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A REVIEW OF ANALYTICAL METHODS FOR ESTIMATION OF LEVOCETIRIZINE AND MONTELUKAST SODIUM IN COMBINED PHARMACEUTICAL DOSAGE FORMS

Y. D. Bhutia, N. R. Bhuyan, B. Shrestha and V. R. Baraily *

Department of Pharmaceutical Analysis, Himalayan Pharmacy Institute, Majhitar - 737132, East Sikkim, India.

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Correspondence to Author:
V. R. Baraily

Assistant Professor, Department of Pharmaceutical Analysis, Himalayan Pharmacy Institute, Majhitar - 737132, East Sikkim, India.

E-mail: Vishalahpi21@gmail.com

ABSTRACT: Beginning from simple analytical methods to the recent development of advanced hyphenated techniques stages, various analytical methods have been designed for the multicomponent analysis of drugs. Simultaneous estimation of drugs in the combined dosage form is vital in the pharmaceutical analysis since it is cost-effective and time-saving. Levocetirizine, the R-enantiomer of Cetirizine, is a peripheral H1-receptor antagonist used as a non-sedative antihistamine in treating chronic idiopathic urticaria, angioedema, and allergic rhinitis. Montelukast Sodium is selective cysteinyl leukotriene I receptor inhibitor that acts as an anti-asthmatic agent in the bronchial tubes and lungs. The combination of Levocetirizine with Montelukast Sodium in the pharmaceutical formulation is frequently used in the treatment of Allergic rhinitis as it has been shown to have additional benefits to the patients in reducing the symptoms efficiently. This review article has compared and addressed a variety of analytical methods applied for estimating Levocetirizine and Montelukast Sodium in the combined dosage form. The methods include UV Spectrophotometry methods, High-Performance Liquid Chromatography (HPLC), Ultra Performance Liquid Chromatography (UPLC), and High-Performance Thin-layer Chromatography (HPTLC). This review article also gives us insight into the development of different analytical techniques for estimating Levocetirizine and Montelukast Sodium combined with other drugs available in the market. The present paper suggests a suitable method for analyzing this pharmaceutical compound and helps optimize various analytical methods for their determination.

INTRODUCTION: Allergic rhinitis, a chronic inflammatory disease, is an IgE-mediated hypersensitivity disease of nasal airways caused mainly by airborne allergens, such as dust, pollen, molds, or animal dander.

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It is also known as hay fever and is characterized by nasal congestion, rhinorrhea, an itchy nose, and sore throat [1]. In this present era, Allergic rhinitis has become a significant health concern globally and has affected about 10-20% of the population throughout the world [2].

Levocetirizine, the R-enantiomer of Cetirizine chemically known as 2-(2-{4-[(R)-(4-chlorophenyl) (phenyl)-methyl] piperazin-1-yl} ethoxy) acetic acid, is a peripheral H1-receptor antagonist used as a non-sedative antihistamine in the treatment of chronic idiopathic urticaria, angioedema and

allergic rhinitis [3, 4]. Levocetirizine Dihydrochloride, having the molecular formula $C_{21}H_{25}ClN_2O_3$. 2HCL is the salt form of Levocetirizine with a molecular weight of 461.8 g/mol. It is a water-soluble, white crystalline powder [5, 6]. This drug is officially listed in IP-2007 [7]. Montelukast Sodium, Monosodium salt of 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl) ethenyl] phenyl]-3- [2-(1-hydroxy-1-methyl ethyl) phenyl] propyl] thio] methyl] cyclopropane acetic acid appears as white to pale yellowish crystalline powder, which is very soluble in alcohol, dimethyl sulfoxide, and freely water-soluble while practically insoluble in acetonitrile. The molecular formula and molecular weight of Montelukast Sodium are $C_{35}H_{35}ClNNaO_3S$ and 608.2 g/mol, respectively [3]. It is officially listed in IP-2010 [8], BP-2016 [9], and USP-2016 [10]. It inhibits the selective cysteinyl leukotriene I receptor in the bronchial tubes and lungs and acts as an anti-asthmatic agent [11].

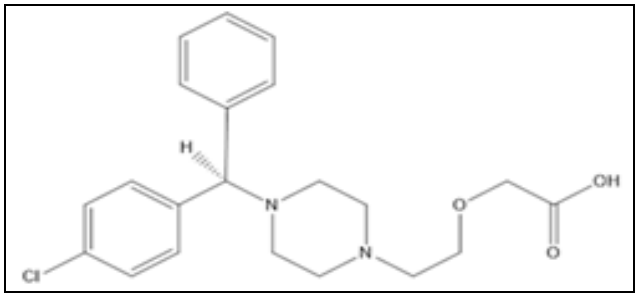

FIG. 1: CHEMICAL STRUCTURE OF LEVOCETIRIZINE

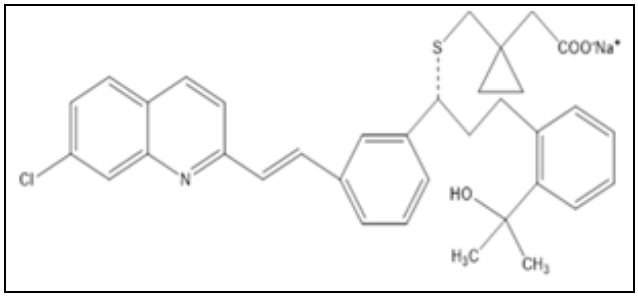

FIG. 2: CHEMICAL STRUCTURE OF MONTELUKAST SODIUM

Levocetirizine with Montelukast Sodium in combined dosage form has been shown to have additional benefits to the patients in efficiently reducing the symptoms of allergic rhinitis [12]. Nowadays, various drugs in combined dosage forms have been researched and developed drastically due to their enhanced activity. The standard analytical procedures designed for these drugs may not be officially included in the pharmacopeia.

Hence, with the increasing demand, the need for new procedures that allow the rapid analysis of combined drugs has also enhanced. The simultaneous estimation of combined drugs ensures that the formulation contains the exact amount of active pharmaceutical ingredients as mentioned on the label. A broad range of simple and advanced analytical methods exist for determining Levocetirizine and Montelukast Sodium simultaneously [1, 13]. A literature survey revealed that this drug product is most routinely determined by both analytical methods, including spectrophotometric and chromatographic methods.

Methodology: This study was conducted using the standard method of data searching using google and yahoo search engines. The obtained data are of standard electronic sources and mostly Scopus, PubMed, Science Direct, listed articles were preferred. The references and information were checked and cross-referenced to rectify errors and present the best-quality data.

Analytical Methods: There are several stages of drug development and manufacturing where analytical method development and validation play a significant role [14]. The main purpose of method development is to establish an analytical method suitable for measuring the concentration of an Active Pharmaceutical Ingredient in a specific compounded dosage form. The method development process includes a method validation process which serves to verify and assure the developed method by studying various validation parameters that include linearity, range, accuracy, precision, specificity, detection limit, quantitation limit, and robustness of the methods, thereby indicating the suitability of the developed method for determination of pharmaceutical compounds from bulk and pharmaceutical formulations [1, 15]. Analytical methods developed for estimating Levocetirizine and Montelukast Sodium are as follows:

Spectrophotometric Method: Spectro-photometric methods for estimating Levocetirizine (LEV) and Montelukast Sodium (MKT) in bulk and combined pharmaceutical dosage forms were studied and have been summarized in **Table 1.**

TABLE 1: UV SPECTROPHOTOMETRY METHOD

Sl. no.	Drug Combination	Method	Descriptions	Ref.
1.	Levocetirizine Hydrochloride and Montelukast Sodium in Tablet Dosage Form	Absorbance correction method	Solvent: Methanol Detection wavelength: 287nm (λ max of MKT) 232nm (λ max of LEV) Linearity range: 2-40 µg/mL (MKT at 287 nm, 232 nm) 1-40 µg/mL (LEV at 232 nm) r^2 value: 0.9997 (MKT at 287 nm) 0.9999 (MKT at 232 nm) 0.9996 (LEV at 232 nm) % RSD (label claim):0.4422 % (MKT) 1.0826 % (LEV) % Recovery range: 99.70 % (MKT) 100.49 % (LEV)	16
2.	Levocetirizine Hydrochloride and Montelukast Sodium in Tablet Dosage Form	Multi-wavelength method	Solvent: Methanol Detection wavelength: 229 nm, 232.2 nm, 232 nm Linearity range: 5-40µg/mL (MKT at 229 nm, 232.2nm) r^2 value: 0.999921(MKT at 229 nm) 0.999795(MKT at 232.2 nm) % RSD (label claim): 1.3069 (MKT) 0.1802 (LEV) % Recovery range: 98.58 % (MKT) 100.49 % (LEV)	16
3.	Levocetirizine Hydrochloride and Montelukast Sodium in Tablet Dosage Form	First-order derivative method	Solvent: Methanol Detection wavelength: 231.1 nm (zero crossing point for LEV) 216.5nm (zero crossing point for MKT) Linearity range: 10-40µg/mL (MKT at 231.1nm) 10-40 µg/mL(LEVat 216.5 nm) r^2 value: 0.99970 (MKT at 231.1 nm) % RSD (label claim): 1.71029 (MKT) 1.0215 (LEV) % Recovery range: 99.76 % (MKT) 99.82 % (LEV)	16
4.	Montelukast Sodium and Levocetirizine Dihydrochloride in Tablet Dosage Form	Ratio derivative spectrophotometricmethod	Solvent: Methanol Detection wavelength: 250.4 nm (MKT) 238.4 nm (LEV) Linearity range: 4-12 µg/mL (MKT) 2-6 µg/mL (LEV) r^2 value: 0.999, 0.997 (MKT, LEV) % Purity:96.86 % (MKT), 99.63 % (LEV) % Recovery Range: 99.79% to 100.68% (MKT) 99.44 % to 100.2 % (LEV) %RSD (Precision): less than 2 % LOD: 0.09 µg/mL (MKT), 0.178 µg/mL (LEV) LOQ: 0.277µg/mL (MKT), 0.591µg/mL(LEV)	17
5.	Montelukast Sodium and Levocetirizine Dihydrochloride in Tablet Dosage Form	AUC curve method	Solvent: Methanol Detection wavelength: 263.6 nm-293.6 nm 222 nm-242nm Linearity range: 5-30 µg/mL for both API r^2value: 0.9969, 0.9988 for MKT at both wavelength range, 0.9991 for LEV at 222 nm-242nm % Purity: 98.90% for MKT 98.75 % for LEV %RSD (Precision): less than 2 % % Recovery: near to 100% LOD (µg/mL): 1.60 at 222 nm-242 nm (MKT) 1.06 at 263.6 nm-293.6 nm (MKT) 1.23 at 222 nm-242nm (LEV) LOQ (µg/mL): 4.80 at 222 nm-24nm (MKT) 3.1 at 263.6 nm-293.6 nm (MKT) 3.71at 222 nm-242nm (LEV)	18
6.	Levocetirizine Dihydrochloride and Montelukast sodium in Tablet Dosage Form	Ratio spectra first derivative spectrophotometricmethod	Solvent: Methanol Detection wavelength:240 nm (LEV) 281 nm (MKT) Linearity range: 2-32 µg/mL (LEV) 3-30 µg/mL (MKT) r^2 value: 0.9995, 1.000 (LCT, MKT) %RSD (Accuracy, Precision): less than 2 % % Purity: Montek-LC: 101.34% (LEV) 99.68 % (MKT) Montair-LC: 100.64% (LEV) 99.48% (MKT) % RSD (Robustness): less than 2 % LOD (µg/mL): 0.2979182, 0.3177621 (LEV, MKT) LOQ (µg/mL): 1.8263959, 2.4459207 (LEV, MKT)	19
7.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	First-orderderivative spectrophotometricmethod	Solvent: 0.5% w/v Sodium Lauryl Sulphate in distilled water Detection wavelength: 350.2 nm (zero crossing point for LEV) 211.8 nm (zero crossing point for MKT) Linearity range: 3-30µg/mL for both API r^2 value: 0.9994 (MKT),0.9999 (LEV) % Purity: Telekast -L®- 98.6 % (MKT) 99.2 % (LEV) Bulk Drug- 101.84% (MKT) 100.88 % (LEV) % Recovery: 98.40 % to 100.50 % (MKT) 99.30 % to 101.25% (LEV) %RSD (Precision): less than 2 LOD: 0.993µg/mL (MKT), 0.361µg/mL (LEV) LOQ: 3.0 µg/mL (MKT), 1.09 µg/mL (LEV)	20
8.	Montelukast Sodium and Levocetirizine Hydrochloride in a binary mixture	Simultaneous equation method	Solvent: Methanol Detection wavelength: 284 nm (λmax of MKT) 229 nm (λmax of LEV) Linearity range: 4-20 µg/mL (MKT) 2-10 µg/mL (LEV) r^2 value: less than 1 for both drug % Purity: 99.08 %-99.87 % (MKT) 98.5 %-101 % (LEV)	21

			% Recovery: 98.5 %-101.1 % % RSD (Precision, Accuracy): less than 2 LOD: 1.1µg/mL(MKT), 3.3 µg/mL (LEV) LOQ: 0.7µg/mL(MKT), 2.1 µg/mL(LEV)	
9.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	Bivariate calibration algorithm Method	Solvent: Methanol Detection wavelength: 220 nm, 230 nm Linearity range: 4–28µg mL^{-1} for both drugs r^2 value: 0.9991 (LEV) 0.9992 (MKT) LOD (µg/mL): 0.261 (LEV) 0.079 (MKT) LOQ (µg/mL):0.893 (LEV) 0.264 (MKT) % RSD (Precision, Accuracy): less than 2 % Recovery: 99.41 % (LEV) 100.58 % (MKT)	22
10.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	Dual wavelength Method	Solvent: Methanol Detection wavelength: 208 nm, 214.4 nm (MKT) 355 nm, 390 nm (LEV) Linearity range: 4–28 µgmL^{-1} for both drugs r^2 value: 0.9990 (LEV at 208 nm, 214.4 nm) 0.9989 (MKT at 355nm, 390 nm) LOD (µg/mL): 0.374 (LEV) 0.273 (MKT) LOQ (µg/mL): 1.249 (LEV) 0.190 (MKT) %RSD (Precision, Accuracy): less than 2 % Recovery: 99.11 % (LEV) 98.62 % (MKT)	22
11.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	Second derivative spectrophotom etric method	Solvent: Methanol Detection wavelength: 244 nm, 293.2 nm, 335.6 nm Linearity range: 4–28 µgmL^{-1} for both drugs r^2 value:0.9990(LEV at 244nm) 0.9986 (MKT at 293.2 nm, 335.6 nm) LOD (µg/mL): 1.177 (LEV at 244 nm) 0.785 (MKT at 293.2 nm) 0.884 (MKT at 335.6 nm) LOQ(µg/mL): 3.921 (LEVat 244nm) 2 .61 (MKT at 293.2nm) 2.818 (MKT at 335.6nm) %RSD (Precision, Accuracy): less than 2% % Recovery: 99.16 % (LEV at 244 nm) 100.53 % (MKT at 293.2 nm) 102.00 % (MKT at 335.6 nm)	22
12.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	Ratio difference method	Solvent: Methanol Detection wavelength: 216 nm, 232 nm (LEV) 296.4 nm, 344.2 nm (MKT) Linearity range: 4–28 µgmL^{-1} for both drugs r^2 value: 0.9979 (LEVat 216 nm, 232 nm) 0.9986 (MKT at 296.4 nm, 344.2 nm) LOD(µg/mL): 0.229 (LEV) 0.352 (MKT) LOQ(µg/mL): 0.764 (LEV) 1.152 (MKT) %RSD (Precision, Accuracy): less than 2 % % Recovery: 100.5 % (LEV) 99.01 % (MKT)	22
13.	Montelukast Sodium and Levocetirizine Hydrochloride in Tablet Dosage Form	Simultaneous equation Method	Solvent: Methanol Detection wavelength: 267 nm (λmax of MKT) 225 nm (λmax of LEV) Linearity range:5-25 µg/mL(MKT) 2.5-12.5 µg/mL (LEV) r^2value: 0.9991 % (MKT) 0.9994 % (LEV) % Purity:99.02% (MKT), 100.04% (LEV) %Recovery: 99 %-100%. %RSD (Precision, Accuracy): less than 2 % L0D (µg/mL): 0.2 (MKT), 0.6 (LEV) L0Q (µg/mL): 0.6 (MKT), 1.8 (LEV)	11
14.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	First-order derivative spectroscopy method	Solvent: 0.1N NaOH Detection wavelength: 291.60 nm (Zero crossing point of LEV) 238.20 nm (Zero crossing point of MKT) Linearity range: 5-30 µg/mL for LEV 10-60µg/mL for MKT r^2 value: 0.9994 for LEV 0.9950 for MKT % Purity: 99.4 % (LEV) 101.73 % (MKT) % RSD (Accuracy, Precision)): less than 2 LOD Value: 1.05µg/mL for LEV 3.69µg/mL for MKT LOQ Value: 3.21 µg/mL for LEV 11.17 µg/mL for MKT	23

To estimate Levocetirizine and Montelukast Sodium levels in combined pharmaceutical formulations, various spectrophotometric methods have been developed over the years. This paper describes the spectrophotometric methods that have been developed from the year 2009 to 2016. Multi-wavelength method, Absorbance correction method, Derivative spectrophotometric method, AUC curve method, Simultaneous equation method, Bivariate calibration algorithm method, Dual-wavelength method, Ratio difference method, and Absorbance Factor method are the developed methods that have been demonstrated for their estimation under different analytical conditions. After reviewing various spectrophotometric methods designed for estimating Montelukast Sodium and Levocetirizine in combined dosage form, it was revealed that methanol is the most used solvent. Wavelengths used were in the range of 200-400nm for their detection. The simultaneous

equation method, also known as Vierordt's method, is frequently used due to its simplicity and also consumes less time compared to other methods requiring tedious sample preparation. The derivative spectrometry method is the most extensively used method where co-formulated drugs come across the problem of interference due to spectral overlapping as derivative spectra show better resolution and help identify the compounds having close λ max to one another. The bivariate calibration algorithm method developed by Noha S. Rashed et al., 2015 proves to be the most sensitive method, having the lowest LOD values with a linearity range of 4-20 µg/ml for Montelukast Sodium and 2-10 µg/ml for Levocetirizine respectively [22]. The ratio derivative spectroscopic method has the advantage of selecting suitable divisor concentration, making it dominant over other methods in terms of sensitivity and accuracy. All the developed spectrophotometric methods for estimating Levocetirizine and Montelukast Sodium were simple, precise, accurate, and reproducible.

Chromatography: Chromatographic methods for estimating Levocetirizine and Montelukast Sodium in bulk and combined pharmaceutical dosage forms were studied and summarized in **Table 2.**

TABLE 2: CHROMATOGRAPHIC METHOD

Sl. no.	Drug combination	Method	Analytical Conditions	Ref.
1.	Montelukast Sodium and Levocetirizine Dihydrochloridein Tablet Dosage Form	HPTLC	Stationary phase: Silica gel $60F_{254}$ aluminum plate (20x 10 cm) Mobile phase: Ethyl acetate: methanol: triethylamine (5:5:0.02 v/v/v) Internal standard: Paracetamol Detection wavelength:240 nm Run time: 7 min R_f value: 0.29, 0.50, 0.6 (LEV, MKT, PARA) Linearity range:400–1200 ng/spot (MKT) 200–600 ng/spot (LEV) r^2value:0.9993 (MTK), 0.9985 (LEV) % RSD (Precision, Accuracy): less than 2 % % Recovery: 90% to 120.0% LOD: 20.63 ng/spot (MKT) 21.12 ng/spot (LEV) LOQ: 62.5 ng/spot (MKT) 64 ng/spot (LEV)	23
2.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	RP-HPLC	Column: SUPELCOSILTM, LC-8 column (15cm x 4.6mm) Mobile phase: 0.02M Potassium dihydrogen phosphate buffer solution: methanol (40:60 v/v) Detection wavelength: 218nm Flow rate: 1.0mL/min Run time: 10 min Retention time: 4.30 min (LEV), 7.408 min (MKT) Linearity range: 5-20 µg/mL (LEV) 10-40µg/mL (MKT) r^2 value: 0.993 (LEV), 0.997 (MKT) % Purity: 99.18 % (LEV), 99.08 % (MKT) %RSD (Precision, Accuracy): less than 2 % LOD: 2.493µg/mL(LEV), 0.489µg/mL(MKT) LOQ: 7.553 µg/mL (LEV), 1.482µg/mL(MKT)	24
3.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	RP-HPLC	Column: BDS Hypersil C_{18}column (250 mmx4.6mm) Mobile phase: Disodium hydrogen phosphate buffer (0.02M): Methanol (25:75 v/v) Detection wavelength: 231 nm, Flow rate: 1.0 mL/min Retention time: 3.558 min, 7.450 min (LEV, MKT) Linearity range: 1 – 10 µg/ mL (LEV) 2 – 20 µg /mL (MKT) r^2 value: 0.9987 (LEV), 0.9980 (MKT) LOD: 0.5 µg/mL (LEV), 0.2 µg/mL (MKT) LOQ: 0.8 µg/mL (LEV), 0.6 µg/mL (MKT) % RSD (Precision): less than 2% % Purity:99.76 % (LEV) 100.15 % (MKT)	25
4.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	RP-HPLC	Column: Waters C_{18}analytical column (15cm × 4.6 mm, 5µ) Mobile phase: Methanol: water (75:25 v/v) Detection wavelength: 235nm Flow rate: 1.0 mL/min Run time: 7 min Retention time: 2.88 min, 3.83 min (LEV, MKT) Linearity range: 50-150 µg/mL (LEV) 100- 300 µg/mL (MKT) r^2 value:0.9991, 0.9994 (LEV, MKT) % Recovery: 100 % (LEV), 99 % (MKT) %RSD (Precision): less than 2 % LOD:0.42 ng/mL, 0.16 ng/mL (LEV, MKT) LOQ: 0.36 ng/mL, 0.12 ng/mL (LEV, MKT)	26
5.	Levocetirizine and Montelukast Sodium in Tablet Dosage Form	RP-HPLC	Column: Atlantis C_{18} analytical column (4.6×150 mm, i.d.5µm) Mobile phase: Acetonitrile: ammonium acetate (65:35 % v/v), Detection Wavelength: 230nm Flow rate: 1.0 mL/min Run time: 13 min Retention time: 3.03min, 6.28 min (LEV, MKT) Linearity range:25-75 µg/mL (LEV) 50-150 µg/mL(MKT) r^2 value: 0.999 % Purity: 99.2%- 102.4 % %RSD (Precision, Accuracy): less than 2 % LOD: 0.05 µg/mL, 0.10 µg/mL (LEV,	27

			MKT) LOQ: 0.17 µg/mL, 0.33 µg/mL(LEV, MKT)	
6.	Levocetirizine Dihydrochloride and Montelukast Sodium in Tablet Dosage Form	RP-HPLC	Column: Hypersil BDS C_{18}column (250×4.6 mm, 5µm) Mobile phase: Phosphate buffer: acetonitrile (40:60% v/v) Detection wavelength: 230 nm Flow rate: 1.0 mL/min Run time: 10 min Retention time:3.06 min,6.76 min (LEV, MKT) Linearity range:12.56–37.68 µg/mL (LEV) 23.78–71.20 µg/mL (MKT) r^2value: 0.9998 % Purity: 99.55 %(LEV), 98.37 % (MKT) %RSD (Precision, Accuracy): less than 2 % LOD: 0.079 µg/mL (LEV), 0.156 µg/mL (MKT) LOQ: 0.239 µg/mL (LEV), 0.473 µg/mL (MKT)	28
7.	Levocetirizine Dihydrochloride and MontelukastSodium in Tablet Dosage Form	HPTLC	Stationary phase: Silica gel60 F_{254}aluminum plate(20 × 10 cm) Mobile phase: Toluene: ethyl acetate: methanol: ammonia (2.5: 7: 2.5: 1,v/v/v/v) Detection wavelength: 231 nm Run time: 25 min R_f value: 0.31, 0.44 (LEV, MKT) Linearity range:500-2500 ng $spot^{-1}$ (LEV) 1000-5000 ng $spot^{-1}$ (MKT) r^2 value: 0.9981 (LEV) 0.9982 (MKT) % (Precision, Accuracy): less than 2% % Purity: 99.72 % (LEV) 100.19 % (MKT) LOD: 90 ng $spot^{-1}$ (LEV), 50 ng $spot^{-1}$ (MKT) LOQ: 200 ng $spot^{-1}$ (LEV), 110 ng $spot^{-1}$ (MKT)	25
8.	Montelukast Sodium and Levocetirizine Hydrochloride in Tablet Dosage Form	HPTLC	Stationary phase: Silica gel 60 F_{254} aluminum sheets (10 x 10 cm) Mobile phase:n- Hexane: chloroform: methanol: acetic acid (3.5:5.0:1.2:0.3 v/v/v/v) Detection wavelength: 302 nm R_f value: 0.29, 0.65 (MKT, LEV) Linearity range: 5-15 µg/mL (MKT) 2.5-7.5 µg/mL (LEV) r^2 value:0.9993, 0.9998 (MKT, LEV) % RSD (Precision): 0.28, 0.31(MKT, LEV) % Purity: 99.02% (MKT), 100.04% (LEV) LOD (ng/spot): 100, 110(MKT, LEV) LOQ (ng/spot): 210, 240 (MKT, LEV)	11
9.	Montelukast Sodium and Levocetirizine Hydrochloride in Tablet Dosage Form	RP-HPLC	Column: Inertsil ODS column (250 x 4.6 mm, 5µ) Mobile phase: Buffer: Methanol (35: 65 v/v) Detection wavelength: 234 nm Flow rate: 1.5 mL/min Run time: 10 min Linearity range: 4-20 µg/mL (MKT) 2-10 µg/mL (LEV) r^2 value: 0.999847 (MKT) 0.999824 (LEV) %RSD (Precision): 0.5 (MKT), 0.3 (LEV) % RSD (Accuracy): 0.4 (MKT), 0.3 (LEV) % Purity: 99.02% (MKT), 100.04% (LEV) LOD: 1.85µg/mL(MKT), 1.63 µg/mL(LEV) LOQ: 3.42 µg/mL(MKT), 4.14 µg/mL (LEV)	11
10.	Levocetirizine Hydrochloride and MontelukastSodium in Tablet Dosage Form	RP-HPLC	Column: HypersilGold L7column (250mm x 4.6mm, 5µm) Mobile phase: 0.05 M Potassium Dihydrogen Phosphate Buffer: Methanol (20:80 v/v) Flow rate: 1.2 mL/min Detection wavelength: 225 nm Retention time:3.2 min, 4.2 min (LEV, MKT) % Purity:99.2%, 100.3% (LEV, MKT) Linearity range (mcg/mL): 10-260 (LEV) 10-350 (MKT) r^2 value: 0.9998, 0.9999(LEV, MKT) LOD (mcg/mL): 2.26 (LEV) 2.41 (MKT) LOQ (mcg/mL): 6.85 (LEV) 7.3 (MKT)	29
11	Montelukast Sodium and Levocetirizine Dihydrochloride in Liquid Dosage Forms	RP-UPLC	Column: AQUITY BEH phenyl column (50mm x 2.1mm, 1.7µm) Mobile phase: Potassium dihydrogen phosphate(2.72 gm) to 1 L of Milli Q water Diluent: Water: methanol (10:90 v/v) Flow Rate:0.4 mL/min Detector: PDA (photo diode array) detector Detection wavelength: 231 nm Run time:3.5 min Retention Time:0.587 min, 1.626 min (LEV, MKT) r^2 value: 0.999 for both API % RSD (Accuracy, Precision): less than2.0 %	30
12	Levocetirizine dihydrochloride and Montelukast sodium in Tablet Dosage Form	RP HPLC	Column: Phenomex-luna 5µ C8 (2) column (100Å, 250 X 4.6 mm) Mobile phase: Acetonitrile: 0.5% triethylamine in water (90:10 v/v) Flow rate: 0.8 mL/min Detection Wavelength: 231 nm Retention time: 3.8 and 5.2 min (LEV and MKT) Linearity range (µg/mL): 2-32, 3-30(LEV, MKT) r^2 value:0.9997, 0.9994(LEV, MKT) % Purity: Montek-LC-99.18%,100.26% (LEV, MKT) Montair LC-99.83%, 98.28% (LEV, MKT) % RSD (Accuracy, Precision): below 2.0 % LOD (µg/mL): 0.00028, 0.0032(LEV, MKT) LOQ (µg/mL): 0.00086, 0.0094 (LEV, MKT)	19

13.	Montelukast Sodium and Levocetirizine Dihydrochloride in Tablet Dosage Form	HPTLC	Stationary Phase: Silica gel 60 F_{254}aluminum plate (10 x 10 cm) Mobile phase: Chloroform: methanol: toluene: glacial acetic acid (10:5:3:0.5v/v/v/v) Detection wavelength: 269.0 nm, 302 nm Linearity range: 400-4500 ng r^2 value: 0.9998 R_f value: 0.89 and 0.64 (MKT and LEV) LOD (µg/mL): 1.536, 2.864 (MKT, LEV) LOQ (µg/mL): 2.536, 3.453 (MKT, LEV)	31
14.	Levocetirizine Hydrochloride and Montelukast Sodium in Tablet Dosage Form	HPTLC	Stationary Phase: Silica gel aluminum plate 60 F_{254} (20 ×10 cm) Mobile phase: Toluene: Ethyl Acetate: Methanol (2.5: 5: 2.5v/v/v) Detection wavelength: 240 nm R_f value: 0.17, 0.76 (MKT, LEV) Linearity range:2-10µL for both API r^2 value: less than0.99 % RSD (Precision):less than 2 % Purity: 99.14 % (LEV), 99.28 % (MKT) LOD (ng $band^{-1}$): 44.43, 29.12 (MKT, LEV) LOQ (ng $band^{-1}$):134.66, 88.24(MKT, LEV)	32
15.	Montelukast and Levocetirizine in Liquid dosage Form	RP-HPLC	Column: Hypersilwaters C18 column (4.6mm × 250mm ×5µm) Mobile phase: Phosphate buffer: acetonitrile (55:45) Flow rate: 1 mL/min Detection wavelength: 228 nm Run time: 6 min Retention time: 2.47 min, 2.823 min (MKT, LEV) Linearity range:40-20 µg/mL for MKT 25-75 µg/mLfor LEV r^2 value: 0.999 % Recovery: 99.10 %, 99.38 % (MKT, LEV) % RSD (Accuracy, Precision): less than 2 % % Purity:98.65%,99% (MKT, LEV)	33
16	Montelukast and Levocetirizine in LiquidDosage Form	RP-HPLC	Column: Hypersil BDS column(250 x 4.6 mm, 5µm) Mobile phase: Potassium di-hydrogen phosphate buffer: Acetonitrile (35:65) Flow rate: 1mL/min Detection wavelength:231nm Retention time: 2.599min, 3.472min (MKT, LEV) Linearity range: 25-150µg/mL (MKT) 12.5-75 µg/mL (LEV) r^2 value: 0.999 for both drugs % RSD: less than2 LOD: 0.04µg/mL,0.08 µg/mL (MKT, LEV) LOQ: 0.11 µg/mL,0.25µg/mL (MKT, LEV) % Recovery: 99.88%, 99.9%for (MKT, LEV)	34
17.	Montelukast Sodium and Levocetirizine Hydrochloride in Tablet Dosage Form	HPTLC	Stationary phase: Silica gel 60F 254 aluminium sheets (20 x 10 cm) Mobile phase: Chloroform: benzene: methanol: toluene (5:7.2:1:0.2 v/v/v/v) Detection wavelength: 286 nm Linearity range: 500-1500 ng spot-1 (MKT) 1000-5000 ng spot-1 (LEV) r^2 value: 0.9992, 0.9995 (MKT, LEV) % RSD (Peak area value): 1.09, 1.17 (MKT, LEV) % Purity: 100.40 % (MKT) 98.40 % (LEV) LOD: 170 ng/spot, 20 ng/spot (MKT, LEV) LOQ: 570 ng/spot, 70 ng/spot (MKT, LEV)	35

Several chromatographic methods estimate Levocetirizine and Montelukast Sodium levels in combined dosage forms. This review covers the chromatographic methods that have been developed from the year 2010 to 2020. After studying various chromatographic methods designed for estimating Levocetirizine and Montelukast Sodium in combined pharmaceutical formulations, it was observed that the RP-HPLC method is the most dominant method over other chromatographic methods due to its specificity and sensitivity. Optimization of the developed analytical methods are carried out under various analytical conditions such as different mobile phase, pH is used, based on resolution, asymmetric factor, and peak area obtained for both LEV and MKT. Methods using water and methanol as mobile phase is found to be economical. Photodiode- Array Detector or PDA detector are commonly used for the detection of compounds in the wavelength range of 200-400 nm. The RP-HPLC method reported by R. Swethan Babu, *et al.*, 2012 can be considered as the most sensitive method among all developed methods having the lowest LOD value for Levocetirizine and Montelukast Sodium, respectively. The separation was achieved using phenomex-luna 5µ C8 Column (100Å, 250 X 4.6 mm) and acetonitrile: 0.5% triethylamine in water (90:10 v/v) as an optimized mobile phase [19]. The RP-UPLC method developed by J. Bharati, *et al.*, 2015 for the estimation of Montelukast Sodium and Levocetirizine seems to be the most rapid method giving a good resolution between two drugs with the shortest run time *i.e.*, 3.5 min and retention time *i.e.*, 0.587min and 1.626 min respectively for Levocetirizine and Montelukast Sodium. In this method, peaks obtained were sharp and had clear baseline separation for both drugs.

The column used was AQUITY BEH Phenyl column (50mm x 2.1mm, 1.7µm) and Potassium dihydrogen phosphate (2.72 gm) to 1 L of Milli Q water was used as mobile phase with a flow rate of 0.4 mL/min [30]. Due to low solvent consumption and rapidity of the method with increased sensitivity and selectivity, we can conclude that the RP-UPLC is the most appropriate method and should be considered major method for their determination as it seems to be more beneficial than RP-HPLC and HPTLC techniques. The high recovery values in the HPTLC method indicate the suitability of the developed method for the determination of Levocetirizine and Montelukast Sodium in the combined pharmaceutical dosage form. An ideal Rf value has been obtained in HPTLC methods published by Ambadas Rote *et al.,* 2011 and Atul S Rathore *et al.,* 2010 [23, 25]. In addition to method development, a force degradation study was carried out in the work reported by Deshpande et al.2016 and Jitendra K. Sonawane *et al.,* 2020 to check the specificity and stability of the drugs [28, 32]. Both drugs were subjected to stress conditions of oxidation, photolysis, acid hydrolysis, base hydrolysis, and thermal degradation. The degradation products obtained in both methods were resolved indicating the specificity of the developed analytical methods.

Analytical Methods for estimation of Montelukast Sodium with Other Drugs in Combined Dosage form: Other than Levocetirizine, Montelukast Sodium is available in the market with many other drugs in the combined pharmaceutical formulation. Doxofylline, Fexofenadine Hydrochloride, Theophylline, Ebastine, Bambuterol Hydrochloride, Loratadine were the most common drugs found in combination with Montelukast Sodium. Both spectro-photometric and chromatographic methods for simultaneous determination of Montelukast with these drugs have been studied and summarized in **Table 3.**

TABLE 3: ANALYTICAL METHODS FOR ESTIMATION OF MONTELUKAST SODIUM

Sl. no.	Drug combination	Method	Descriptions	Ref.
1.	Montelukast Sodium and Doxofyllinein Tablet Dosage Form	HPLC	Column: C_{18} analytical column (150 mm × 4.6 mm, 5$\mu\mu$m) Mobile phase: Methanol: phosphate buffer (10:90) Flow rate: 1.0 mL/min Detection wavelength: 280 nm Run time: 20 min Retention time: 4.78 min (MKT) 1.97 min (DOX) Linearity range:0.005-0.015 mg/mL (MKT) 0.2-0.6 mg/mL (DOX) r^2 value: 0.9941 (MKT) 0.9935 (DOX) % Purity: 99.8 %-100.3%	36
2.	Montelukast Sodium and Fexofenadine Hydrochloride in Tablet Dosage Form	RP-HPLC	Column: X-bridge C_{18} column (250 mm x 4.6 mm, 5 mm) Mobile phase: Sodium acetate buffer: acetonitrile: methanol (25:35:40) Flow rate: 1.0 mL/min Detection wavelength: 210 nm Retention time: 3.43 min (MKT) 8.22 min (FEX) Linearity range: 12.5-37.5 mg/mL (MKT) 150-450 mg/mL (FEX) r^2 value: 0.9997(MKT) 0.9994 (FEX) % RSD (Accuracy, Precision): less than 2 % % Purity: 99.73 % (MKT) 100.06 % (FEX)	37
3.	Montelukast Sodium and Fexofenadine Hydrochloride in Tablet Dosage Form	Simultaneous equation method	Solvent: Methanol Detection wavelength: 259.60 nm 283.00 nm Linearity Range: 30-120 mg/mL(FEX) 6-20 mg/mL(MKT) r^2 value: 0.9927 (FEX) 0.9985 (MKT) %RSD (Accuracy, Precision): less than 2 %	38
4.	Theophylline and Montelukast Sodium in Tablet Dosage Form	RP- HPLC	Column:ODS C- 18 Kromacil column (250 mm × 4.60 mm) Mobile Phase: Methanol Detection Wavelength: 210nm Retention time: 4.173 min (TPH) 2.910 min (MKT) r^2 value: 0.9960 for both API %RSD (Accuracy, Precision): less than 2 %	39
5.	Montelukast Sodium and Ebastine inTablet DosageForm	Absorbance correction method	Solvent: Methanol Detection wavelength: 345 nm, 253 nm Linearity range: 5-25 µg/mL for both drugs r^2 value:0.9993 at 345 nm 0.9999 at 253 nm %RSD (Accuracy, Precision): less than 2 % % Purity:99.75 (MKT) 99.89 (EBA)	40
6.	Montelukast Sodium and Bambuterol Hydrochloride in	Dual wavelength method	Solvent: Chloroform Detection wavelength:322.0 nm (MKT) 266.0 nm(BAM) Linearity range: 10-80 µg/mL for MKT 40-240 µg/mL for BAM r^2 value:0.9997 (BAM) 0.9998 (MKT) % Recovery: 98.9 %-99.2 % %RSD (Accuracy, Precision): less	41

	Tablet Dosage Form		than 2 %	
7.	Montelukast Sodium and Loratadinein Tablet Dosage Form	HPLC	Column: Symmetry C_{18} column Mobile phase: Sodium phosphate buffer: acetonitrile (20:80, v/v) Flow rate: 1.0 mL/min. Detection wavelength: 225 nm Internal standard:5-Methyl 2-nitrophenol Linearity range: 100-600mg/mL (MKT) 116-580mg/mL (LTD) r^2 value: less than 1 %RSD (Accuracy, Precision): less than 2%	42
8.	Montelukast and Ebastine in Tablet Dosage Form	RP-HPLC	Column: Grace Smart RP C_{18} column (250 mm × 4.6 mm I.D. 5µ particle size) Mobile phase: Methanol: water (0.1% triethylamine) (90:10) Flow rate: 1.2 mL/min Detection wavelength: 246 nm Retention time: 2.36 min (MKT) 4.90 min (EBA) Linearity range: 5-15 µg/mL(MKT, EBA) r^2 value: 0.999	43
9.	Bambuterol Hydrochloride and Montelukast Sodium in Tablet Dosage Form	RP-UPLC	Column: BEH C18 Acquity UPLC column(100×2.1 mm, 1.7 µ) Mobile phase: 0.025% (v/v) trifluoroacetic acid in water and acetonitrile Detection wavelength: 210 nm Flow rate: 0.3mL/min Run time: 6.0 min Retention time: 1.40 min (BAM) 3.42 min (MKT) Linearity range: 6.25-37.5 µg/mL for both drugs r^2 value:0.999 % Recovery: 99.1-100.0% (BAM) 98.0-101.6% (MKT)	44
10.	Montelukast Sodium and FexofenadineHydrochloride in Tablet Dosage Form	RP-HPLC	Column: Lichrospher® 100RP-18e column Mobile phase: Methanol:0.1% o-phosphoric acid (90:10 v/v) Flow rate: 1 mL/min Detection wavelength: 226 nm Retention time: 10.16 min (MKT) 12.03 min (FEX) Linearity range: 2-10 µg/mL (MKT) 24-120 µg/mL (FEX) % Recovery: 99.09, 99.81% (MKT, FEX)	45
11.	Fexofenadine Hydrochloride and Montelukast Sodium in Tablet Dosage Form	Simultaneous equation method	Solvent: 0.1N NaOH Detection wavelength: 259 nm (λ max of FEX) 344.5 nm (λ max of MKT) Linearity range: 50- 180 µg/mL(FEX) 1-35 µg/mL(MKT) r^2 value: 0.998 % Purity: 101.88 % (FEX) 100.07 % (MKT)	46

Analytical Methods for estimation of Levocetirizine with Other Drugs in Combined Dosage form: Levocetirizine (as Levocetirizine Hydrochloride and Levocetirizine Dihydrochloride) is available with many other drugs such as Diethylcarbamazine, Ambroxol, Pseudoephedrine, Phenylephrine Hydrochloride, Phenyl-propanolamine Hydrochloride in the combined pharmaceutical formulation **Table 4.**

Represents both spectrophotometric and chromatographic methods designed for the simultaneous estimation of Levocetirizine with these drugs in the combined dosage form.

TABLE 4: ANALYTICAL METHODS FOR ESTIMATION OF LEVOCETIRIZINE

Sl. no.	Drug combination	Method	Description	Ref.
1.	Diethylcarbamazine and Levocetirizine Dihydrochloride in Tablet Dosage Form	RP-HPLC	Column: Princeton Sphere-100C_{18}column (250×4.6 mm. 5 µ) Mobile phase: Potassium dihydrogen orthophosphate buffer: acetonitrile (50:50 v/v) Internal standard: Losartan potassium Flow rate: 1 mL/min Detection wavelength: 224 nm Elution time: 2.12 min (DEC) 4.27 min (LEV) Linearity range: 5 to 30 µg/mL for DEC 0.1 to 1 µg/mL for LEV r^2 value: 0.9949 for DEC 0.9979 for LEV	47
2.	Ambroxol and Levocetirizine in Tablet Dosage Form	RP-HPLC	Column: Phenomenex C_{18} column (150 × 4.6 mm, 5µ) Mobile Phase: 0.01M Potassium dihydrogen orthophosphate: Acetonitrile (60:40 v/v) Flow rate: 1 ml/min Detection wavelength: 230nm Retention time: 3.60min (LEV) 4.68min (AMB) Linearity range:12-120 µg/mL for AMB 1-10µg/mL for LEV r^2 value: 0.9991 for both drugs % Purity: 100.2 %, 98.2 % (AMB, LEV)	48
3.	Levocetirizine and Pseudoephedrine in Tablet Dosage	Simultaneous equation method	Solvent: Distilled water Detection wavelength:231 nm, 257 nm Linearity range:5-30 µg/mL (LEV) 120-960 µg/mL (PSEUDO) r^2 value: 0.9992 (LEV) 0.9991 (PSUEDO) % Purity: 100.03 %	49

	Form		(LEV) 100.31 % (PSUEDO) % RSD (Accuracy, Precision): less than 2 %	
4.	Levocetirizine and Pseudoephedrine in Tablet Dosage Form	Absorbance ratiomethod	Solvent: Distilled water Detection wavelength: 231 nm, 257 nm Linearity range: 5-30 µg/mL (LEV) 120-960 µg/mL (PSEUDO) r^2 value: 0.9994 (LEV) 0.9993 (PSUEDO) % Purity: 101.81 (LEV) 100.04 (PSUEDO) %RSD (Accuracy, Precision): less than 2 %	49
5.	Levocetirizine Dihydrochloride and Phenylephrine Hydrochloride in Tablet Dosage Form	First-order derivative spectrophotom etric method	Solvent: Methanol Detection wavelength: 240nm, 283.2nm Linearity range:4–24 μg/mL (LEV) 8–48 μg/mL (PHE) r^2 value: 0.9964 ,0.9972 (LEV, PHE) % Purity: Levocet-D: 99.66 % (LEV, PHE) Rinostat-L: 99.63 %, 100.3 % (LEV, PHE) %RSD (Accuracy, Precision): less than 2 %	50
6.	Levocetirizine and Phenylephrine in Tablet Dosage Form	RP-HPLC	Column: C_{18} analytical column Mobile phase: Phosphate buffer: Methanol: Acetonitrile (40:20:40) Flow rate: 1mL/min Detection wavelength: 231 nm. Retention time:2.85min (PHE) 6.51 min (LEV) Linearity range: 2-10 µg/mL (LEV) 5-25 µg/mL (PHE) %RSD (Accuracy, Precision): less than 2 % % Recovery: 99.5 % (LEV) 101.1 % (PHE)	51
7	Levocetirizine and Phenylephrine Hydrochloride in Tablet Dosage Form	RP-HPLC	Column: Luna 5u C_{18}column (20mm X 4mm) Mobile phase: Methanol: potassiumdihydrogen phosphate buffer(70:30) Detection wavelength: 251nm Flow rate: 1.0 mL/min Retention time: 8.42 min (LEV) 2.70 min (PHE) Linearity range: 30 -150% r^2 value:0.9984, 0.9983 (LEV, PHE) % Recovery: 100.64 % (LEV) 100.40 % (PHE)	52
8.	Ambroxol Hydrochloride and Levocetirizine Dihydrochloride in Tablet Dosage Form	Simultaneous equation method	Solvent: Distilled water Detection wavelength: 242 nm, 231 nm Linearity range:10-50 µg/mL (AMB) 8-24 µg/mL (LEV) r^2 value: 0.999 for both API % Recovery: 99.13 to 99.52% (AMB) 98.88 to 99.42% (LEV) %RSD (Accuracy, Precision): less than 2 %	53
9.	Levocetirizine and Phenylpropanolami ne HydrochlorideTable t Dosage Form	RP-HPLC	Column: Phenomenex Luna C_{18} column (25 cm × 4.6 mm i.d., 5 µ) Mobile phase: Acetonitrile: 0.5%triethylamine (70:30 v/v) Flow rate: 1.2 mL/min Detection wavelength: 220 nm Retention time: 1.8 min (PPA) 2.6 min (LEV) % Recovery: 98.17- 103.56 % (PPA) 98.893 to 10.422 % (LEV)	54
10	Levocetirizine hydrochloride and Phenylephrine Hydrochloride in Tablet Dosage Form	First-order derivative method	Solvent: Methanol Detection wavelength: 216 nm, 230 nm Linearity range: 3-9µg/mL (LEV) 6-18 µg/mL (PHE) r^2 value: 0.9993 (LEV) 0.9996 (PHE) % RSD (Precision, Accuracy): less than 2 % % Purity: 99.19 % (PHE) 99.88 % (LEV)	55
11.	Levocetirizine and Phenylephrine in Tablet Dosage Form	RP-HPLC	Column: Eclipse Plus C_{18} column (4.6 mm × 150 mm) Mobile phase: Methanol: water (50:50 v/v) Flow rate: 1 mL/min Detection wavelength: 277 nm Retention time: 3.37 min (LEV) 6.40 min (PHE) Linearity range: 5-25µg/mL (LEV) 2.5-12.5µg/mL (PHE) r^2 value: 0.999	56

Analytical Methods for estimation of Levocetirizine and Montelukast Sodium with Other Drugs in Combined Dosage form: For simultaneous determination of Montelukast Sodium and Levocetirizine combined with other drugs have been studied and summarized in **Table 5.**

TABLE 5: ANALYTICAL METHODS FOR ESTIMATION OF LEVOCETIRIZINE AND MONTELUKAST SODIUM

Sl. No	Drug Combination	Method	Description	Ref.
1.	Montelukast Sodium, Levocetirizine Dihydrochloride and Acebrophylline in Tablet Dosage Form	RP-HPLC	Column: Hypersil ODS C_{18} column (250 × 4.6 mm, 5µm) Mobile phase: Methanol, acetonitrile and 20 mM ammonium acetate buffer (60:30: 10v/v) Flow rate: 0.8 mL/min Elution time: 10 min Linearity range: 2-12 µg/mL for MKT and LEV 20-120µg/mL ABP r^2 value:	57

2.	Ambroxol, Montelukast, and Levocetirizine in Tablet Dosage Form	RP-HPLC	0.999 % Purity: 99.89(LEV) 100.30%(ABP) 100.59% (MKT) % RSD (Precision, Accuracy): less than 2 % Column: C_{18} column Mobilephase: Triethylamine buffer: ACN: methanol (20:30:50v/v) Detection wavelength: 280 nm Linearity range: 7.7-22.5 µg/mL (AMB) (r^2=0.999) 1.25-3.75 µg/mL (MKT) (r^2=0.998) 5-15 µg/mL (LEV) (r^2=0.997) % Purity: 98.81% (AMB) 102.56% (MKT) 98.6 % (LEV)	58
3.	Acebrophylline, Montelukast and Levocetirizine DihydrochlorideForm	Simultaneous equation method	Solvent: Methanol Detection wavelength:250.14 nm ((λ max of ABP) 284.79 nm((λ max of MKT) 231.27 nm ((λ max of LEV) Linearity range: 6-18 µg/mL (ABP, MKT) 3- 12µg/mL for (LEV) r^2 value: 0.999 for all drugs % Purity: 100 % (ABP) 101 % (MKT) 99 %(LEV) % RSD (Precision): less than 2 %	59
4.	Doxofylline, Montelukast, and Levocetirizine Dihydrochloride in Tablet Dosages Form	RP-HPLC	Column: C_{18} (150 x 250 x 4.6 mm) Agilent column Mobile phase: Ammonia acetate Buffer: ACN) pH 3.5 Retention time: 4.425 min (DOX) 7.409 min (MKT) 8.558 min (LEV) Linearity range: 10-15 µg/mL for all drugs r^2 value: less than 1 % Purity: 101.21 % (DOX) 98.90 % (MKT) 100.40 % (LEV)	60

CONCLUSION: In recent years, various analytical methods have reported various analytical methods for quantitative estimation of drugs in combined pharmaceutical dosage forms under spectrophotometric and chromatographic methods. This article provides a summary of reported analytical methods for simultaneous estimation of Levocetirizine and Montelukast Sodium in bulk, combined pharmaceutical formulation, and a combination of these drugs with other different drugs available in the market. The literature review reveals that RP- HPLC is the most frequently used method over different spectroscopic methods and other chromatographic methods for their determination. RP-UPLC with a PDA detector gives good resolution between two drugs and is the most rapid analytical method for determining pharmaceutical compounds. Therefore, we can conclude that RP-UPLC and RP-HPLC should be the most preferred method for the simultaneous estimation of Montelukast sodium and Levocetirizine in terms of sensitivity, rapidity, and reliability. Spectrophotometric methods are economical, non-sophisticated, show a high level of accuracy and precision, and can be used as an alternative method to overcome the demerits of Chromatographic methods, which are complex, time-consuming, require expensive setup, and require a skilled operator. Overall, both spectrophotometric and chromatographic methods can be successfully used to simultaneously estimate the pharmaceutical drug product in bulk and combined pharmaceutical dosage form. All the developed methods for Levocetirizine and Montelukast Sodium were validated per ICH guidelines, and the methods met its acceptance criteria.

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