Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/6kj48b91

A REVIEW ON ANALYTICAL METHODS FOR ESTIMATION OF A FIX DOSE COMBINATION OF CIPROFLOXACIN AND CELECOXIB

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Abstract
In pharmaceutical development, fixed-dose combinations (FDCs) have drawn more attention due to their ability to reduce pill burden, enhance patient compliance, and produce synergistic therapeutic effects. A promising medication combination for the treatment of antimicrobial therapy complicated by inflammation, such as in antibiotic-loaded scaffolds (ALS) and infection-associated pain, is celecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, and ciprofloxacin, a fluoroquinolone antibiotic. Due to variations in chemical structure, polarity, solubility, and UV absorption properties, analytical estimation of such a combination presents difficulties. The chemical and pharmacological profiles of celecoxib and ciprofloxacin, their combined therapeutic justification, and the analytical ramifications of creating reliable estimation techniques are all critically summarized in this review. With a focus on spectrophotometric, chromatographic, and advanced hyphenated methods, reported analytical techniques for both individual and combined estimation are examined. Since it is still the most dependable, sensitive, and repeatable method for simultaneously quantifying these medications in bulk, formulations, and biological matrices, special attention is paid to reverse-phase high-performance liquid chromatography (RP-HPLC). In order to overcome analytical difficulties and guarantee precision, adherence to regulations, and clinical suitability in fixed-dose combinations, the review also identifies potential approaches for method development and validation.

Key words: Ciprofloxacin, Celecoxib, Fixed-dose combination, PrimeC, Analytical methods, RP-HPLC, LC–MS/MS, UV–Vis spectrophotometry, Green analytical chemistry, Amyotrophic lateral sclerosis, Method validation

❖ Introduction

Motor neurons, the nerve cells that regulate muscle movement, are progressively harmed by amyotrophic lateral sclerosis (ALS), a dangerous neurological disorder. This continuous loss causes progressive paralysis and muscle weakness, and the disease usually kills its victims within two to five years of its onset.(1)

Although the precise cause of ALS is still unknown, it is believed that a number of overlapping biological processes play a role in its development. Among these are RNA-binding protein dysfunction, aberrant iron accumulation, neuroinflammation, and disruptions in microRNA regulation. The progressive damage to nerve cells is thought to be caused by a combination of mechanisms, as no single pathway can adequately explain the disease. The necessity for therapeutic approaches that target several pathways at once is highlighted by this intricate, multifactorial origin. (2)

PrimeC is a combination treatment that combines precisely calibrated dosages of celecoxib and ciprofloxacin. By addressing the three main pathological pathways, this formulation aims to slow down the progression of ALS and target the key disease mechanisms involved.

Because it inhibits DNA gyrase and topoisomerase IV, the well-known fluoroquinolone antibiotic ciprofloxacin (CIP) is frequently prescribed to treat both Gram-positive and Gram-negative bacteria (3). Because of its wide range and superior oral bioavailability, it is frequently used as a first-line treatment in clinical settings for gastrointestinal, respiratory, and urinary tract infections (4). In contrast, celecoxib (CLX) is a selective cyclooxygenase-2 (COX-2) inhibitor that is frequently used to treat inflammatory diseases like rheumatoid arthritis and osteoarthritis (5). The combined use of an antimicrobial with an anti-inflammatory agent is a frequent clinical practice, particularly in treating infection-related inflammation, in postoperative care, or in fixed-dose formulations aimed at enhancing patient compliance[6].

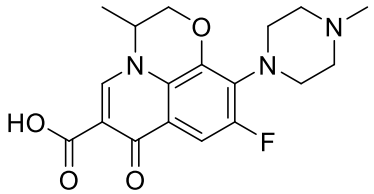
From an analytical standpoint, simultaneous determination of CIP and CLX presents notable challenges due to their markedly different physicochemical properties. CIP is amphoteric, carrying both acidic and basic groups, and demonstrates appreciable solubility in water under physiological pH[7]. On the other hand, CLX is highly lipophilic, poorly water-soluble, and strongly bound to plasma proteins (>97%)[5,8]. Their UV absorption spectra further complicate analysis: CIP exhibits absorption maxima at approximately 278 and 320 nm, whereas CLX absorbs intensely near 254–255 nm, leading to spectral overlap[9]. This overlap often necessitates the use of advanced chemometric tools, mathematical corrections, or chromatographic separation to achieve accurate quantification.

The creation of trustworthy simultaneous analytical techniques is especially crucial for pharmacokinetic studies, therapeutic monitoring, and quality control of fixed-dose formulations. For comparable drug pairs, numerous methods have been investigated over time, including capillary electrophoresis, high-performance liquid chromatography (HPLC), chemometric approaches, ratio-spectra, UV spectrophotometry, and spectrofluorimetry (10). The concepts of green analytical chemistry have gained more attention in recent years, with an emphasis on reducing the use of organic solvents and switching to economical, environmentally friendly substitutes like micellar spectrofluorimetry or chemometric-assisted UV techniques [11].

❖ Chemical and Pharmacological Profiles

Because amyotrophic lateral sclerosis (ALS) involves intertwined processes of neuroinflammation, oxidative stress, and disrupted proteostasis, the fixed-dose combination of celecoxib (CLX) and ciprofloxacin (CIP), often known as PrimeC, is being evaluated in early clinical trials. The co-formulation's acceptable safety and signals on exploratory biomarkers were reported in an open-label, year-long safety/tolerability study, which has encouraged more controlled trials (12). Details of the protocol and the reasoning behind it are available in the corresponding trial registry (13). In light of this translational context, method development, PK interpretation, and product quality control all depend on an understanding of the chemistry, pharmacology, and analytical behavior of each drug.

❖ **Ciprofloxacin (CIP)**



Chemical Profile

- **IUPAC Name:** 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-quinoline-3-carboxylic acid
- **Molecular Formula:** $C_{17}H_{18}FN_3O_3$
- **Molecular Weight:** 331.34 g/mol
- **Chemical Class:** Second-generation fluoroquinolone antibiotic
- **Structure:** Contains a quinoline core with substitutions including:
  - Cyclopropyl group at N-1
  - Carboxylic acid group at C-3
  - Ketone group at C-4
  - Fluorine at C-6
  - Piperazine ring at C-7
- **Physical Properties:**
  - White to slightly yellow crystalline powder
  - Solubility: Slightly soluble in water, more soluble in acidic solutions
  - Melting point: ~255–257 °C [14]

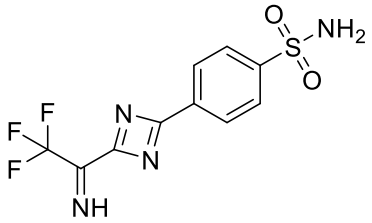
Mechanism and clinical role: Ciprofloxacin is a widely used fluoroquinolone antibiotic with potent activity against many Gram-negative pathogens and selected Gram-positive organisms. Its antibacterial effect results from stabilization of cleavage complexes formed by **DNA gyrase and topoisomerase IV**, which blocks DNA replication and produces bactericidal strand breaks. [16,17]

Spectroscopic and physicochemical characteristics: A piperazinyl moiety and carboxyl functionality have replaced the molecule's quinolone core, making CIP amphoteric and pH-sensitive in solubility and ionization. This characteristic has a significant impact on extraction, chromatographic retention, and UV behavior in analytical procedures. pH-dependent shifts in λmax (such as a principal band around ~278 nm and shifts in different media) are reported in studies that characterize the spectral behavior of solid states and solutions. This allows for UV detection and cautions that mixed samples may exhibit spectral overlap with other drugs unless separated or mathematically deconvolved [18].

Pleiotropic / off-target effects with potential relevance to ALS: Effects that are pleiotropic or off-target and may be related to ALS In addition to their antimicrobial properties, fluoroquinolones have been shown in recent studies to modulate inflammatory mediators, particularly by lowering the production of MMP-9 in stimulated cells via MAPK-linked pathways. This effect has been suggested as part of the justification for quinolone repurposing in non-infectious contexts (e.g., cancer models). A believable mechanistic connection to neuroprotection ideas in ALS is provided by such MMP-9 modulation, which is pertinent to blood–brain barrier integrity and neuroinflammatory cascades [12].

Pharmacokinetics and dosing considerations The absorption, distribution, and elimination of CIP in a variety of patient groups—including elderly or critically ill populations—are summarized by recent population PK studies and scoping reviews. These reports highlight the need to take tissue penetration into account when interpreting CNS or biomarker results in clinical studies, as well as exposure variability and renal elimination [16, 17]. The absorption, distribution, and elimination of CIP in a variety of patient groups—including elderly or critically ill populations—are summarized by recent population PK studies and scoping reviews. These reports highlight the need to take tissue penetration into account when interpreting CNS or biomarker results in clinical studies, as well as exposure variability and renal elimination.

❖ Celecoxib (CLX)



Chemical Profile

- **IUPACName:** 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide
- **Molecular Formula:** $C_{17}H_{14}F_3N_3O_2S$
- **Molecular Weight:** 381.37 g/mol
- **Chemical Class:** Selective COX-2 inhibitor (nonsteroidal anti-inflammatory drug, NSAID)
- **Structure Features:**
  - Pyrazole ring system
  - Trifluoromethyl group at position 3
  - Para-methylphenyl substituent
  - Benzenesulfonamide moiety
- **Physical Properties:**
  - White to off-white crystalline powder
  - Melting point: ~157–159 °C
  - Poorly soluble in water, but soluble in ethanol and DMSO [14]

Mechanism and therapeutic rationale: Celecoxib is a selective COX-2 inhibitor of the diaryl pyrazole class that inhibits downstream inflammatory signaling and prostaglandin synthesis. COX-2 contributes to microglial activation and neuronal injury in models of neuroinflammation and hypoxic injury; in cellular and animal studies, selective COX-2 blockade with celecoxib decreases these cascades, bolstering a case for research in conditions where neuroinflammation is pathogenic. [13, 15]

Physicochemical and ADME profile: Celecoxib is lipophilic, poorly water-soluble and extensively protein-bound; it is predominantly metabolized by hepatic CYP enzymes. These properties drive formulation strategies (solubility enhancement, surfactants, nanoparticle approaches) and make dose adjustments or interaction-monitoring relevant in populations with variable CYP2C9 activity (illustrated in recent reviews and formulation studies) [13, 15].

Formulation and analytical consequences: Modern research has concentrated on nano- and particle-based strategies to improve oral availability and dissolution rate because CLX is BCS class II (low solubility, high permeability). Analysts should confirm extraction recovery, matrix effects, and method linearity under representative formulation and biological conditions because the same formulations and sample-preparation decisions (cosolvents, surfactants, and solid dispersions) change chromatographic behavior and UV response. [15, 16].

❖ Combination of CLX and CIP in ALS

When paired with a medication exhibiting potential MMP-9 and stress-pathway modulation, the combination offers a multimodal therapeutic hypothesis: reduce neuroinflammation (CLX) while modifying proteolytic/inflammatory mediators and stress responses (CIP). ALS pathology includes persistent neuroinflammation and molecular stress pathways that may be amenable to modulation by anti-inflammatory agents. The current clinical program is empirically supported by early clinical safety/tolerability results and the biological justification from preclinical studies (such as fluoroquinolone-induced MMP-9 suppression and COX-2-linked neuroinflammation models). [15]

❖ Official / Reported Analytical Methods for Ciprofloxacin

Matrix	Method	Column / Principle	Mobile phase / Reagent (typical)	λ / Detector	tR / Output	Ref
Bulk drug / Tablets	RP-HPLC (stability-indicating)	C18 (150–250×4.6 mm)	Phosphate buffer : ACN (acidic)	UV 278 nm	4-8 min	16
Human plasma	UPLC-MS/MS (total & unbound)	UPLC C18 + triple quad	Protein precip/SPE; ACN:Water + 0.1% FA	MS/MS (MRM)	1-4 min	17
Human plasma (multi-analyte)	LC–MS/MS multi-antibiotic panel	UPLC C18	ACN:H2O gradient; MRM	MS/MS	Short	18
Environmental water	SPE + LC–MS/MS	SPE (HLB) + UPLC	SPE elution MeOH/ACN; gradient LC-MS	MS/MS	-	19
Tablets / formulations	Green UPLC (CIP + NSAIDs)	BEH C18, 2.1×150 mm	ACN:Water 65:35 (pH adj)	DAD/UV 210–278 nm	CIP ~2.75 min	20
Meat/tissues	Capillary electrophoresis (CZE)	Fused silica capillary	Phosphate/borate buffer	UV 278 nm	minutes	21
Point-of-care / sensors	Electrochemical sensor (DPV)	Modified carbon electrode (Cu-Fe/rGO)	PBS	Current / peak potential	-	18
Fluorescent probe	Gold nanocluster fluorescence / synchronous fluorescence	Nanocluster probe	Aqueous buffer; Al3+ enhancer	Ex 360 / Em 448 & 612 nm	-	20
Spectrophotometric/colorimetric	Colorimetric spectrophotometry	No column	Sodium nitroprusside reagent	UV-Vis	-	21
Microbiological potency	Agar diffusion / turbidimetric bioassay (updated)	Agar plates	Culture media	Zone diameter	-	22

- LC–MS/MS for Total & Unbound Ciprofloxacin in Plasma

Both the bound and unbound fractions of ciprofloxacin in human plasma can be measured using the quick LC–MS/MS assay described in this method. This is accomplished by first separating the free drug using ultrafiltration, and then precisely quantifying the result by protein precipitation using a deuterated internal standard. With a validated concentration range of 0.02-5.0 mg/L, the entire analysis only takes 1.5 minutes. This approach is very dependable for pharmacokinetic research and clinical therapeutic drug monitoring because accuracy and precision were continuously within allowable bounds (intraday ≤7.6%, interday ≤9.8%). [23].

- LC–MS/MS for Multiple Antibiotics Including Ciprofloxacin

Matrix	Method	Column / Principle	Mobile phase / Reagent (typical)	λ / Detector	tR / Output	Ref
Drug substance / impurities	RP-HPLC (AQbD impurity profiling)	C18 (250×4.6 mm)	ACN : Buffer gradient; pH adjusted	DAD 252–254 nm	-	27
Plasma (PK)	UHPLC-MS/MS	UPLC C18 + triple quad	Protein precip/LLE; ACN:Water + FA	MS/MS (MRM)	1-4 min	28
Nanocarrier formulations (NLC)	HPLC-MS/MS quantitation	UPLC/LC-MS	Gradient LC-MS; extraction LLE/SPE	MS/MS	-	29
Formulations / tablets	RP-HPLC (stability-indicating)	C18	ACN:Water or MeOH:Water	UV 252–254 nm	5-9 min	30
Eco-friendly spectrophotometry	Multi-spectrophotometric green methods	No column	Water/ethanol mixtures	Derivative UV	-	31
Controlled delivery quantitation	HPLC for β-CD inclusion complex quantitation	C18	MeOH:Water	UV 252 nm	-	32
Electrochemical	Modified electrodes	GCE with	BR buffer	Voltammogram	-	33

sensors	voltammetry	nanomaterials		peaks		
TLC / HPTLC	HPTLC densitometry	Silica gel GF254	Toluene:EtOAc:MeOH systems	Densitometer UV	Rf	34
Method improvement discussion	HPLC-MS method optimization	UPLC/ LC–MS	Gradient acetonitrile/water	MS/MS or DAD	-	34
Sustainable HPLC	Green RP-HPLC with greenness appraisal	C18/ green solvents	Lower-organic mobile phases	UV 252 nm	-	35

Ciprofloxacin is one of nine antibiotics that can be measured in plasma samples using a multi-analyte LC–MS/MS technique. The technique enables high-throughput and effective sample preparation by combining Turboflow online extraction with protein precipitation. The technique is reliable enough for therapeutic drug monitoring in hospital and research settings, despite the fact that ciprofloxacin is examined alongside other antibiotics. [24].

- HPLC–FLD–DAD for Fluoroquinolones in Plasma & Urine

This validated HPLC method measures fluoroquinolones like levofloxacin, ciprofloxacin, moxifloxacin, and gemifloxacin in biological fluids using both fluorescence (FLD) and diode-array (DAD) detection. A pentafluorophenyl core-shell column is used for the separation, which takes 7.5 minutes to complete. The technique exhibits good stability and precision, recovery ranging from 79 to 103%, and strong linearity ($r \geq 0.9989$). It is helpful in pharmacokinetic and clinical monitoring studies because it can be applied to both plasma and urine. [25].

- Multi-Antibiotic LC–MS/MS Panel

In a single run of roughly 3.8 minutes, ten antimicrobials, including ciprofloxacin, were to be quantified using a different LC–MS/MS-based assay. Before being separated using gradient elution on a Waters Acquity BEH C18 column, plasma samples are subjected to protein precipitation. This high-throughput workflow is effective for clinical pharmacology and therapeutic drug monitoring because it enables the simultaneous monitoring of several antimicrobial classes. [26].

❖ Official / Reported Analytical Methods for Estimation of Celecoxib

- LC–MS/MS for simultaneous quantification of celecoxib and amlodipine in rat plasma

Celecoxib and amlodipine together can be measured in rat plasma using a contemporary, fully validated LC–ESI-MS/MS technique. After cleaning with protein precipitation, the assay separates analytes on an Agilent C18 column using acetonitrile–water (70:30) and 0.1% formic acid, and it runs for 10 minutes. It is ideal for preclinical PK studies due to its high sensitivity (20–800 ng/mL for celecoxib), precision (intra- and inter-day CV under ~7%), and accuracy (87.9–100.3%). [36]

- HPLC (UFLC) for amlodipine and celecoxib in rat plasma

Ultra-fast liquid chromatography (UFLC) is a quick and accurate HPLC technique that measures celecoxib and amlodipine from rat plasma. It uses UV detection at 228 nm, a C18 Eclipse Plus column, and a methanol–acetate buffer (70:30, pH 4.5). Run time is 15 minutes, recovery rates are approximately 89–94%, and celecoxib calibration ranges are 600–4200 ng/mL. This approach to pharmacokinetic sample analysis is straightforward and reliable. [37]

- RP-HPLC with UV detection for celecoxib in tablet formulations (fixed-dose combination)

A validated reverse-phase HPLC-UV method to simultaneously determine amlodipine and celecoxib in combined tablet dosage forms. The assay uses a Flowrosil C18 column with an 80:20 acetonitrile–water mobile phase at 1 mL/min. Detection is at 250 nm, with celecoxib linear over 50–300 µg/mL and recovery above 99.5%. The technique is accurate, precise, and ideal for routine QC of fixed-dose products. [38]

- UPLC-MS/MS for celecoxib (plus analgesic co-drugs) in beagle plasma

Celecoxib, dezocine, and dexmedetomidine can all be measured simultaneously in beagle dog plasma using a quick and extremely sensitive UPLC-MS/MS technique. The assay makes use of gradient elution, separation on an Acquity UPLC BEH C18 column, and acetonitrile protein precipitation. With recovery above 79% and inter- and intra-day RSD < 8%, precision and accuracy

are well within FDA bioanalytical standards. Because of this, it is reliable and perfect for preclinical pharmacokinetic research. (39)

❖ Official / Reported RP-HPLC Methods for Ciprofloxacin with other drugs

Matrix	Method	Column / Principle	Mobile phase / Reagent (typical)	λ / Detector	tR / Output	Ref
Human plasma (CIP + DIC + IBU)	Green UPLC-DAD simultaneous method	BEH C18, 2.1×150 mm	ACN:Water 65:35 pH adj	DAD 210–278 nm	CIP~2.75; DIC~3.42; IBU~3.75	16
Tablets (CIP + IBU)	UV derivative / chemometrics	No column	Methanol/buffer	UV wavelengths	-	40
Tablets (CIP + NSAID)	RP-HPLC isocratic simultaneous	C18	ACN : Phosphate buffer (acidic)	UV multiwavelength	Separation	41
Plasma (multi-drug panels)	LC–MS/MS multi-analyte	UPLC C18	Gradient + MRM	MS/MS	Short	42
Environmental co-monitoring	SPE + LC–MS/MS	SPE + UPLC	SPE elution; gradient LC	MS/MS	-	19
Tablet (CIP + DIC)	TLC–densitometry	Silica gel	Chloroform:MeOH	Densitometer UV	Rf	43
Sensors (CIP + NSAID)	Electrochemical multipeak detection	Modified electrodes	PBS	Voltammogram	-	44
UPLC rapid assay (PK)	UPLC-DAD rapid 4-min assay	BEH C18	ACN:Water 65:35	DAD 278 nm	CIP 2.75 min	16
CE simultaneous	Capillary electrophoresis	Fused silica capillary	Phosphate/borate buffers	UV/DAD	minutes	17
Multi-analyte LC-MS	LC–MS/MS for plasma multi-drug panels	UPLC C18	ACN:H2O + modifiers	MS/MS	Short	41

❖ Official / Reported RP-HPLC Methods for Celecoxib with other drugs

Matrix	Method	Column / Principle	Mobile phase / Reagent (typical)	λ / Detector	tR / Output	Ref
Tablet (CEL + LEV)	RP-HPLC isocratic/gradient	C18	MeOH/ACN : Buffer	UV 252 & 293 nm	Resolved	30
Plasma (CEL + FQ)	LC–MS/MS simultaneous	UPLC + triple quad	Protein precip / SPE; gradient	MS/MS	1–4 min	44
Tablet (CEL + OFX)	Capillary electrophoresis	CZE	Phosphate buffer	UV 254 nm	Minutes	2
Tablet (CEL + MOXI)	RP-HPLC	C18	ACN:Buffer	UV 254–296 nm	Resolved peaks	45
Sensors (CEL + FQ)	Electrochemical mixed detection	GCE/MIP electrodes	BR buffer	Voltammogram	-	46
TLC-densitometry	HPTLC	Silica gel	Toluene:EtOAc:MeOH	Densitometer UV	Rf	41
UPLC-DAD rapid assay	UPLC C18	ACN:Buffer gradient	DAD 254–278 nm	2–5 min	Rapid QC for combined formulations	47
LC-MS environmental/trace	SPE + LC–MS/MS	SPE + UPLC MS/MS	Gradient	MS/MS	-	4
AQbD template for combined method development	AQbD HPLC development (DoE)	C18 + DoE	Buffer/ACN	DAD	-	27

- **Prospective Strategies for Simultaneous Quantification of Celecoxib and Ciprofloxacin**

The celecoxib + ciprofloxacin (PrimeC) combo is pioneering. Currently, there are **no marketed analytical methods** specifically for this combination - so we must rely on proximate strategies and one breakthrough method as proof-of-concept.

1. Proven SSF Method

Celecoxib and ciprofloxacin are directly measured in plasma using SDS micelles and $\Delta\lambda = 80$ nm in a 2025 SSF study. With the least amount of solvents, it achieves remarkable sensitivity—LODs as low as 0.58 ng/mL for celecoxib and 0.24 ng/mL for ciprofloxacin. For this particular pair, this approach is the only validated, environmentally friendly analytical solution. [48]

2. Multi-Analyte LC–MS/MS Strategies

Although PrimeC does not yet have an LC–MS/MS, methods for measuring ciprofloxacin in single runs with other antibiotics (such as panels of ten antibiotics) provide a framework for adding celecoxib transitions and creating a highly sensitive dual assay. [49]

3. HPLC with Fluorescence Detection

Fluoroquinolones in plasma or urine can be effectively separated using HPLC techniques that use fluorescence, particularly when combined with dual detection. By optimizing the wavelength, these can be modified for simultaneous celecoxib estimation [50].

4. Chemometric Models for Spectral Overlap

Chemometric techniques applied to synchronous fluorescence or UV-Vis data can resolve celecoxib and ciprofloxacin signals when spectra overlap. These low-cost, high-throughput substitutes are beneficial for the initial stages of method development. [51]

5. Smart Sample Prep: QuEChERS & Cleanup

It has been demonstrated that QuEChERS or protein precipitations can produce pure extracts for fluorescence or LC analyses of NSAIDs and fluoroquinolones in complex matrices. For combo samples, this method is reliable and flexible. [52]

❖ Applications of Analytical Methods for Simultaneous Estimation of Celecoxib and Ciprofloxacin

The development of analytical methods for simultaneous estimation of celecoxib (a selective COX-2 inhibitor) and ciprofloxacin (a fluoroquinolone antibiotic) has significant pharmaceutical and clinical applications. Since these drugs are increasingly investigated for potential combination therapies (especially in cancer-related infections and inflammatory disorders), robust methods are critical across several domains:

1. Fixed-Dose Combination (FDC) Development & Quality Control

Using multi-analyte HPLC or LC–MS/MS platforms speeds up formulation screening and ensures dosage accuracy. [53]

2. Therapeutic Drug Monitoring & Pharmacokinetics

Multi-analyte LC–MS/MS assays streamline simultaneous drug level measurement in plasma (including ciprofloxacin), essential for PK profiling. [54]

3. Stability & Forced-Degradation Testing

Quality-by-Design (QbD)-based RP-HPLC methods support separation of actives from degradation products—critical for stability-indicating assays. [53]

4. Green and High-Throughput Analytical Methods

Multiplex LC–MS/MS strategies enable efficient TDM with minimal solvents and rapid turn-around. [55]

5. Method Adaptations in Complex Matrices (Food/Biological)

QuEChERS-HPLC and chemometric techniques support clean extraction and simultaneous estimation even in complex sample types. [56]

6. Regulatory Compliance & Validation Workflow

Applying validated multi-analyte methods with an ICH/QbD approach aligns both quality and regulatory expectations. [53]

7. Monitoring Drug Combinations in Multi-Drug Therapies

Multi-drug therapies are common, and robust analytical methods help verify product integrity and detect degradation/contamination. [57]

8. Ultra-Fast Antibiotic Susceptibility Testing

Rapid antibiotic assays (e.g., using Raman or fluorescence) can inform therapeutic decision-making. While not a quantitation method per se, they showcase rapid drug-related analytics in co-treatment settings. (58)

9. Tracking Herb–Drug Interaction Effects on Ciprofloxacin Pharmacokinetics

Quantifying changes in ciprofloxacin's PK profile when co-administered with other substances highlights the importance of precise, simultaneous monitoring. (57)

10. Simultaneous Dual-Drug Estimation in Complex Matrices

Demonstrates that two very different APIs (celecoxib + docetaxel) can be separated and quantified using validated HPLC–UV in formulations and plasma. (53)

Conclusion

Because of their different physicochemical characteristics, ciprofloxacin and celecoxib simultaneous estimation in fixed-dose formulations poses a significant analytical challenge. Existing techniques, particularly RP-HPLC, have proven to be reliable for quantifying these medications either alone or in conjunction with other substances. A substantial research gap is indicated by the scant reports on direct simultaneous estimation. For such FDCs to have quality control, regulatory approval, and therapeutic efficacy, validated methods must be standardized. To improve sensitivity, lower solvent consumption, and satisfy regulatory requirements, future viewpoints should prioritize the integration of sophisticated chromatographic techniques, green analytical approaches, and hyphenated methods. In addition to aiding pharmaceutical research, the creation of strong analytical techniques will make it easier to translate ciprofloxacin- celecoxib combinations into clinical settings, which will ultimately improve patient outcomes.

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