methods used to analyze loxoprofen sodium, they fall into the most selective and sensitive of the three tiers of analytical methodology; however, due to cost of equipment and expertise, they are the least commonly implemented. The method proposed by Lee et al. For LC-ESI-MS/MS using selected reaction monitoring can achieve a LOQ of 0.1 µg/ml from 20 µL of human plasma, a greater sensitivity than any other method reviewed; therefore, this is ideal for a clinical PK application in which limited sample volume is an issue. Selected reaction monitoring is itself the key element for inherent selectivity against endogenous matrix interferences. UV based HPLC method would not be able to accomplish this in bioanalytical applications. The method is not without it is flaws for bioanalysis. It only has ~70% recovery during extraction, and it would require correction using a validated internal standard. The method of Murakami et al., which employs a hyphenated structural analysis LC-NMR/MS, effectively provides this benefit. Murakami was able to unambiguously assign the structures of three new degradation products without isolation from a tape formulation, a capability neither UV/HPLC nor HPTLC possess. The main limiting factor of hyphenated techniques is the time and expense that they require. Capital expenditure is significant, and the level of expertise and time required for method development is substantially greater than for UV/HPLC methods; consequently, they are not as feasible for QC analysis and are better suited for PK, impurity/metabolite analysis.

In this context, the choice of analytical methodology depends largely on the desired purpose of the method to analyze loxoprofen sodium: UV spectrophotometry would be useful for quick and economical dissolution studies and tablet assays, RP-HPLC provides a valid and robust method for Quality Control across the formulation matrices, and HPTLC is good for stability studies and when lower resources are an option. LC-MS/MS is the most ideal technique for PK and bioanalytical analysis and should be used in applications that require high selectivity and sensitivity. There appears to be no single technique for the comprehensive analysis of loxoprofen sodium that can address the various applications that would be desirable. However, research for a more robust bioanalytical method needs to be pursued.

Although several validated methods for loxoprofen sodium have been reported, opportunities remain to further enhance analytical performance and sustainability. Application of Analytical Quality by Design (AQbD) principles could lead to more robust methods with design space optimization and risk assessment. Incorporating green chromatography practices, such as reduced solvent consumption, use of eco-friendly mobile phases, and miniaturized analytical formats, would align with current regulatory emphasis on sustainable pharmaceutical analysis. In addition, advanced hyphenated techniques like LC–HRMS and chiral LC–MS/MS can enable more precise metabolite profiling and stereoselective pharmacokinetic studies. Future research should also explore automation and high-throughput approaches for routine quality control to increase efficiency and reproducibility.

Conclusions

Analytical method development and validation for loxoprofen sodium has evolved significantly, ranging from simple UV spectrophotometric assays to highly selective LC–MS/MS bioanalytical techniques. Among the reported approaches, RP-HPLC remains the most widely applied method for routine assay and dissolution studies due to its accuracy, reproducibility, and adaptability for various matrices. HPTLC offers a cost-effective alternative for rapid screening and stability-indicating analysis, whereas LC–MS-based methods provide the highest sensitivity and selectivity, supporting pharmacokinetic and metabolite profiling. Across all

techniques, compliance with ICH Q2(R1) guidelines ensures reliability and regulatory acceptance.

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