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An In-Depth Survey of Analytical Techniques for Quantifying Antihistamines and Antiasthmatics in Diverse Dosage Forms.

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Analytical Methods, Validation Parameters, Combined Drugs.

Abstract: This article presents a comprehensive examination of various analytical methodologies employed in the quantification of antihistamines and antiasthmatics, specifically desloratadine, levocetirizine hydrochloride, fexofenadine hydrochloride, and montelukast sodium, in both dosage forms and biological matrices. The analytical techniques encompass electrometric methods, UV spectroscopy, mass spectroscopy, thin-layer chromatography, high-performance liquid chromatography (HPLC), and high-performance thin-layer chromatography (HPTLC). The investigation systematically addresses the essential analytical validation parameters applicable to each methodology. The study reveals that HPLC and UV-Vis spectrophotometry emerged as the predominantly utilized analytical techniques by the researchers.

Introduction:

Allergic conditions, such as allergic rhinitis, hay fever, and anaphylaxis, are immunological disorders triggered by hypersensitive reactions to external factors like environmental allergens. Manifesting symptoms include itchy skin, red eyes, sneezing, and shortness of breath. Immunoglobulin E antibodies (IgE), binding to allergens and activating mast cells in the body, initiate the immunological response. Asthma, a chronic inflammatory disease primarily affecting the respiratory system's airways, leads to symptoms like bronchospasm, coughing, chest constriction, wheezing, and difficulty breathing. The root causes of asthma involve environmental elements, allergens, and genetic interactions. Leukotriene, a precursor to IgE, plays a pivotal role. Notably, a leukotriene modifier serves as a preventive and therapeutic agent for allergic diseases [122].

Anti-histaminic and anti-asthmatic drugs:

Desloratadine, represented as 8-chloro-6, 11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine (Fig. 1), functions as a non-sedative antihistamine providing symptomatic relief for allergic conditions, including rhinitis and urticaria [120].

Levocetirizine, a third-generation non-sedating antihistamine, is chemically characterized as 2-[2-[4-[(R)-(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid (Fig.2). Primarily utilized in the treatment of idiopathic recurrent urticaria and allergic rhinitis, it represents the active enantiomer of cetirizine. Cetirizine, an oral histamine receptor antagonist, is distinguished by its potency, selectivity, prolonged action, and lack of anticholinergic effects [3].

Fexofenadine hydrochloride, chemically known as (±)-4-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]–dimethyl benzene acetic acid hydrochloride (Fig.3), serves as an antihistamine employed in the treatment of hay fever and related allergy symptoms. Developed as a safer alternative

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to terfenadine, it avoids potentially hazardous side effects. Distinguished by its reduced propensity to traverse the blood-brain barrier compared to first-generation histamine receptor antagonists, it belongs to the second and third generations of antihistamines. Its mechanism of action involves functioning as an H_1 receptor antagonist [4].

Montelukast Sodium, designated as [R-(E)]-1-[[[1-[3-[2-(7-Chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropaneacetic acid monosodium salt (Fig.4), operates as a specific antagonist of a leukotriene receptor. This compound finds application in the management of chronic asthma, allergic rhinitis, and the prophylaxis of exercise-induced asthma [121].

The primary objective of this comprehensive review is to collate and present documented analytical methodologies for desloratadine (DESLO), fexofenadine (FEX), levocetirizine (LCTZ), and montelukast sodium (MTKT). These analytical approaches are explored both individually and in combination, specifically in bulk and various medicinal dosage forms such as tablets and capsules. Additionally, the review encompasses analytical methods applied to biological samples, including human plasma, human serum and sheep plasma, The aim of this overview is to facilitate swift access to a diverse array of analytical techniques employed for the quantification of antihistamines and anti-asthmatic medications across different matrices, ensuring the requisite levels of accuracy and precision.

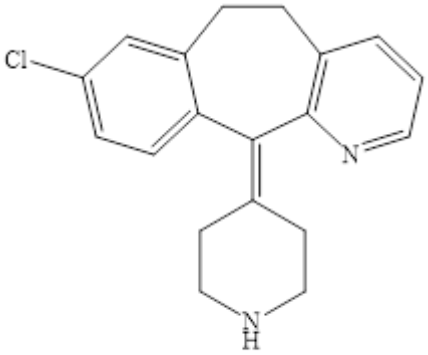

Figure 1: Desloratadine

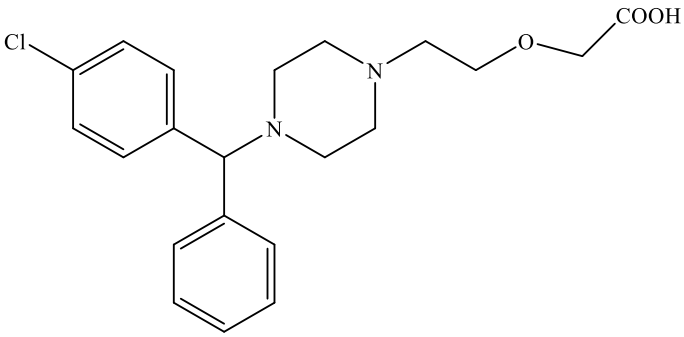

Figure 2: Fexofenadine

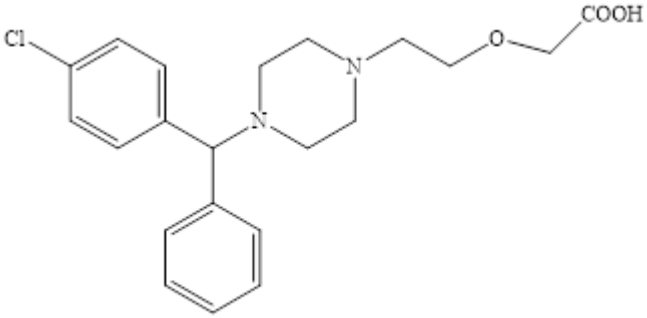

Figure 3: Levocitrizine

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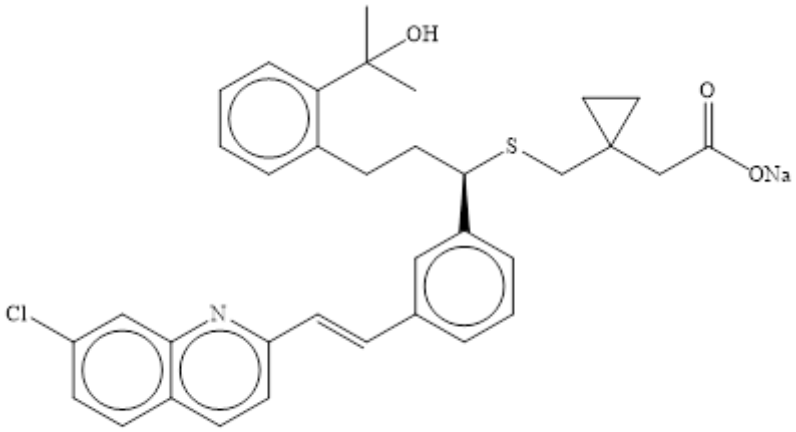

Figure4: Montelukast sodium

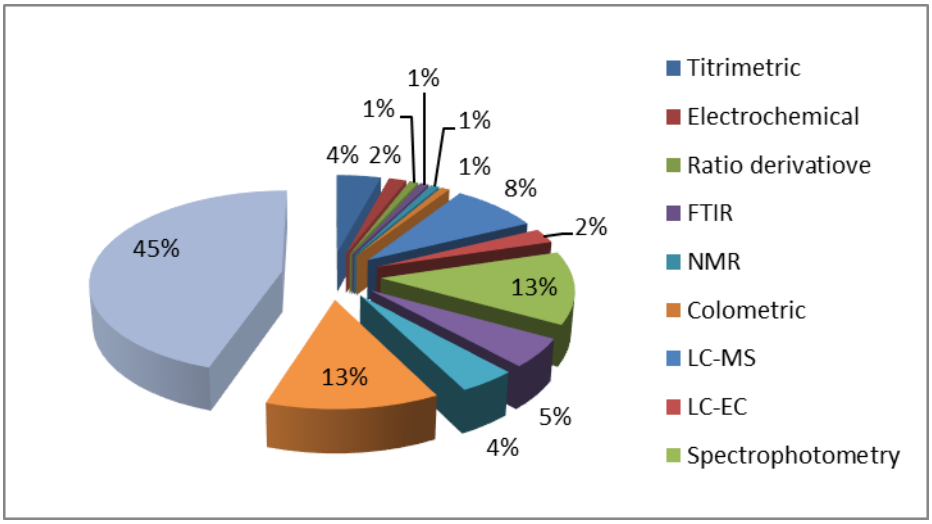

Figure 5: Various analytical methods employed for the analysis of anti-histaminic and anti-asthmatic substances.

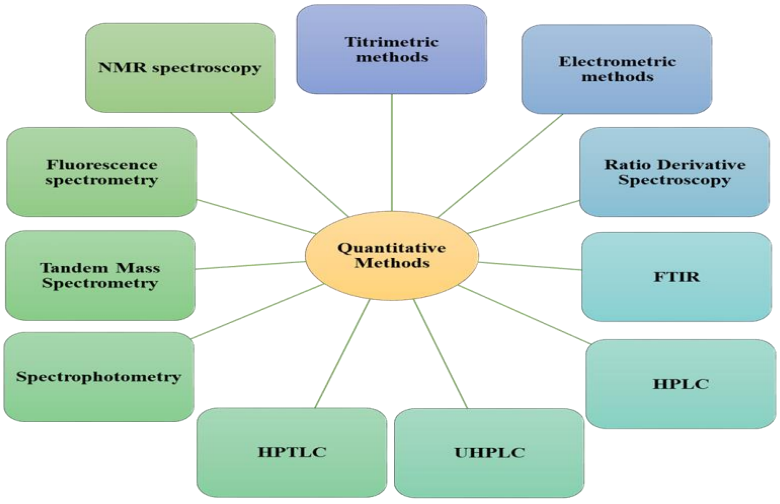

Figure 6: Visual depiction of the different techniques explored.

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Quantitative Methods Review for the Detection of Antihistamines and Antiasthmatics:

Titrimetric Techniques:

El-Enanyn et al. [5] have devised four specialized and highly sensitive titrimetric methods for the detection of desloratadine (DSL). In Methods I and II, DSL is coupled with 4-chloro-7-nitrobenzo-2-oxa-1,3-diazole in a pH 7.6 borate buffer, yielding a yellow reaction product detectable spectrophotometrically at 485 nm (Method I). Alternatively, the same product can be identified spectrofluorimetrically at 538 nm after excitation at 480 nm (Method II). In Methods III and IV, desloratadine undergoes derivatization with 2,4-dinitrofluorobenzene in a pH 9.0 borate buffer, resulting in a yellow product with maximum absorption at 375 nm (Method III). Following separation via High-Performance Liquid Chromatography (HPLC), the identical derivative is identified (Method IV). A comparable technique has been employed by other researchers for the quantification of montelukast sodium in pharmaceutical and bulk formulations [6-7].

Raghu M. S. et al. [8] have established two spectrophotometric methods, including a titrimetric approach, for quantifying the presence of fexofenadine hydrochloride in tablets and other pharmaceuticals. In Method A, fexofenadine hydrochloride is titrated with a known excess of a bromate-bromide mixture in an acidic medium, and the unreacted bromine is subsequently determined by iodometry. Using spectrophotometry, liberated iodine (I_3) is detected at 360 nm (Method B), or iodine reacts with starch before being detected at 570 nm to ascertain the residual bromine amount (Method C). In a similar vein, A.K. Pandey et al. [9] introduce a titrimetric technique for antihistamine drugs utilizing pyridinium fluorochromate as a chromogenic agent. Following the iodometric principle, a chromogenic agent and potassium iodate are employed to oxidize an organic functional group in the analyte molecule within a sulfuric acid-containing solution.

Electrometric methods:

Rajan R. et al. [10] introduced a non-aqueous potentiometric titration method for the identification of fexofenadine within pharmaceutical formulations. A standardized solution of 0.1 N perchloric acid served as the titrant. The proposed technique underwent validation, demonstrating analyte molecule recovery between 99.739% and 101.724%, with an RSD of less than 1 and an r^2 value of 0.999. A parallel potentiometric titration was developed by Aslan et al. to quantify montelukast sodium in pharmaceutical formulations, utilizing hydrochloric acid as the titrant. The protonation constants were determined to be approximately 6.25 and 200, yielding RSD values of 0.38%, 0.24%, and 0.74% for visible and conductometric methods, respectively.

In this series of review articles authored by N. Aslan et al. [11] an innovative potentiometric titration method for assessing montelukast sodium in pharmaceutical dosage forms is presented and rigorously validated. The study focused on conducting potentiometric titrations of standard montelukast sodium, utilizing hydrochloric acid as the titrant. The developed method exhibited remarkable accuracy and precision, with a relative standard deviation of less than 1.0%. The stoichiometric protonation constant was determined based on titration data obtained in 40% ethanol-60% water and 60% ethanol-40% water (v/v) mixtures, maintaining a constant temperature of 25.0 °C and an ionic strength of 1.0×10-1 M NaCl. The protonation constant was identified as 6.25 in the 40% ethanol-60% water mixture and 5.95 in the 60% ethanol-40% water mixture. Moreover, the method demonstrated its applicability by successfully analyzing commercial pharmaceuticals containing 10.0 mg montelukast sodium. To further validate the method, recovery studies involving standard additions to a tablet solution were conducted, yielding highly satisfactory results. These findings underscore the reliability and robustness of the developed potentiometric titration method for the determination of montelukast sodium in pharmaceutical formulations.

Ratio Derivative Spectroscopy:

Choudhari V. et al. [12] devised and validated a spectrophotometric technique utilizing ratio derivative spectroscopy for the simultaneous determination of montelukast and levocetirizine in a combined tablet form. This method involves measuring the amplitude of the first derivative ratio

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spectra at 250.4 nm for montelukast and 238.4 nm for levocetirizine as two estimation wavelengths. The Beer's law is observed in the concentration range of 4–12 or 2–6 µg/ml for montelukast or levocetirizine, respectively. The respective LOD values for montelukast and levocetirizine are 0.09 µg/ml and 0.178 µg/ml, while the LOQs are 0.591 g/mL and 0.277 µg/ml.

Fourier Transform Infrared spectroscopy:

Padmavathi Y. et al. [13] employed chemometric Fourier transform infrared (FTIR) spectroscopy to determine the presence of montelukast sodium and fexofenadine hydrochloride in pharmaceutical dosage forms. Solid pellets were created using geometric mixing with potassium bromide (KBr). Spectra were gathered using a reduced path length in absorbance mode. D.S. Agha and Hind El-Zien [14] utilized FTIR spectrophotometry to assess the compatibility of montelukast and levocetirizine in a solid dose form. The KBr disc approach was employed, revealing spectral alterations indicative of non-covalent hydrogen bond formation and potential molecular complex development, influencing chemical stability or solubility.

NMR spectroscopy:

Gulsel Yurtda Krmlolu [15] employed 1H NMR spectroscopic techniques utilizing Ultrashield CPMASNMR (Bruker, Germany) to ascertain the enantiomeric purity of desloratadine. Deuterated dimethyl sulfoxide served as the solvent in this analysis.

Fluorescence spectrometry:

In a study conducted by Ragab, M. A. A., and Youssef, R. M. [16], a novel hybrid chemometric method has been implemented for analyzing emission response data. This innovative approach involves the convolution of emission data using 8-point sine xi polynomials, which are discrete Fourier functions, following the derivative treatment of the emission data. The application of this new method proved effective for the simultaneous determination of Fexofenadine and Montelukast in both bulk and pharmaceutical preparations. Notably, it demonstrated significant advantages in resolving partially overlapping emission spectra within this mixture. The utility of this chemometric method extended to addressing various challenges commonly encountered in spectrofluorimetry, such as overlapping emission spectra and self-quenching. The application of this approach not only involved the treatment of emission data but also subjected the obtained results to non-parametric linear regression analysis, specifically using Theil's method. This comprehensive methodology represents a noteworthy advancement in the field, showcasing its potential to enhance the accuracy and reliability of emission data analysis in pharmaceutical and bulk material assessments..

Liquid Chromatography:

Tandem Mass Spectrometry (LC-MS/MS) methods:

In the study conducted by Ponnuru V. S. et al. [17], Desloratadine-d5 served as an internal standard for the determination of desloratadine levels in human plasma using liquid chromatography-tandem mass spectrometry. Chromatographic separation employed an Xbridge C18 column with a flow rate of 0.7 ml/min, utilizing an isocratic mobile phase comprising 10 mM ammonium formate and 20 mM methanol. Proton adducts for desloratadine and the internal standard were detected at m/z 311.2-259.2 and 316.2-264.3, respectively, in positive mode multiple response monitoring. The method exhibited robustness with an r^2 correlation coefficient of 0.9994 over a linear concentration range of 5.0-500.0 pg/ml. Accuracy ranged between 101.4%-102.4% and 99.5%-104.8%, with intraday precision between 0.7%-2.0% and 0.7%-2.7%. Simultaneous analysis of desloratadine and its active metabolite, 3-hydroxydesloratadine, has also been reported by Muppavarapu R. et al. [18] and others [19–21].

For the analysis of levocetirizine in human plasma, Wisut Wichitnithad et al. [22] introduced a method utilizing LC-MS/MS. Chromatographic separation occurred on a reverse-phase column with an isocratic mobile phase of acetonitrile and 10 mM ammonium formate pH 3.5 (80:20) at a flow rate of 1.0 m1/min. The method demonstrated a dynamic range and lower limit of quantification of 100-500 ng/ml. Yamane N. et al. [23] developed a technique for quantifying fexofenadine in human plasma using LC-MS/MS during a clinical trial. Chromatographic separation on an X-Bridge C18 column utilized acetonitrile and 2 mM ammonium

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acetate (91:9) as the mobile phase at a flow rate of 0.6 ml/min. The calibration curve was linear in the range of 10-1000 ng/ml. Hofmann et al. [24] reported employing a cyano column to detect fexofenadine in human plasma and urine.

In a study by Muppavarapu R. et al. [25], a method was developed for the simultaneous measurement of montelukast and fexofenadine in human plasma using internal standards montelukast-d6 and fexofenadine-d10. Chromatographic separation was achieved on a Chromolith RP18e column with an isocratic mobile phase of 20 mM ammonium formate and acetonitrile (20:80, v/v) at a flow rate of 1.2 ml/min. LC-MS/MS with electrospray ionization in multiple-reaction monitoring mode was employed. The calibration curve exhibited linearity in the range of 2.00-1000 ng/ml. Other researchers [26–27] have reported using similar LC-MS/MS methods for the analysis of montelukast sodium.

Liquid chromatography with electrochemical detection (LC-EC):

In a study by Sakur A. A. et al. [28] fabrication of three carbon paste electrodes is detailed for the quantitative measurement of third-generation antihistamines, namely fexofenadine (FEX), desloratadine (DES), and levocetirizine (LEV. The proposed potentiometric method introduces an environmentally friendly, rapid, uncomplicated, and sensitive approach for determining these drugs in their pure and pharmaceutical forms. Utilizing the constructed carbon paste electrodes enabled the quantitative determination of antihistamine drugs. The analytical method exhibited linearity within the concentration range of e (5×10^{-6}–1×10^{-2}) M for FEX and DES, and, (1×10^{-5} – 1×10^{-2}) M for LEV. Nernstian slopes (-57.40, -29.01, -56.01) mV/decade indicated close proximity to the ideal Nernstian slope value. The limits of quantification (LOQ) were (2.17×10^{-8} - 6.31×10^{-8} - 3.3×10^{-8}) M, respectively. The electrodes demonstrated good selectivity, repeatability (RSD<2%), stability, and a fast response time. The method underwent validation and was applied to determine the studied drugs in pharmaceutical dosage forms, yielding average recovery values of (99.13–99.53–99.90) % for FEX, DES, and LEV, respectively. Additionally, Sakur A. A. et al. [29] investigated Fexofenadine, Desloratadine, and levocetirizine. The study revealed that carbon paste electrodes surpassed conventional ion-selective electrodes, offering an accurate, precise, environmentally friendly, reliable, and economically advantageous analytical approach.

In another study by Dania Nashed et al. [30] presents a pioneering electrochemical approach for concurrently determining Fexofenadine hydrochloride and Montelukast sodium through the development of three novel graphite electrodes coated with a polymeric membrane. The first electrode, designed for Fexofenadine determination, incorporated ammonium molybdate reagent as an ion pair with the Fexofenadine cation. The second electrode, tailored for Montelukast determination, utilized cobalt nitrate as an ion pair with the Montelukast anion. The third electrode, a composite of the first two, was sensitized to both Fexofenadine and Montelukast drugs. The polymeric film coating included Poly Vinyl Chloride (PVC), Di-butyl phthalate as a plasticizer (DBP), and ion pairs of drugs with the previously mentioned reagents. The electrodes exhibited Nernstian responses, with mean calibration graph slopes of [59.227, 28.430, (59.048, and 28.643)] $mV.decade^{-1}$ for the three pencil electrodes, respectively. Detection limits were recorded at 0.025 µM for Fexofenadine and 0.019 µM for Montelukast, surpassing the performance of reported methods for this drug combination. The electrodes demonstrated effective functionality over a pH range of (2–4.5) for Fexofenadine hydrochloride and (5–9.5) for Montelukast sodium. Selectivity coefficient values indicated negligible interference from proposed interfering species. The electrodes maintained effectiveness over a period of 45–69 days. The suggested sensors demonstrated useful analytical features for the determination of both drugs in bulk powder, in laboratory prepared mixtures and their combined dosage form. We have validated the method following ICH protocol, and we have reached very signifcant results in terms of the linearity, accuracy, selectivity, and precision of the method.

Spectrophotometry:

Spectrofluorometry, also known as fluorimetry, is a branch of emission spectroscopy that focuses on

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studying samples producing fluorescence. This analytical technique is particularly valuable for the sensitive determination of organic compounds present in air or water.

In a study conducted by Etta Naveen Kumar et al., [31] the identification of montelukast and desloratadine was carried out at specific wavelengths, namely 283 nm and 269 nm in methanol, respectively. The analysis encompassed various analytical parameters, including linearity, precision, accuracy, and ruggedness. Desloratadine and montelukast both demonstrated linearity at their respective wavelengths within concentration ranges of 5-30 µ/ml and 2-22 µ/ml.

Table 1: Summarizes reported spectrophotometric techniques utilized for the examination of various antihistamines and anti-asthmatics, emphasizing the diverse applications of spectrofluorometry in this analytical domain.

Compound	Solvent	λ max (nm)	Linearity range µg /ml	LOD µg/ml	LOQ µg /ml	Reference
DESLO MTKT	Methanol	218.6 262	5-40 5-40	0.72 0.17	1.2 0.52	[32]
DESLO MTKT	Methanol	245 285.6	2–12 4-24	-	-	[33]
FEX MKT	0.1N NaOH.	259 344.5	50-180 1-35	-	-	[34]
FEX MKT	Methanol	221.20 287.52	6-26 4-24	0.7137 0.6339	2.1628 1.938	[35]
FEX MKT	Methanol	289.12 288.17	24-120 2-10	0.144 0.1043	0.371 0.31	[36]
FEX	Alkaline Kmno4	610	2.5–50.	0.055	0.183	[37]
LCTZ MKT	Methanol	225 267	2.5-12.5 5-25	0.6 0.2	1.8 0.8	[38]
LCTZ MKT	0.5 % w/v SLS in distilled water	211.8 350.2	03-30 03-30	0.361 0.993	1.09 3.0	[39]
LCTZ MKT	Methanol	284.0 229.0	2-10 4 -20	3.3 1.1	2.1 0.7	[40]
LCTZ MKT	Methanol	287 232	2-40 2-40	-	-	[41]
LCTZ MKT	Methanol	229 232.2	5-40 5-40	-	-	[41]
LCTZ MKT	Methanol	231.1 216.5	10-40 10-40	-	-	[41]
LCTZ	Methanol	247-255	5-25	0.53	1.59	[42]

High performance thin layer chromatography (HPTLC):

In a research study conducted by TK Ravi et al. [44] a novel high-performance thin-layer chromatographic (HPTLC) method has been introduced for the bioestimation of Desloratadine (DSLR) and Montelukast (MON) in their combined dosage form. The separation process utilized Merck HPTLC aluminum plates coated with silica gel G60 F254, featuring a thickness of 250 µm. The mobile phase consisted of ethanol, methanol, ammonia formate solution, and ammonia in a ratio of 9:1:0.5:0.5 (v/v/v/v). The HPTLC separation of both drugs was conducted, and densitometric measurements were performed in absorbance mode at 287 nm. The satisfactory resolution of both drugs was achieved with Rf values of 0.19 ± 0.03 for DSLR and 0.86 ± 0.03 for MON. Calibration

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curves were established within the concentration ranges of 0.06 µg/spot to 0.36 µg/spot for DSLR (r2 > 0.996) and 0.12 µg/spot to 0.72 µg/spot for MON (r2 > 0.999). The developed method underwent thorough validation encompassing accuracy, precision, linearity, limit of detection, and limit of quantification. This HPTLC method, once validated, can be effectively applied for the estimation of DSLR and MON in both bulk drug and drug formulations, showcasing its potential utility in pharmaceutical analysis.

Hitesh vekaria et al. [45] have successfully devised a straightforward, precise, specific, and accurate high-performance thin-layer chromatographic (HPTLC) technique for concurrently assessing Fexofenadine hydrochloride (FEXO) and Montelukast sodium (MONT) in pharmaceutical dosage forms. The separation process utilized Merck HPTLC aluminum plates coated with silica gel G60 F254 (20 × 10 cm) and 250 µm thickness. The mobile phase consisted of ethyl acetate: methanol: ammonia (30%) (7: 3: 0.5, v/v/v/v). HPTLC separation of the two drugs, followed by densitometric measurement, was performed in the absorbance mode at 215 nm. The drugs exhibited satisfactory resolution with Rf values of 0.84 ± 0.01 and 0.24 ± 0.01 for MONT and FEXO, respectively. Linear regression analysis of the calibration plots indicated a robust linear relationship, with R2 values of 0.9988 and 0.9995 for FEXO and MONT, respectively, within the concentration range of 1800-9000 ng/spot for FEXO and 150-750 ng/spot for MONT. Validation of the method encompassed assessments of accuracy, precision, specificity, and robustness. The limit of detection and quantitation were determined as 100.6079 and 304.8726 ng/spot, respectively, for FEXO, and 40.0191 and 121.8456 ng/spot, respectively, for MONT.

Tandulwadkar S. S. et al. [46] developed a precise and accurate HPTLC method for simultaneous determination of FEX and MTKT in pharmaceutical dosage forms. Silica gel G60 F254-coated Merck HPTLC aluminum plates (20×10 cm, 250 µm thickness) were used with toluene: ethyl acetate: methanol: ammonia (30%) (0.5: 7: 2: 0.5, v/v/v/v) as the mobile phase. HPTLC separation occurred at 220 nm in the absorbance mode. FEX and MTKT exhibited satisfactory resolution with Rf values of 0.21±0.01 and 0.59±0.01, respectively. Linear regression analysis showed a strong linear relationship (r2 = 0.9996 for FEX and 0.9998 for MTKT) within concentration ranges of 2400–10800 ng spot−1 for FEX and 200–900 ng spot−1 for MTKT. Validation included precision, robustness, specificity, and accuracy assessments. Limits of detection and quantitation were 100 and 300 ng spot−1 for FEX and 50 and 100 ng spot−1 for MTKT. This HPTLC method is applicable for identifying and quantifying FEX and MTKT in bulk drug and drug formulations, presenting a reliable analytical approach.

Atul S. Rathore et al. [47] presented two chromatographic methods for the simultaneous determination of levocetirizine dihydrochloride and Montelukast sodium in tablets. The first method involved high-performance thin-layer chromatography (HPTLC) separation, followed by densitometric measurements on normal phase silica gel 60 F254. The second method employed high-performance liquid chromatography (HPLC) separation on a BDS Hypersil C18 column, utilizing a mobile phase of disodium hydrogen phosphate buffer (0.02 M): Methanol (25: 75, v/v) with pH adjusted to 7 using ortho-phosphoric acid. Both methods were validated according to ICH guidelines and successfully applied for the determination of the investigated drugs in tablets. This research offers reliable chromatographic approaches for the simultaneous analysis of levocetirizine dihydrochloride and Montelukast sodium in pharmaceutical formulations.

Ambadas R. Rote and Vaishali S. Niphade [48] have introduced two straightforward, expeditious, precise, and reproducible methods for concurrently determining montelukast sodium and levocetirizine dihydrochloride in a combined tablet dosage form. The first method utilized high-performance thin-layer chromatography (HPTLC) with paracetamol as an internal standard. The stationary phase was a precoated silica gel 60F254 aluminum plate, and the mobile phase consisted of a mixture of ethyl acetate: methanol: triethylamine (5:5:0.02, v/v/v). Detection occurred at 240 nm, and Beer's law was adhered to in the range of 400–1200 ng/spot for montelukast sodium and 200–600 ng/spot for

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levocetirizine dihydrochloride. The second method involved first derivative spectrophotometry, employing the zero-crossing technique for determining montelukast sodium at 291.60 nm and levocetirizine dihydrochloride at 238.20 nm. Both methods successfully passed f tests and t tests.

Katarzyna Bober et al. [49] established an HPTLC method for desloratadine analysis using ethyl acetate, n-butanol, ammonia, and methanol as the mobile phase. Silica gel 60F254 pre-coated HPTLC plates were employed, and quantification was achieved through spectrodensitometric analysis at the determined wavelength of 276 nm. This method proved effective for the quantitative assessment of desloratadine in various pharmaceutical preparations.

Ultra high performance liquid chromatography (UHPLC):

In a study by Rao D. D. et al. [50], a specialized stability-indicating gradient reverse-phase ultra-performance liquid chromatographic (RP-UPLC) method was developed to assess the purity of desloratadine in the presence of contaminants and forced degradation products. The approach utilized a Waters Acquity BEH C18 column with a mobile phase consisting of a gradient mixture of solvents A and B. The eluted chemicals were monitored at 280 nm, allowing for clear isolation of desloratadine and its five impurities over an 8-minute run duration. The method involved subjecting desloratadine to various stress conditions, including oxidative, acidic, basic, hydrolytic, thermal, and photolytic processes. Results showed that desloratadine significantly degraded under oxidative and thermal stress, while maintaining stability under acidic, basic, hydrolytic, and photolytic conditions. The degradation byproducts were effectively separated from the primary compound.

Mustafa M. et al. [51] introduced a rapid, simple, and sensitive gradient ultra-performance liquid chromatographic (UPLC) technique for determining fexofenadine HCl and montelukast sodium. The operation employed a Thermo Scientific UPLC system and a Waters (symmetrical) C18 column (1.8 microns, 4.6 x 50 mm). The mobile phase consisted of orthophosphoric acid, acetonitrile, and 20 mM potassium dihydrogen phosphate in a ratio of 80:30 (v/v) adjusted to a pH of 5.5. Detection occurred at 230 nm, and the separation was completed within ten minutes. Retention durations for montelukast sodium and fexofenadine HCl were found to be 1.022 and 3.281, respectively. The proposed approach exhibited linearity in the concentration ranges of 96-144 µg/mL for montelukast sodium and 80-120 µg/mL for fexofenadine HCl.

In their publication, Mangamma Kuna and Gowri Sankar Dannana [52] described the development of a rapid, sensitive, selective, precise, and accurate stability-indicating UPLC method with photodiode array detection. This method was designed for the simultaneous determination of montelukast and fexofenadine in both bulk drug and pharmaceutical formulations. The analytical column employed was an HSS C18 (2.1 mm × 100 mm, 1.8 µm), with the mobile phase consisting of 0.1% orthophosphoric acid and acetonitrile (50:50 v/v). Detection and analysis were performed using a photodiode array detector set at 269 nm.The calibration curves demonstrated a strong linear relationship in the concentration range of 2.5-15 µg/ml for montelukast and 30-180 µg/ml for fexofenadine, as indicated by linear regression analysis data. The validation of the method followed the International Conference on Harmonization guidelines, assessing parameters such as selectivity, precision, accuracy, robustness, specificity, limit of detection (LOD), and limit of quantitation (LOQ).

In the research article by J. Bharati et al. [53], a stability-indicating reversed-phase ultra-performance liquid chromatography (RP-UPLC) method was established for the simultaneous determination of Montelukast sodium and Levocetirizine dihydrochloride in liquid pharmaceutical dosage forms. Chromatographic separation was accomplished on an AQUITY BEH Phenyl column (50mm x 2.1mm, 1.7µm) using gradient elution with a detector wavelength set at 231 nm. The optimized mobile phase was prepared by dissolving 2.72 grams of Potassium dihydrogen phosphate in 1 L of Milli Q water, followed by thorough mixing. To this solution, 2 ml of Triethyl amine was added, and the pH was adjusted to 6.5 using O-phosphoric acid. The resulting solution was filtered through a 0.22µ membrane filter and

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degassed by sonication, serving as solvent-A, while acetonitrile was utilized as solvent-B. The developed RP-UPLC method achieved efficient separation of Montelukast sodium and Levocetirizine dihydrochloride within a short runtime of 3.5 minutes.

Validation of the RP-UPLC method was conducted in accordance with the International Conference on Harmonization (ICH) guidelines. The validated method was successfully applied for the simultaneous estimation of Montelukast sodium and Levocetirizine dihydrochloride in various commercially available dosage forms.

High-Performance Liquid Chromatography (HPLC):

High-Performance Liquid Chromatography (HPLC) stands as the most commonly employed chromatographic method for the scrutiny of pharmaceuticals. This methodology is extensively utilized in the examination of related compounds outlined in pharmacopoeias and various assay techniques. The following table provides an overview of distinct HPLC methods validated through scientific research for the determination of antihistamines and antiasthmatics drugs, whether individually or in combination.

Table 2: Verified HPLC Techniques for the Quantification of Antihistaminic and Antiasthmatics in Isolation or Combination.

Matrix	Mobile Phase	Column	λ max (nm)	Flow rate (ml/min)	Linearity Range (µg/ml)	LOD (µg/ml)	LOQ (µg/ml)	Reference
DESLO	acetonitrile: bidistilled water (40:60)	Nucleosil 120-5 (4.0 mm x 150 mm, 5 µm)	242	0.75	1-100	0.4115	1.2469	[56]
DESLO	acetonitrile: bidistilled water (40:60)	Nucleosil 120-5 (4.0 mm x 150 mm, 5 µm)	242	0.75	5–100	-	-	[57]
DESLO MTKT	0.3 % triflouroacetic acid with water: acetonitrile (20:80)	ODS hypersil C18 (250 mm × 4.6 mm, 5µ)	230	1	40-60 80-120	4.066 11.51	12.32 34.89	[55]
DESLO MTKT	methanol: water: Acetic acid (90:10:0.05)	C 18 (250 mm × 4.8 mm ,5µm)	280	1	20-70 40-140	0.87 0.69	2.54 2.09	[69]
DESLO MTKT	Waters & Methanol (60:40) using K2HPO4buffer (PH: 8.6)	ECLEPSE XDB C8 (4.6 x 150 mm, 5µm)	261	0.8	50-150 50-150	2.759	9.19	[70]
DESLO MTKT	Orthophosporic acid (PH-2.1): Methanol (40:60)	YMC C18 (250, 4.6, 5µ)	278	1	05-15 10-30	0.429 0 .6593	1.429 2.1978	[71]
DESLO MTKT	Orthophosphoric acid and water (20:80)	Hypersil BDS C18 (250 mm × 4.6 mm 5)	280	1	05-15 10-30	0.087 0.176	0.292 0.587	[72]
DESLO MTKT	Acetonitrile : Methanol : water (35:40:25)	C18 (250 x 4.6 mm, 5µ)	256	1	50 - 300 100 – 600	9.78 15.62	29.66 46.88	[73]
DESLO MTKT	mixed buffer: methanol (40: 60) (pH 6.0 ±0.1 adjusted by using Ortho-	Zodiac C18 (100 x4.6 mm, 5µ)	261	1	2.5 – 15 5 - 30	0.081 0.084	0.246 0.254	[74]

	phosphoric acid)							
DESLO MTKT	0.01N pot.dihydrogen ortho-phosphate buffer and acetonitrile (40:60)	DS C8 (150 × 4.6mm, 5 µm)	280	1	2.5-15 5-30	0.01 0.01	0.04 0.03	[75]
DESLO MTKT	Acetonitrile:Methanol: water (15:80:05)	Imp Sil, C18 HS(250 mm x 4.6 mm 5µm)	280	1	2-10 10 – 50	0.522 1.384	0.584 1.268	[76]
MTKT	Acetonitrile: 0.1 *M* ammonium acetate (10:90)	Capcell pak MF Ph-1 (PC; 50 x 4.6 mm)	350	1	1–500	1	30	[58]
FEX	1% triethylamine phosphate (pH 2.7): acetonitrile: methanol (60:40 :)	i) Hypersil BDS C18 (250 × 4.6 mm,5 µm)	215	1.5	0.1-50	0.02	0.05	[59]
FEX	Phosphate buffer pH 7.4: methanol (35:65)	ii)KROMASIL-100-5 C-18 (250 x 4.6 mm 5 µm) ii) C18 Phenomenex (250 mm x 4.6 mm 5 µm) iii) NUCLEOSIL 100-5 C18 (250 x 4.6 mm 5 µm) iv) Discovery C18 (250 x 4.6 mm 5 µm) v) Hypersil ODS (250 x 4.6 mm 5 µm)	218	1	5–15	0.03	0.1	[77]
FEX	acetonitrile: water (50:50)	Cap Cell Pack C18 (250 mm × 4.5 mm, 5µ)	224	1	50-175	0.27	0.84	[86]
FEX	Methanol : water (80:20)	C18 column (4.6×250mm,5µm)	220	1.2	7.5-40	0.603	1.829	[93]
FEX MTKT	0.5% Orthophosphoric acid pH adjusted to 6 (tri ethyl amine): Acetonitrile(40:60)	phenomenex C18 (150mm × 4.6 mm, 5 µm)	240	1	72-120 06-10	3.83 0.21	11.62 0.64	[60]
FEX MTKT	methanol : O-phosphoric acid (90:10) PH 6.8	Lichrospher® 100, RP-18e (250×4.6 mm, 5 µm)	226	1	2-10 24-120	0.28357 0.03622	0.859303 0.10975	[61]
FEX MTKT	methanol: acetonitrile: 1%	Hypersil ODS C18 (250 mm × 4.6	225	1	10-60 10-60	0.158	0.026	[62]

	trifluoroacetic acid (80:10:10)	mm, 5 µ)						
FEX MTKT	Methanol: Acetonitrile: Water (44:44:12)	Kromasil C18, 250 × 4.6 mm, 5 µm	241	1	0.6-120 0.05-10	0.094 0.6	0.028 0.89	[78]
FEX MTKT	phosphate buffer (pH 6.0) : methanol (25: 75)	Hypersil BDS C-18 (250 × 4.6 mm, 5 µm).	220	1	84–156 7–13	0.29 0.16	0.16 0.49	[79]
FEX MTKT	0.1M potassium dihydrogen orthophosphate buffer (pH 5.0) : methanol (60:40)	Phenomenex C18 (150 × 4.6 mm, 5µ)	220	1	10-100 5-15			[80]
FEX MTKT	acetonitrile: Triethylamine (80:20)	C18 (250×4.6 mm id, 5 µm particle size)	220	1	12-144 1-12	1.41 0.02	4.29 0.06	[81]
FEX MTKT	0.05 M NaH2PO4 in water pH 6.8 : Methanol (55:45)	C18 (250×4.6 mm id, 5 µm particle size)	258	1	60-80 5-15	1.9 0.9	3.1 1.3	[82]
FEX MTKT	0.05 m potassium di hydrogen ortho phosphate: acetonitrile (35:65)	C18 (250×4.6 mm id, 5 µm)	226	1	0.4 – 2.4 4.8 - 28.8	-	-	[83]
FEX MTKT	Sodium acetate buffer: acetonitrile : methanol (25:35:40)	X-bridge C18 (250 mm x4.6 mm, 5 mm	210	1	150- 450 12.5-37.5	3.0070 0.2931	9.1123 0.8884	[84]
FEX MTKT	Phosphate buffer pH-3 and Acetonitrile (20:80)	Hypersil BDS C18 (250 mm x 4.6 mm 5µm)	250	1	4.8-28.8 0.4-2.4	0.026 0.131	0.0814 0.3977	[85]
FEX MTKT	Phosphate buffer:acetonitrile (40:60,15:85 and 30:70) at different pH (3.5, 5.5 & 6.5)	C18 (4.6 mm × 150 mm, 5µm)	210	1.2	10-30 10-50	1.11796 2.2437	3.3877 7 6.7992	[14]
FEX MTKT	Acetonitrile: Phosphate buffer (pH2.8) (70:30)	ARP-C18 (250 mm × 4.5 mm, 5µ)	245	1	10-50.	0.003 0.09	9.78 9.96	[87]
FEX MTKT	Acetonitrile: phosphate buffer (75:25)	Chromasol C18 (250 mm × 4.5 mm, 5µ)	240	1	48-240 4-20	0.0130 0.0043	0.0070 0.0023	[88]
FEX MTKT	Triethylamine : acetonitrile (20:80)	shim-pack-solar C8 (4.6 x 250mm, 5µm)	226.	0.8	4-20 10-30	1.035 0.961	3.137 2.91	[89]
FEX	water : methanol	Hypersil-BDS C18	259	1	20-80	1.14	3.42	[90]

MTKT	(70:30)	(250mm × 4.6mm,5µ)				1.51	4.58	
FEX MTKT	Acetonitrile: buffer: methanol (50:30:20)	X bridge C18 (250 × 4.6 mm, 5 µm)	248	1.5	0.020-0.100 0.016-0.064	0.07 0.04	0.023 0.11	[91]
FEX MTKT	Acetonitrile: Water (40:60)	Hypersil C18 (4.6 x 250mm, 5µm)	220	1.0	75-375 5-25	13.8 0.7	41.8 2.1	[92]
LCTZ	acetonitrile & water (50:50)	Supelco C-18 (250mm x4.6mm, 0.5 mm)	230	1	5–40	0.75	5	[66]
LCTZ	Ammonium Acetate Buffer (pH 5.0) Methanol and Acetonitrile (20:55:25)	Prontosil C-18 (250mm ×4.6 mm, 5µ)	232	1	2--10	0.0057	0.174	[109]
LCTZ	acetonitrile: methanol: 20mM ammonium acetate buffer pH-5 (25:55:20)	Thermo C-18 (250mm x 4.6mm, 5µ)	232	1	2--10	0.0057	0.174	[110]
MTKT	o-phthaldialdeyde (OPA): Methanol (10:90)	Princeton SPHER ULTIMA C18 (250 x 4.6 mm, 5µm)	284	1	1-6	0.0011	0.0033	[68]
MTKT	Acetonitrile and ammonium acetate buffer (20 mM, pH adjusted to 5.5) (80:20)	Phenomenex Luna C18 (250mm x4.6mm x 5 mm)	345	1	20-2000	10	20	[116]
MTKT	2ml of Trifluroacetic acid: Mixture of Acetonitrile 250 ml and methanol 400 ml (350:650).	Meteoric core C18 (100mm x 4.6 mm,2.7µm)	255	1.5	120.39-802.57	-	-	[117]
MTKT	PH 6.6 buffer & acetonitrile (mobile phase A, (70:30) and pH 6.6 buffer & acetonitrile (mobile phase B (15:85).	Agilent Eclipse XDB C18 (octadecylsilane)100 mm × 4.6 mm, 5 µm)	220	1	0.1,1.3,2.6,3.9 and5.2	0.007	0.024	[118]
MTKT	Acetonitrile: Phosphate buffer (pH 3.0)	Phenomenex Luna C18 (250 × 4.6 mm, 5µm)	255	1	0-16	0.607	1.821	[119]
LCTZ MTKT	methanol: Trichloroacetic acid: Acetonitril (90:5:5)	Phenomenex (Torrance, CA) C18 (250 mm × 4.6 5 µm)	231	1	0.5-30 0.5-30	0.22 0.32	0.56 0.72	[63]

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LCTZ MTKT	ammonium acetate buffer of pH 3.5 (pH adjusted with glacial acetic acid) and methanol (15:85)	Macherey-Nagel C18 (4.6 mmx250 mm,5 µm)	230	0.6	3–12 6–18	0.52 0.28	1.6 0.9	[64]
LCTZ MTKT	0.02M phosphate buffer and Methanol, (20:80)	Inertsil extended C18 (250 x 4.6 mm, 5µm)	226	1.5	10-100 20-200	0.3 0.4	0.9 1.23	[65]
LCTZ MTKT	disodium hydrogen phosphate buffer (0.02 M): Methanol (25: 75) pH adjusted to 7 with ortho-phosphoric acid	BDS Hypersil C18 (250 x 4.6 mm, 5µm)	231	1	1-10 2-20	0.5 0.2	0.8 0.6	[47]
LCTZ MTKT	mixture of 0.05 (M) Potassium Dihydrogen Phosphate Buffer of pH 7.5 and Methanol in (20:80)	L7 column Hypersil Gold (250 mm × 4.6 mm, 5µm)	225	1.2	10-260 10-350	2.26 2.41	6.85 7.3	[95]
LCTZ MTKT	acetonitrile: 0.5 % triethylamine in water (90:10) pH adjusted to 5.5with orthophosphoric acid	phenomex-luna (250 mm × 4.6 mm, 5µ)	231	0.8	2-32 3-30	0.00028 0.0032	0.0008 6 0.0094	[96]
LCTZ MTKT	0.02M potassium dihydrogen phosphate buffer solution : methanol (40:60, pH 5.0)	SUPELCOSILTM, LC-8 (15cm × 4.6 mm, 5 5µm)	218	1	5.0 - 20.0 10.0 - 40.0	2.493 0.489	7.553 1.482	[97]
LCTZ MTKT	10 Mm acetonitrile: ammonium acetate (65:35) pH 4.2 was adjusted with orthophosphoric acid)	Atlantis C-18 (4.6 mm ×150 mm, 5µm)	230	1	25-75 50-150	0.05 0.10	0.17 0.33	[98]
LCTZ MTKT	methanol and sodium hydrogen phosphate and orthophosphoric acid buffer (pH 7.0) (75:25)	Hypersil BDS C18 (250 mm × 4.6 mm, 5 µ)	230	1.2	4-14 8-28	0.0525 0.0173	0.188 0.056	[99]
LCTZ MTKT	Ammonium acetate: acetonitrile (40:60)	Phenomenox-RPC18 (250 mm × 4.6 mm, 5 µ)	215	1.5	4–20 8–40	0.125 0.005	0.38 0.015	[100]
LCTZ MTKT	Buffer and methanol (70:30)	Symmetry C18 (4.6× 150 mm, 3.5 mm)	232	1	25 – 150 12.5 – 75	0.18 0.31	0.75 1.21	[101]
LCTZ MTKT	phosphate buffer (pH 4) :	XTerra C8 (4.6 x 150 mm, 3.5 µm)	230	0.8	30-70 30-70	3.36 9.90	3.2 9.86	[102]

	acetonitrile (60:40)							
LCTZ MTKT	Buffer and acetonitrie (90: 10)	Hypersil C18 (100 x 4.6 mm, 3 µm)	230	1	6.22-37.34 12.42-74.52	-	-	[103]
LCTZ MTKT	Buffer: Methanol (35: 65)	Inertsil ODS (250 x 4.6 mm, 5µ)	234	1.5	2-10 4-20	1.63 1.85	4.14 3.42	[38]
LCTZ MTKT	triethyl amine: Methanol (25:75)	Inertsil ODS C18 (150 × 4.6 mm, 5µm)	240	0.8	25-150 50-300	3.06 3.15	9.29 9.55	[104]
LCTZ MTKT	phosphate buffer: acetonitrile (40:60)	Kromasil C-18, (250 ×4.6 mm, 5µm)	225	1	5 – 30 10 - 60	0.02 0.08	0.06 0.25	[105]
LCTZ MTKT	Phosphatebuffer: acetonitrile (55:45)	HypersilC18 (250mm × 4.6mm ,5µm)	228	1	25-75 40-120	-	-	[106]
LCTZ MTKT	Ammonia acetate Buffer pH3 : acetonitrile (15:85)	Agilent C18 (150mmx 250mm 4.6)	230	1.2	4-24 4-24	0.97 1.12	2.94 3.39	[107]
LCTZ MTKT	Phosphate buffer:acetonitrile (40:60)	Hypersil BDS C18 (250 mm × 4.6 mm, 5 µm)	230	1	12.56–37.68 23.78–71.20	0.079 0.156	0.239 0.473	[108]
LCTZ MTKT	methanol, acetonitrile and 20 mM ammonium acetate buffer (60:30: 10)	Hypersil ODS C18 (250 × 4.6 mm, 5µm)	232	0.8	20-120 2-12	0.21 0.35	0.63 1.07	[111]
LCTZ MTKT	phosphatebuffer :acetonitrile (30:70 pH 3.6)	Thermosil C18 (150mm ×4.6 mm, 3.5µm)	232	1	50-90 100-140	0.11 0.04	0.36 0.12	[112]
LCTZ MTKT	0.02Mpotassium dihydrogen phosphate buffer solution: methanol (40:60, pH 5.0).	SUPELCOSILTM, LC-8 (15mm × 4.6 mm, 5 µm)	218	1	5.0 to 20 10 - 40	2.493 0.489	7.553 1.482	[113]
LCTZ FEX	Phosphate buffer pH 6.0 and Acetonitrile (68:32)	C18 (150 mm × 4.6mm, 5µm)	230	1	5–40 6–48	6.8 9.0	22.7 30.0	[114]
LCTZ MTKT	methanol:10 mMammonium acetate buffer pH 4.0 (85:15)	KinetexC 18 (150 mm x 4.6 mm, 5 µm)	240	1	0.5-100 0.5-100	0.16 0.05	0.47 0.16	[115]
LCTZ FEX	Methanol : water (80:20) at pH 3.5	Purospher STAR RP18 end-capped (25 cm × 0.46 cm, 5 µm)	230	1	5–50 0.553–50	0.16 0.19	0.55 5.00	[94]

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Conclusion:

Various analytical techniques are available for the evaluation of antihistamine and anti-asthmatic medications in pharmaceutical dosage forms and biological samples such as serum and plasma. In comparing the suggested UV strategies, which are practical for routine assessments due to their cost-effectiveness and speed, with the provided High-Performance Liquid Chromatography (HPLC) approaches, it becomes evident that the latter are more straightforward, accurate, and reliable. Moreover, HPLC methods offer enhanced sensitivity in the detection of analyte chemicals. As a result, HPLC stands out as the preferred choice for the analysis of these medicines. The advantages of HPLC extend beyond its accuracy and reliability, encompassing the simultaneous evaluation of multiple components. This feature adds significant value to the analytical process, making HPLC an indispensable tool in pharmaceutical analysis, especially when dealing with complex formulations or biological matrices. The robustness, precision, and versatility of HPLC methodologies make them indispensable for ensuring the quality, safety, and efficacy of antihistamine and anti-asthmatic drugs in diverse formulations and clinical samples.

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Reference:

1. Galli, S. J.; Tsai, M.; Piliponsky, A. M. The development of allergic inflammation. Nature 2008, 454(7203), 445–454.
2. Ibrahim, F. A.; El-Enany, N.; El-Shahenya, R. N.; Mikhail, I. E. Simultaneous determination of desloratadine and montelukast sodium using second derivative synchronous fluorescence spectrometry enhanced by an organized medium with applications to tablets and human plasma. Luminescence 2014, 30(4), 485-494.
3. Kumar, N. R.; Vaidhyalingam, V. Development and validation for the simultaneous quantification of montelukast and levocetirizine by UV, RP-HPLC, and HPTLC methods in a tablet. JPAR 2016, 5(3), 487-496.
4. Sreejith, K. R.; Rajagopal, P. L.; Neethu, N.; Ashraf, F. A comprehensive review on analytical methods for the simultaneous estimation of montelukast sodium and fexofenadine hydrochloride. WJPLS 2018, 8, 193-200.
5. El-Enany, N.; El-Sherbiny, D.; Belal, F. Spectrophotometric, Spectrofluorometric, and HPLC determination of desloratadine in dosage Forms and Human Plasma. Chem. Pharm. Bull. 2007, 55(12), 1662-1670.
6. Aslan, N.; Erden, P. E.; Canel, E.; Kilic, E. Development and validation of a potentiometric titration method for the determination of montelukast sodium in a pharmaceutical preparation and its protonation constant. Bulgarian Chem. Commun. 2014, 46(3), 497–502.
7. Sheikh, E. R.; Hassan, S. W.; El-Gabry, M. M.; Gouda, A. A.; Idris, S. S.; Salem, M. O.; Ali, S. I. Development and validation of spectrophotometric methods for the determination of leukotriene receptor antagonist montelukast sodium in bulk and pharmaceutical formulations. Asian J. Pharm Clin Res. 2020, 13(5), 86-92.
8. Raghu, M. S.; Shantaram, C. S.; Kumar, Y. K. Application of bromate-bromide mixture as a green brominating agent for the determination of fexofenadine hydrochloride in pharmaceutical dosage form. J Anal Pharm Res. 2018, 7(1), 14-21.
9. Pandey, K. A.; Dwivedi, D. A Validated Titrimetric Method for the Quantitative Estimation of Fexofenadine Hydrochloride in Pure form and in their Pharmaceutical Preparations with Pyridinium Fluoro Chromate (PFC) as Reagent. I J ChemTech Research. 2017, 10(10), 236-240.
10. Rajan, V. R.; Swapnil, S. A. A validated non-aqueous potentiometric titration method for quantitative determination of fexofenadine from pharmaceutical

preparation. J. Chem. Pharm. Res. 2013, 5(4), 286-289.

11. Aslan, N.; Erden, P. E.; Canel, E.; Kilic, E. Development and validation of a potentiometric titration method for the determination of montelukast sodium in a pharmaceutical preparation and its protonation constant. Bulgarian Chem. Commun. 2014, 46(3), 497–502.
12. Choudhari, V.; Kale, A.; Abnawe, S.; Kuchekar, B.; Gawli, V.; Patil, N. Simultaneous determination of montelukast sodium and levocetirizine dihydrochloride in Pharmaceutical Preparations by ratio derivative spectroscopy. Int. J. PharmTech Res. 2010, 2(1), 04-09.
13. Padmavathi, Y.; Babu, R. N.; Rohini, K.; Khanam, A. A.; Padmavathi, R. Development and validation of chemometric assisted Fourier Transform Infrared Spectroscopic method for simultaneous determination of montelukast Sodium and fexofenadine hydrochloride in pharmaceutical dosage forms. RJPT. 2022, 15(5), 2261-2267.
14. Agha, S. D.; El-Zien, H. Solid-state compatibility studies between montelukast Sodium and levocetirizine. Asian J. Pharm Clin. Res. 2018, 11(33), 368-374.
15. Yurtdaş-Kırımlıoğlu, G. A promising approach to design thermosensitive in situ gel based on solid dispersions of desloratadine with Kolliphor ® 188 and Pluronic ® F127. J. Thermal Analy. and Calorimetry. 2021, 147(22), 1307–1327.
16. Ragab, A. A. M.; Youssef, M. R. Simultaneous determination of montelukast and fexofenadine using Fourier transform convolution emission data under non-parametric linear regression method. J. Fluoresc. 2013, 23(6), 1329–1340.
17. Ponnurua, S. V.; Challa, B. R.; NadendR. Quantification of desloratadine in human plasma by LC-ESI-MS/MS and application to a pharmacokinetic study. J. Pharm. Analysis. 2012, 2(3), 180–187.
18. Muppavarapu, R.; Guttikar, S.; Kamarajan, K. LC-MS/MS method for the simultaneous determination of desloratadine and its metabolite 3-hydroxydesloratadine in human plasma. IJPBS. 2014, 4(2), 151-161.
19. Xu, H.; Li, X.; Chen, W.; Chu, N. N. Simultaneous determination of desloratadine and its active metabolite 3-hydroxydesloratadine in human plasma by LC/MS/MS and its application to pharmacokinetics and bioequivalence. JPBA. 2007, 45(4), 659–666.
20. Yang, L.; Clement, P. R.; Kantesaria, B.; Reyderman, L.; Beaudry, F.; Grandmaison, C.; Donato, D. L.; Masse, R.; Rudewicz, J. P. Validation of a sensitive and automated 96-well solid-phase extraction liquid chromatography–tandem mass spectrometry method for the determination of desloratadine and 3-hydroxydesloratadine in human plasma. J. Chrom B. 2003, 792(2), 229–240.
21. Srinubabu, G.; Patel, S. R.; Shedbalkar, P. V.; Rao, A. A.; Rao, N. M.; Bandaru, R. V. V. Development and validation of high-throughput liquid chromatography–tandem mass spectrometric method for simultaneous quantification of loratadine and desloratadine in human plasma. J. ChromB. 2007, 860(2), 202–208.
22. Wichitnithad, W.; Jithavech, P.; Sanphanya, K.; Vicheantawatchai, P.; Rojsitthisak, P. Determination of Levocetirizine in Human Plasma by LC–MS-MS: Validation and Application in a Pharmacokinetic Study. J. Chroma. Scie. 2015, 53(10), 1663–1672.
23. Yamane, N.; Tozuka, Z.; Sugiyama, Y.; Tanimoto, T.; Yamazaki, A.; Kumagai, Y. Microdose clinical trial quantitative determination of fexofenadine in human plasma using liquid chromatography/electrospray ionization tandem mass spectrometry. J. Chrom B. 2002, 766(2), 227–233.
24. Hofmann, U.; Seiler, M.; Drescher, D.; Fromm, F. M. Determination of fexofenadine in human plasma and urine by

liquid chromatography–mass spectrometry. J. Chrom. B. 2002, 766(2), 227–233.

25. Muppavarapu, R.; Guttikar, S.; Rajappan, R.; Kamarajan, K.; Mullangi, R. Sensitive LC-MS/MS-ESI method for simultaneous determination of montelukast and fexofenadine in human plasma: application to a bioequivalence study. Biomed. Chromato. 2014, 28(8), 1048–1056.
26. Papp, R.; Luk, P.; Wayne M. Mullett, E. K. A rapid and sensitive method for the quantitation of montelukast in sheep plasma using liquid chromatography/tandem mass spectrometry. J. Chrom. B. 2007, 858(1-2), 282–286.
27. Bharathi, V. D.; Hotha, K. K.; Jagadeesh, B.; Mullangi, R.; Naidu, A. Quantification of montelukast, a selective cysteinyl leukotriene receptor (CysLT1) antagonist in human plasma by liquid chromatography–mass spectrometry validation and its application to a human pharmacokinetic study. Biomed. Chromatogr. 2009, 23(8), 804–810.
28. Sakur, A. A.; Nashed, D.; Noureldin, I. Green potentiometric determination of some of the third-generation antihistamines fexofenadine, desloratadine, and levocetirizine by using new carbon paste electrodes. Talanta Open. 2022, 5(0), 1–6.
29. Sakur, A. A.; Nashed, D.; Noureldin, I. Selective Consecutive Determination of desloratadine and montelukast sodium in their pure and binary dosage form based on pencil graphite electrochemical sensors. J. of Analy. Metho. Chem. 2021, 4(1), 1–8.
30. Nashed, D.; Noureldin, I.; Sakur, A. A. New pencil graphite electrodes for potentiometric determination of fexofenadine hydrochloride and montelukast sodium in their pure, synthetic mixtures, and combined dosage form. BMC Chemistry. 2020, 14(60), 1–9.
31. Kumar, N. E.; Sireesha, D.; Bakshi, V.; Haque, A. M.; Harshini, S. Simultaneous estimation of desloratadine and montelukast in combined pharmaceutical dosage form by UV spectroscopy. IJIPSR 2014, 2(11), 2765-2772.
32. Bankar, M. R.; Patel, B. D. Simultaneous estimation of montelukast sodium and desloratadine by ratio spectra derivative spectrophotometry method in combined dosage forms. J. Chem. Pharm. 2013, 5(1), 193-199.
33. Jain, R. R.; Patil, P. O.; Bari, S. B. Simultaneous estimation of montelukast sodium and desloratadine in bulk and in tablet formulation by UV-spectrophotometry. Indian Drugs 2013, 50(3), 30-35.
34. Sowjanya, G.; Sastri, T. K. UV spectrophotometric method development and validation for simultaneous determination of fexofenadine hydrochloride and montelukast sodium in tablets. WJPPS 2017, 6(10), 780-789.
35. Sharma, K.; Bhatia, R.; Anghore, D.; Singh, V.; Khare, R.; Rawal, K. R. Development and validation of UV spectrophotometric and RP-HPLC Methods for Simultaneous estimation of fexofenadine hydrochloride, montelukast sodium, and ambroxol hydrochloride in tablet dosage form. TACL 2018, 8(6), 829 - 843.
36. Chabukswar, R. A.; Choudhari, P. V.; Sharma, N. S.; Bari, A. N.; Ghuge, R. Ratio derivative spectrophotometry method for simultaneous estimation of montelukast and Fexofenadine HCl in their combined dosage form. Asian J. Research Chem. 2012, 5(5), 637-641.
37. Ashour, S.; Khateeb, M. New kinetic spectrophotometric method for the determination of fexofenadine hydrochloride in pharmaceutical formulations. Inte. J. Spectro. 2014, doi.org/10.1155/2014/308087.
38. Kumar, R. N.; Vaidhyalingam, V. Development and validation for the simultaneous quantification of montelukast and levocetirizine by UV, RP-HPLC, and HPTLC methods in tablets. IJPA 2016, 5(3), 487-496.

39. Patel, K. N.; Chouhan, P.; Paswan, K. S.; Soni, K. P. Development and validation of a UV spectrophotometric method for simultaneous estimation of the combination of Montelukast sodium in the presence of levocetirizine. Der Pharmacia Lettre 2014, 6(3), 313-321.
40. Tamilselvi, N.; Idris, H. S. A.; Basheer, M.; Nidhin, L. L. Development and validation of a spectrophotometric method for simultaneous determination of montelukast Sodium and levocetirizine hydrochloride. J. Pharm. Inn. Res. June-2015, 2(2), 6-10.
41. Sankar, A. S. K.; Baskar, G. N.; Nagavalli, D.; Anandakumar, K.; Vetrichelvan, T. Simultaneous estimation of montelukast sodium and levocetirizine hydrochloride from tablet dosage form. ReseJ. Pharm. and Tech. Oct.-Dec. 2009, 2(4), 743-745.
42. Mali, D. A.; Patil, M. Estimation of levocetirizine in bulk and formulation by second order derivative area under curve UV-Spectrophotometric Methods. Asian J. Pharm. Res. 2015, 5(3), 51-56.
43. Mali, D. A.; Bathe, R.; Patil, M.; Tamboli, A. Zero order and area under curve spectrophotometric methods for determination of Levocetirizine in pharmaceutical formulation. IJASR 2015, 1(6), 270-276.
44. Ravi, T. K.; Gandhimathi, M.; Varghese, A. Simultaneous estimation of desloratadine and montelukast sodium by HPTLC. RRJPPS June 2021, 10(6), 17-26.
45. Vekaria, V.; Muralikrishna, S. K.; Sorathiya, M. Development and validation of HPTLC method for simultaneous estimation of montelukast sodium and fexofenadine hydrochloride in combined dosage form. Der Pharmacia Lettre 2012, 4(3), 755-762.
46. Tandulwadkar, S. S.; More, J. S.; Rathore, S. A.; Nikam, R. A.; Sathiyanarayanan, L.; Mahadik, R. K. Method development and validation for the simultaneous determination of fexofenadine hydrochloride and montelukast sodium in drug formulation using normal phase high-performance thin-layer chromatography. ISRN Analy. Chem. 2012, 1-7. doi:10.5402/2012/924185.
47. Rathore, S. A.; Sathiyanarayanan, L.; Mahadik, R. K. Development of validated HPLC and HPTLC methods for simultaneous determination of levocetirizine dihydrochloride and montelukast sodium in bulk drug and pharmaceutical dosage form. Pharm. Analyti. Acta 2010, 1(1), 1-6.
48. Rote, R. A.; Niphade, S. V. Determination of montelukast sodium and levocetirizine dihydrochloride in combined tablet dosage form by HPTLC and first-derivative spectrophotometry. J. Liquid Chromat. & Rel. Tech. 2011, 34(3), 155–167.
49. Bober, K.; Płonka, M.; Miszczyk, M. Desloratadine analysis as a pharmaceutical preparation and after accelerating ageing. Curr. Iss. Pharm. Med. Sci. 2015, 28(3), 181-185.
50. Rao, D. D.; Satyanarayana, V. N.; Reddy, M. A.; Sait, S. S.; Chakolea, D.; Mukkanti, K. A validated stability-indicating UPLC method for desloratadine and its impurities in pharmaceutical dosage forms. J. Pharm. &Biomed. Analy. 2010, 51(3), 736–742.
51. Mustafa, M.; Amuthalakshmi, S.; Nalini, C. N. Simultaneous UPLC of Fexofenadine HCl and Montelukast Sodium Tablets. RJPT 2017, 10(2), 557-561.
52. Kuna, M.; Dannana, S. G. Stability-indicating UPLC method for estimation of montelukast and fexofenadine simultaneously in the presence of stress degradation products. J. Global Trends Pharm Sci. 2017, 8(4), 4542-4553.
53. Bharati, J. Naidu, C. B.; Sumanth, M.; Rajana, N. A rapid, RP-UPLC assay method for simultaneous determination of montelukast sodium and levocetirizine dihydrochloride in pharmaceutical dosage forms. WJPPS 2015, 4(11), 1409-1421.
54. Sangeetha, S.; Alexandar, S.; Jaykarn, B. Simultaneous estimation of acebrophylline, montelukast Sodium, and levocetirizine by

RP-UPLC method in combined dosage forms. Acta Scienti. Pharma. Scien. 2020, 4(10), 52-55.

55. Mistry, M.; Patel, K.; Shah, K. S. Stability Indicating HPLC Method for the simultaneous estimation of montelukast sodium and desloratadine in its dosage form. Inventi Rapid Phar. Anal. & Q. A. 2015, 4, 1-5.
56. Kirimlioglu, Y. G. Host-guest inclusion complex of desloratadine with 2-(hydroxy) propyl-β-cyclodextrin (HP-β-CD) Preparation, binding behaviors and dissolution properties. J Res Pharm. 2020, 4(5), 693-707.
57. Yurtdas Kirimlioglu, G. A promising approach to design thermosensitive in situ gel based on solid dispersions of desloratadine with Kolliphor and Pluronic. J. Thermal Anal. & Calorimet. 2022, 147(1), 1307–1327.
58. Ochiai, H.; Uchiyama, N.; Takano, T.; Hara, K.; Kamei, T. Determination of montelukast sodium in human plasma by column-switching high-performance liquid chromatography with fluorescence detection. J. Chrom. B. 1998, 713(2), 409–414.
59. Maher, M. H.; Sultan, A. M.; Olah, V. I. Development of validated stability-indicating chromatographic method for the determination of fexofenadine hydrochloride and its related impurities in pharmaceutical tablets. Chem. Central J. 2011, 5(76), 1-10. doi: 10.1186/1752-153X-5-76.
60. Tamilselvi, N.; Sruthi, K. Development of validated HPLC method for simultaneous estimation of fexofenadine hydrochloride and montelukast sodium in tablet dosage form. IJPSR. 2012, 3(12), 4876-4881.
61. Pankhaniya, M.; Patel, P.; Shah, S. J. Stability indicating HPLC method for simultaneous determination of montelukast and fexofenadine hydrochloride. Indian J. Pharm Sci. 2013, 75(3), 284-290.
62. Chundawat, S. R.; Sarangdevot, S. Y.; Rathore, S. P. R; Sisodiya, S. D.; Rathore, S. U. Method development and validation for simultaneous estimation of montelukast and fexofenadine in pharmaceutical dosage form by HPLC method. Resea J. Pharm. and Tech. 2013, 6(10), 1102-1106.
63. Patel, K. N.; Patel, S.; Pancholi, S. S. HPLC method development and validation for simultaneous estimation of montelukast sodium and levocetirizine dihydrochloride in pharmaceutical dosage forms. 2012, 4(2), 241-243.
64. Mittal, M.; Upadhyay, Y.; Anghore, D.; Kumar, A.; Rawal, K. R. Simultaneous estimation of acebrophylline, montelukast and levocetirizine dihydrochloride in marketed formulation by high-performance liquid chromatography method. Pharm Aspire. 2018, 10(1), 23-28.
65. Harish, V.; Sahu, S. Method development and validation of cetirazine HCl and montelukast sodium. Euro. J. of Mole & Clini. Medi. 2020, 7(7), 5855-5874.
66. Gunjal, P. R.; Raju, G.; Babu, R A.; Mallikarjun, N.; Shastri, N.; Srinivas, R. HPLC and LC-MS studies on stress degradation behavior of levocetirizine and development of a validated specific stability-indicating method. J. Liq. Chro. & Rel Tech. 2011, 34(12), 955–965.
67. Shakya, K. A.; Arafat, A. T.; Hakooz, M. N.; Abuawwad, N. A.; Al-Hroub, H.; Melhim, M. High-performance liquid chromatographic determination of montelukast sodium in human plasma, application to Bioequivalence Study. Acta Chrom. 2014, 26(3), 457-472.
68. Phadtare, G. D.; Pawar, R. A.; Kulkarni, R. R.; Patil, K. G. Method development and validation of montelukast sodium in bulk and tablet formulation by HPLC. Asian J. Research Chem. 2016, 9(7), 339-342.
69. Chhatrala, R. V.; Patel, J. Simultaneous estimation of montelukast sodium and desloratadine by RP-HPLC in their

marketed formulation. Intern. J. of ChemTech Rese. 2012, 4(4), 1402-1407.

70. Mallesham.; Geetha, K.; Rao, M. U. V.; Ramarao, N. Simultaneous estimation of desloratadine and montelukast in bulk and pharmaceutical formulations by RP-HPLC. IJITR. 2014, 2(5), 1181-1186.
71. Mastanamma, S.; Rambabu, G.; Saidulu, P.; Tejaswini, I. S. Designing of forced degradation studies and development of validated stability-indicating method for simultaneous estimation of desloratadine and montelukast sodium in their formulation. Der Pharmacia Lettre. 2015, 7(3), 39-47.
72. Gandhi, M. B.; Rao, L. A.; Rao, V. J. Method development and Validation for Simultaneous Estimation of Montelukast Sodium and Desloratadine by RP-HPLC. AJAC. 2015, 6(8), 651-658.
73. Patel, K. K.; Suthar, B.; Luhar, V. S.; Narkhede, B. S. Development and Validation of Stability Indicating RP-HPLC Method for Montelukast Sodium and Desloratadine in Pharmaceutical dosage Form. J PharmSciBioscientific Res. 2016, 6(3), 291-299.
74. Challa, R.; Naidu, S. V. N. Development and validation of stability indicating RP-HPLC method for simultaneous determination of desloratadine and montelukast sodium in pharmaceutical dosage form. IJPAR. 2016, 5(2), 294-309.
75. Mamatha, J.; Devanna, N.; RP-HPLC-PDA Method for Simultaneous quantification of montelukast, acebrophylline, and desloratadine tablets. AJCHM. 2018, 30(6), 1383-1386.
76. Kishore, N. R.; Anjaneyulu, N.; Sri, T.; Swetha, V. B.; Bhavani, M. Method development and validation for simultaneous estimation of desloratadine and montelukast sodium by RP-HPLC. wjpps. 2018, 7(6), 641-653.
77. Arayne, S. M.; Sultana, N.; Shehnaz, H.; Haider, A. RP-HPLC method for the quantitative determination of fexofenadine hydrochloride in coated tablets and human serum. Med Chem Res. 2009, 20(1), 55-61.
78. Chabukswar, R. A.; Choudhari, P. V.; Jagdale, C. W.; Sharma, N. S.; Bari, A. N.; Pagare, D. B. Simultaneous Estimation of Montelukast Sodium and Fexofenadine HCL in Pharmaceutical Formulation by RP-LCPDA. IJPSR. 2012, 3(1), 241-248.
79. Kakade, C. T.; Rathore, S. A.; Lohidasan, S.; Mahadik, R. K. Separation and determination of fexofenadine hydrochloride and montelukast sodium in tablet dosage form using RP-HPLC. AIJRPLS. 2016, 1(1), 54-65.
80. Kumar, P. K.; Haque, A. M.; Kumar, P. T.; Nivedita, G.; S. Amrohi, H.; Prasad, V. V. L. N.; Diwan, V. P. Simultaneous determination of montelukast sodium and fexofenadine hydrochloride in a combined dosage form by using RP-HPLC method. World J. Chem. 2012, 7(2), 42-46.
81. Godavarthi, M.; Sujana, K.; Rani, P. A. Method development and validation for the simultaneous determination of fexofenadine hydrochloride and montelukast sodium using RP-HPLC. IOSR J. Pharmacy. 2012, 5, 41-48.
82. Singh, R. R.; Rathnam, V. M. A stability indicating RP-HPLC method for the estimation of montelukast sodium and fexofenadine hydrochloride in pharmaceutical preparations. Int. J. of Pharm. Pharm. Sci. 2012, 4(2), 587-593.
83. Ravisankar, M.; Uthirapathy, S.; Thangadurai, A.; Munusamy, J.; Dhanapal. Simultaneous estimation of fexofenadine hydrochloride and montelukast sodium in bulk drug and marketed formulation by RP-HPLC method. IRJP. 2012, 3(4), 356-359.
84. Vekaria, H.; Limbasiya, V.; Patel, P. Development and validation of RP-HPLC method for simultaneous estimation of montelukast sodium and fexofenadine hydrochloride in combined dosage form. Jopr. 2013, (6)1, 134-139.
85. Swarnalatha, G.; Vijayakumar, B.; Jothieswari, D.; Poojitha, M.;

Chandrakumar, R.A.; Krishnan, G. P. RP-HPLC method development and validation for simultaneous estimation of montelukast sodium and fexofenadine HCl in a pharmaceutical dosage form. IJMCA. 2016, 6(1), 44-51.

86. Malothu, N.; Paladugu, T.; Katamaneni, P. Development and validation of RP-HPLC method for determination of fexofenadine in pharmaceutical dosage form by using levocetirizine as an internal standard. IJPBSTM. Jul-Sep 2018, 8(3), 619-625.
87. Mohite, P.; Deshmukh, V.; Pandhare, R.; Dhonde, P. Development and validation of RP-HPLC method for the simultaneous estimation of montelukast and fexofenadine. Open J. of Pharm. Scienc. 2021, 1(1), 1-7.
88. Jayaseelan, S.; Kannappan, N.; Ganesan, V. Simultaneous optimization of the resolution and analysis time in RP-HPLC of fexofenadine and montelukast using Derringer's desirability function. Annals of R.S.C.B. 2021, 25(2), 3597–3615.
89. Niharika, S.; Ravichandran, S. Analytical method development and validation for simultaneous estimation of montelukast sodium, fexofenadine hydrochloride, and acebrophylline in bulk and their formulation by RP-HPLC. IJRSR. 2022, 13(3), 700-705.
90. Khatri, S. Bioanalytical method development and validation for the estimation of levocetirizine in blood plasma by using RP-HPLC. JDTT. 2018, 8(5-s), 288-292.
91. Kumar, P. R.; Kumar, R. R. Validated stability-indicating isocratic RP-HPLC method of estimation of montelukast sodium and fexofenadine hydrochloride in bulk and in solid dosage by Vieordt's method. J. Chem. Pharm. Res. 2017, 9(5), 237-243.
92. Ukundamma, V.; Vageesh, N. M.; Kistayya, C. Simultaneous estimation of montelukast and fexofenadine in pure and pharmaceutical dosage form by using RP-HPLC method. Innov. Inter. J.of Medic. & Pharm. Sci. 2018, 3(1), 14-17.
93. Chinababu, D.; Supraveena, K.; Reddy, S. S. L.; Chetty, M. C.; Gopal, M. N. Stability indicating method development and validation of fexofenadine hydrochloride in bulk and its pharmaceutical dosage form by using RP-HPLC. IAJPS. 2021, 8(11), 202-207.
94. Arayne, S. M.; Sultana, N.; Mirza, Z. A.; Siddiqui, A. F. Simultaneous determination of gliquidone, fexofenadine, buclizine & levocetirizine in dosage formulation and human serum by RP-HPLC. J. of Chromato Sci. May-Jun 2010, 48(5), 382-385.
95. Basu, A.; Basak, K.; Chakraborty, M.; Rawat, S. I. Simultaneous RP-HPLC estimation of levocetirizine hydrochloride and montelukast Sodium in tablet dosage Form. Int. J. ChemTech Res. 2010, 3(1), 405-410.
96. Babu, S. R.; Bharadwaj, A. K.; Arjun, N. C.; Nagaraj; Prasad, V. A Validated Comparative LC and ratio first derivative spectrophotometric method for the simultaneous determination of levocetirizine dihydrochloride and montelukast sodium in bulk and Pharmaceutical dosage forms. JAPS. 2012, 2(8), 243-249.
97. Somkuwar, S.; Pathak, A. K. Simultaneous estimation of levocetirizine dihydrochloride and montelukast sodium by RP-HPLC method. Pharmacia. 2012, 1(3), 90-94.
98. Raja, T.; Rao, L. A. Development and validation of a Reversed Phase HPLC method for simultaneous determination of levocetirizine and montelukast sodium in tablet dosage form. IJRPC. 2012, 2(4), 1057-1063.
99. Gupta, N. K.; Babu, A. M.; Gupta, P. Simultaneous estimation of montelukast sodium and levocetirizine HCl by RP-HPLC method development in pharmaceutical tablet dosage form. Int. J. of Pharm. Erudi. Feb 2013, 2(4), 32-39.
100. Srividya, P.; Tejaswini, M.; Sravanthi, D.; Nalluri, N. B. Simultaneous analysis of levocetirizine dihydrochloride, ambroxol hydrochloride, and montelukast sodium by

RP-HPLC-PDA method. J. Liqu. Chro. & Relat. Tech. 2013, 36(20), 2871–2881.

101. Kumar, R. B. K.; Girija, S. V.; Komala, G.; Priyadarshini, P.; Naresh, P. A Novel validated stability indicating Chromatographic method for the simultaneous estimation of levocetrizine and montelukast in the combined dosage form by RP-HPLC. Int. J. Chem. Pharm. Sci. 2013, 1(2), 80-93.
102. Rao, P. M.; Srilakshmi, M.; Teja, R. B.; Rao, N. D. Analytical method development and validation of levocetirizine hydrochloride and montelukast sodium in combined tablet dosage form by RP-HPLC. RJPBCS. 2014, 5(6), 1010-1021.
103. Jayasimha, N.; Reddy, K. V.; Goud, K. S. Development and validation of RP-HPLC method for simultaneous determination of montelukast sodium and levocetirizine dihydrochloride tablets. Der Pharmacia Sinica. 2015, 6(9), 8-14.
104. Gohil, U. R.; Chudhary, A.; Raval, J. R. Development and validation of RP-HPLC method for estimation of montelukast sodium and levocetirizine hcl in tablet. Wjpps. 2016, 5(6), 880-894.
105. Penta, S. C. D.; Sankar, G. D.; Forced degradation studies of combination of levocetrizine, ambroxol and monteleukast by validated RP-HPLC method. iajpr. 2017, 7(7), 2231-6876.
106. Naaz, A.; Vani, R. Simultaneous estimation of montelukast and levocetirizine in its bulk and liquid dosage form by RP- HPLC. iajpr. 2015, 5(10), 3338-3347.
107. Kumar, N.; Anghore, D.; Rawal, K. R.; Pandey, A. RP-HPLC and UV method development for simultaneous estimation of doxofylline, montelukast and levocetirizine dihydrochloride in pharmaceutical dosages form. TACL. 2018, 8(2), 195 - 204.
108. Sonawane, J. K.; Patil, D. A.; Jadhav, S. B.; Jadhav, S. L.; Patil, B. P. Stability Indicating RP-HPLC method development and validation for simultaneous quantification of antihistaminic & anti-asthmatic drug in bulk and tablet dosage form. jjbps. January-June 2020, 8(1), 12-22.
109. Jain, N.; Jain, K. D.; Jain, R.; Patel, V. K.; Patel, P.; Jain, K. S. Bioanalytical method development and validation for the determination of levocetirizine in pharmaceutical dosage form and human plasma by RP-HPLC. JAPS. 2016, 6(10), 063-067.
110. Khatri, S. Bioanalytical method development and validation for the estimation of levocetirizine in blood plasma by using RP-HPLC. J. Drug Deli & Therap. 2018, 8(5-s), 288-292.
111. Butala, S.; Khan, T. Development and validation of RP-HPLC method for simultaneous estimation of montelukast sodium, levocetirizine dihydrochloride and acebrophylline in fixed-dose combination tablets. IJPSR. 2021, 12(9), 4851-4857.
112. Harika, C. H.; Vijaykumar, G.; Harinadhbabu, K. Development and validation of a RP-HPLC method for estimation of levocetirizine and montelukast in pharmaceutical dosage form. Int. J. Pharm. 2012, 2(3), 675-678.
113. Somkuwar, S.; Pathak, A. K. Simultaneous estimation of levocetirizine dihydrochloride and montelukast sodium by RP-HPLC method. Pharmacia. June 2012, (3), 90-94 I.
114. AlAani, H.; Alashkar, I. Development and validation of Stability-indicating RP-HPLC method for the analysis of levocetirizine dihydrochloride and fexofenadine hydrochloride in the Presence of Parabens in Liquid Dosage Forms. Int. J. Pharm. Sci. Rev. Res. Nov – Dec 2013, 23(92), 64-71.
115. Erkmen, C.; Kurnali, Z. S.; Uslu, B. Development of reverse phase liquid chromatographic method by using core shell particles column for determination of montelukast and levocetirizine from pharmaceutical capsule dosage forms. Revue Roumaine de Chimie. 2019, 64(10), 859-866.
116. Ranjan, P. O.; Nayak, Y. U.; Reddy, S. M.; Dengale, J. S.; Musmade, B. P.; Udupa, N. Development and validation of RP-HPLC method with ultraviolet detection for

estimation of montelukast in rabbit plasma: Application to preclinical pharmacokinetics. J. Young Pharmaci. 2013, 5(4), 133-138.

117. Patil, R. H.; Patil, N. P. Development and Validation of Stability Indicating Assay Method of Montelukast Tablet by RP-HPLC. IJTSRD. 2019, 4(1), 2456–6470.
118. Barnabas, S. K.; Suvaitha, P. S.; Dhinagaran, G.; Venkatachalam, K.; A novel stability indicating method for determination of related substances of montelukast sodium in a pharmaceutical dosage form using RP HPLC. Chromatographia. June 2021, 84(7), 645–662.
119. Shireesha, T.; Narmada, V.; Shyamsunder, R. A new simple RP-HPLC method development, validation and stability studies for the simultaneous estimation of montelukast and ebastine in pure form and combined tablet formulation. IJPBS. 2019, 9(4), 396-407.
120. Bachert, C. Therapeutic points of intervention and clinical implications: role of Desloratadine. Eur. J. Allergy Clin. Immunol. 2002, 57, 13-8.
121. Food and Drug Administration. Singulair® (montelukast sodium) Tablets, Chewable Tablets, and Oral Granules: Approved Label 2002. [Available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-409_Singulair_Prntlbl.pdf].
122. MSD Manuals. Overview of Allergic and Atopic Disorders. [Available from: https://www.msdmanuals.com/en-in/professional/immunology-allergic-disorders/allergic,-autoimmune,-and-other-hypersensitivity-disorders/overview-of-allergic-and-atopic-disorders].