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Review on RP-HPLC Method Development and Validation of Cefixime and Azithromycinin Pharmaceutical Dosage Form

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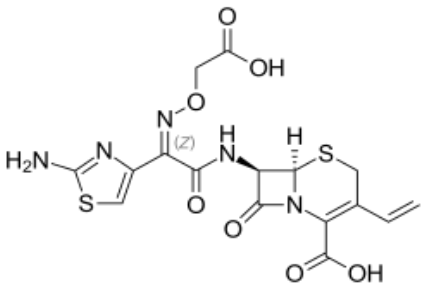
ABSTRACT

A variety of simple, precise, and robust RP-HPLC methods have been developed and validated for the simultaneous estimation of azithromycin and cefixime, both in bulk and in pharmaceutical dosage forms. Across different studies, methods using different columns (C8 and C18) and mobile phase compositions (phosphate buffers with acetonitrile or methanol) have shown excellent linearity, accuracy, precision, and specificity, complying with ICH guidelines. Stress testing confirmed the stability-indicating capability of the developed methods, with minimal interference from excipients. The methods demonstrated strong recovery rates, low LOD and LOQ values, and rapid analysis times, making them reliable for routine quality control and stability studies. Overall, these developed HPLC methods offer a cost-effective, sensitive, and reproducible approach for the simultaneous analysis of azithromycin and cefixime in pharmaceutical formulation.

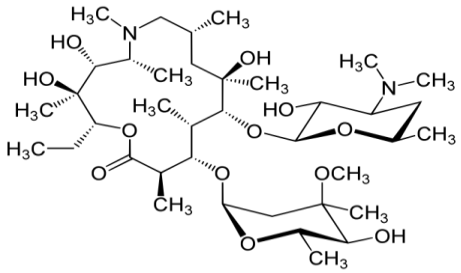
Keywords: RP-HPLC, Azithromycin, Cefixime, Linearity.

I. INTRODUCTION TO DRUG PROFILE

Cefixime (CFI) is an orally active third-generation cephalosporin antibiotic ($C_{16}H_{15}N_5O_7S_2 \cdot 3H_2O$**,** molecular weight 507.50 g/mol) that inhibits bacterial cell wall synthesis. It is widely used to treat respiratory tract infections, urinary tract infections, sinusitis, otitis media, and Helicobacter pylori infections.



Azithromycin (AZT), a macrolide antibiotic ([9-deoxy-9a-aza-9a-methyl-9a-homoerythromycin A dihydrate]**)**, blocks bacterial protein synthesis by binding to the 50S ribosomal subunit. It is effective against respiratory infections, cystic fibrosis, COPD-related inflammation, malaria (with other antimalarials), typhoid fever, and Neisseria gonorrhoeaeinfections.



Both drugs are official in the **Indian Pharmacopoeia (2010)**. While various analytical methods like **HPLC**, **LC-MS/MS**, **micellar chromatography**, **UV spectrophotometry**, and **HPTLC** have been reported for individual estimation, no method has been documented for their simultaneous analysis in pharmaceutical formulations.

II. Summary of Analytical Methods

Reported analytical methods for Cefixime and Azithromycin

SLno no	Drug	Method	Brief description
1	Cefixime and Azithromycin	RP-HPLC	**Column:** Phenomnex C18 column (250 x 4.6mm, 5µm) **Mobile phase:**0.02M Potassium dihydrogen phosphate (KH2PO4): Acetonitrile in the ratio of 65:35 (v/v) **Detected Wavelength:** 227 nm **Flow rate:** 1 ml/min **Retention time**:6.94 & 5.22 min **Linearity range**: 40-60 & 50-70 µg/ml
2	Cefixime	RP-HPLC	**Column:** C18 (zodiac company) **Mobile phase:**Methanol:Acetonitrile (30:70) **Detected Wavelength:** 243 nm **Flow rate:** 1.1 ml/min **Run time**: 2.9mins **Linearity range**: 100-600 µg/ml
3	Azithromycin and Cefixime	RP-HPLC	**Column:** AgilantZorbax C8, 5 µ column having 150 x 4.6mm **Mobile phase:** 0.1M Dipotassium Hydrogen Phosphate Buffer : methanol (60:40 %v/v pH: 8.0 adjusted with Ortho phosphoric acid **Detected Wavelength:** 230 nm **Flow rate:** 1.1 ml/min **Retention time**:2.7 & 4.6 min **Linearity range**: 250-750µg/mL and 200-600 µg/mL
4	Cefixime and Azithromycin	RP-HPLC	**Column:** Inertsil -ODS C18(250 x 4.6 mm, 5 µ) **Mobile phase:** Methanol : Buffer (85:15) **Detected Wavelength:** 275 nm **Flow rate:** 1 ml/min **Retention time**:2.186 & 3.968 min **Linearity range**: 20-80µg/ml
5	Azithromycin and Cefixime	RP-HPLC	**Column:** Supleco C18 (25cm×4.6 mm, 5 µm) **Mobile phase:** 80:20 Na2HPO4: Methanol **Detected Wavelength:** 273 nm **Flow rate:** 1 ml/min **Retention time**:2.77 & 4.93 min **Linearity range** 50-150 µg/ml
6	Azithromycin and Cefixime	RP-HPLC	**Column:** Kromasil C18 column **Mobile phase:** Ortho Phosphoric Acid buffer and Methanol in the ratio of 70:30 v/v **Detected Wavelength:** 292 nm **Flow rate:** 1 ml/min **Retention time**:2.8 & 3.9 min **Linearity range:**0.5 1.5 mg/ml., 0.4-1.2 mg/ml
7	Azithromycin	RP-HPLC	**Column:** Column ODS-3 (250 mm × 4.6 mm x 5 µm) **Mobile phase:** Methanol: Phosphate buffer (9:1, v/v) **Detected Wavelength:** 210 nm **Flow rate:** 1.2 ml/min **Linearity range:** 0.5 1.5 mg/ml., 0.4-1.2 mg/ml

III.CONCLUSION:

Several RP-HPLC methods have been developed for the estimation of Cefixime and Azithromycin individually and simultaneously, mostly using C18 columns with different mobile phases comprising phosphate buffers combined with methanol or acetonitrile. Detection wavelengths varied between 210 nm and 292 nm, depending on the method, and flow rates ranged from 1.0 to 1.2 mL/min, ensuring efficient separations. Retention times for Cefixime and Azithromycin were generally short, between approximately 2 to 7 minutes, allowing rapid analysis. Linearity ranges covered a broad spectrum from low µg/mL levels (20–80 µg/mL) to high mg/mL levels (0.5–1.5 mg/mL), making the methods suitable for different types of pharmaceutical analyses. Overall, the methods are efficient, sensitive, and flexible, and the choice of method can be tailored based on required sensitivity, sample concentration, and analysis time.

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