A REVIEW ON ANALYTICAL METHODS FOR SIMULTANEOUS ESTIMATION OF LEVOCETIRIZINE HYDROCHLORIDE WITH OTHER COMBINATION DRUGS IN BULK DOSAGE FORM

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Abstract

Levocetirizine is a second-generation, non-sedative antihistamine known for its potent effects and fast onset of action, which lasts longer compared to other antihistamines. A review article explores various analytical methods for determining levocetirizine dihydrochloride in amalgamation with other drugs such as Ambroxol hydrochloride, montelukast sodium, salbutamol sulphate, pseudoephedrine, phenylephrine hydrochloride, phenylpropanolamine hydrochloride, and acebrophylline. These combination drugs are commonly used for treating conditions like rhinitis, chronic obstructive pulmonary disease, seasonal allergies, and asthma. The study's findings indicate that the proposed methods, which include spectroscopic techniques and chromatographic techniques like UV-Spectroscopy, HPLC, RP-HPLC, and HPTLC, are precise, accurate, and reproducible for the, immediate approximation of levocetirizine and the above mentioned drugs in tablet dosage form.

Keywords: levocetirizine dihydrochloride, ambroxol hydrochloride, montelukast sodium, salbutamol sulphate, pseudoephedrine, phenylephrine hydrochloride, phenylpropanolamine hydrochloride, acebrophylline, UV-spectroscopy, HPLC, RP-HPLC, HPTLC.

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INTRODUCTION

Levocetirizine dihydrochloride is the chemical name for the R-(+)-enantiomer of cetirizine dihydrochloride. It is a crystalline powder that dissolves readily in water but has limited solubility in acetone and methylene chloride. Levocetirizine dihydrochloride is an approved drug listed in the Indian Pharmacopeia and British Pharmacopeia.[3] Its molecular formula is C21H25ClN2O3·2HCl, with a molecular weight of 461.8 g/mol. It is commonly prescribed for the action of situations such as sensitive rhinitis, rash, and rose fever. [6]

Mucolytic agent known as Trans-4-[(2-amino3,5-dibromobenzyl) amino]-cyclohexanol hydro-chloride. It is found as a white or yellowish crystalline powder that readily dissolves in methanol, has limited solubility in water, and is almost insoluble in methylene chloride. Through a molecular mass of 378.1028 g/mol and a molecular formula of C13H19Br2ClN2O, ambroxol hydrochloride is an approved compound.

The medication mentioned is included in the Indian Pharmacopeia [4] and British Pharmacopeia as an approved drug. It is commonly prescribed for the behaviour of conditions such as cough, respiratory disorders related with thick phlegm, acute and recurrent bronchitis, and chronic obstructive pulmonary disease [8].

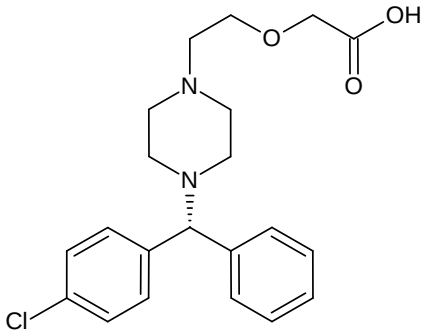
Montelukast sodium is the chemical name [11] for a leukotriene receptor antagonist that is effective in controlling and preventing symptoms associated with asthma, such as wheezing, coughing, difficulty in breathing, and chest tightness. It is an approved drug listed in the Indian Pharmacopeia and British Pharmacopeia Montelukast sodium appears as a white to whitish powder and exhibits high solubility in ethanol, methyl alcohol, and water. Conversely [31], it is practically insoluble in methylene chloride. With a molecular mass of 608.2 g/mol molecular formula of C35H35ClNO3S.Na, montelukast sodium is widely used for managing asthma symptoms.

Salbutamol sulphate, chemically recognized as (RS)-1-(4-hydroxy-3-hydroxy-methylphenyl)-2-(tert-butylamine) ethanol sulphate, is categorized as a short-acting ß2-adrenergic receptor agonist. It holds official status in both the Indian Pharmacopeia and British Pharmacopeia. With a molecular weight of 576.7 g/mol and a molecular formula of (C13H21NO3) H2SO4, salbutamol sulphate is characterized as an almost white or white crystalline powder It exhibits high solubility in water, slight solubility in ethanol, and is practically insoluble in dichloromethane. This drug is primarily utilized in the action of respiratory asthma and COPD (chronic obstructive pulmonary disease).The molecular weight of the compound listed in the British Pharmacopeia and Indian Pharmacopeia [4] is 165.23 g/mol, and its molecular formula is C10H15NO. It appears as a fine, white to off-white crystal or powder The compound exhibits high solubility in benzene, is freely soluble in ethanol, and has limited solubility in water.

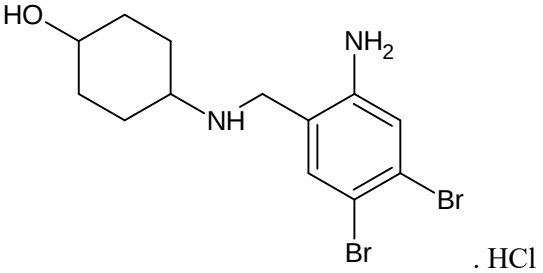
Phenylephrine hydrochloride is the chemical name for a selective alpha-1 adrenoreceptor agonist. It is recognized as an official drug in the British Pharmacopeia and Indian Pharmacopeia. With a molecular weight of 203.66 g/mol and a molecular formula of C9H14ClNO2, phenylephrine hydrochloride exists as a white crystalline powder. It is commonly prescribed for the treatment of nasal congestion sinus conditions, and respiratory ailments such as bronchitis, allergies, and hay fever.

Phenylpropanolamine hydrochloride, also known as benzenethiol, α-(1-aminoethyl)-hydrochloride, (R*, S*)-, or (±) Norephedrine hydrochloride, is a white to creamy white crystalline powder It is classified as an indirectly acting sympathomimetic drug and is commonly prescribed for the treatment of cold symptoms, nasal congestion, hay fever, and sinus irritation. With a molecular weight of 187.66 g/mol and a molecular formula of C9H14ClNO, phenylpropanolamine hydrochloride is utilized to alleviate various respiratory conditions.

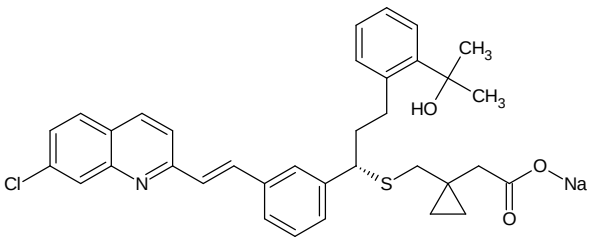
Acebrophylline is a chemical compound with the following chemical composition: 4-[(2-amino-3,5dibromophenyl) methylamino] cyclohexan-1-ol; 2-(1,3-dimethyl-2,6-dioxopurin-7-yl) acetic acid. It functions as both a mucolytic agent and a bronchodilator, primarily used for treating conditions like asthma and COPD (chronic obstructive pulmonary disorder). The molecular weight and molecular formula of acebrophylline are dependent on the specific arrangement of atoms in the compound. Acebrophylline has a molecular bulk of 616.3 g/mol and a molecular formula of C22H28Br2N6O5. This compound is recognized as an official drug in the Indian Pharmacopeia, British Pharmacopeia, and United States Pharmacopeia.



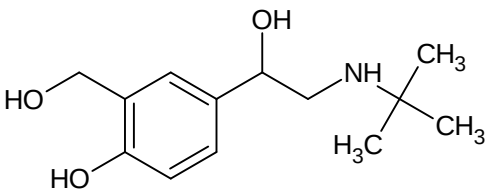
Levocetirizine



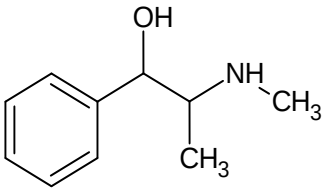
Ambroxol hydrochloride



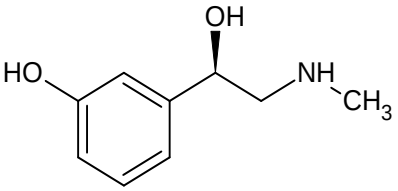
Montelukast sodium



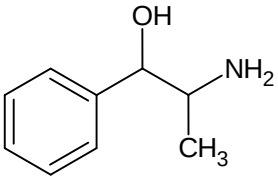
Salbutamol sulphate



Pseudoephedrine



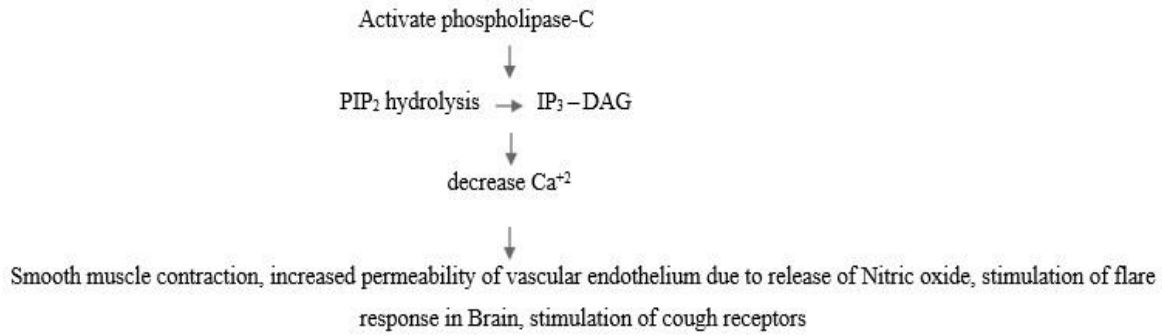
Phenylephrine hydrochloride



Propylamine hydrochloride

Mechanism of Action

Levocetirizine dihydrochloride exerts its effects by selectively inhibiting histamine H1 receptors. This specific act thwarts the activation of the receptor by histamine, thereby averting consequences such as even strength reduction, enlarged perviousness of vascular endothelium, histidine uptake in basophils, stimulation of cough receptors, and stimulation of flare responses in the nervous system. Additionally, levocetirizine dihydrochloride is known to activate phospholipase-C, leading to the hydrolysis of PIP2 into IP3 and DAG. This cascade ultimately results in a decrease in intracellular calcium levels. Consequently, the overall impact of levocetirizine dihydrochloride includes preventing smooth muscle contraction, reducing vascular endothelial permeability through the release of nitric oxide, dampening flare responses in the brain, and inhibiting the stimulation of cough receptors.



COMBINATIONS OF LEVOCETIRIZINE DIHYDROCHLORIDE:

1. Levocetirizine dihydrochloride + Montelukast sodium
2. Levocetirizine dihydrochloride + Ambroxol hydrochloride
3. Levocetirizine dihydrochloride + Paracetamol
4. Levocetirizine dihydrochloride + Phenylephrine hydrochloride
5. Levocetirizine dihydrochloride + Phenylpropanolamine hydrochloride
6. Levocetirizine dihydrochloride + Montelukast sodium + Ambroxol
7. Levocetirizine dihydrochloride + Montelukast sodium + Acebrophylline
8. Levocetirizine dihydrochloride + Salbutamol sulphate + Ambroxol hydrochloride
9. Levocetirizine dihydrochloride + Phenylephrine hydrochloride + Paracetamol
10. Levocetirizine dihydrochloride + Pseudoephedrine + Ambroxol

RP-HPLC method

The aim of this work is to develop an accurate, specific and validated HPLC method for simultaneous determination of Levocetirizine dihydrochloride and Montelukast Sodium from tablet dosage form. The proposed method was validated as per the International Conference on Harmonization (ICH) guidelines.

Materials and methods

Methanol used was of HPLC grade of Merck and Milli Q water was used for the preparation of the mobile phase. All other reagents like KH2PO4, KOH, H3PO4 used were of AR/GR grade. All the glass wares used were of standard quality.

Instrumentation

An Isocratic Waters HPLC with a 515 pump, 2487 dual λ UV-Visible detector and L7 column (Hypersil Gold: 250mm x 4.6mm, 5µm) were used for the analysis. The HPLC system was well equipped with Empower 2 software for data processing.

Summary of chromatographic condition: Parameters Condition- Column Hypersil Gold L7 (4.6 x 250 mm, 5µm), Mobile Phase 0.05 M KH2PO4, Buffer pH 7.5: Methanol 20: 80 v/v, Flow Rate ml/min, Temperature 35°C, Detection Wavelength 225 nm, Injection Volume 10 µl Diluent Mobile phase.

CONCLUSION:

The stated RP-HPLC method was proved to be simple, rapid and reproducible. The validation data indicate good precision, accuracy and reliability of the method. The developed method offers several advantages in terms of simplicity in mobile phase, isocratic mode of elution, easy sample preparation steps and comparative short run time which makes the method specific and reliable for its intended use in simultaneous determination of Levocetirizine dihydrochloride and Montelukast sodium in tablet dosage forms.

HPLC method MATERIALS AND METHODS

Chemicals and reagents: Analytically pure sample of LEVO and MONT were purchased. The pharmaceutical dosage form used in this study was Lemont tablets labelled to contain 5 mg of LEVO and 10 mg of MONT, Toluene, Ethyl Acetate and Methanol (AR grade).

Instrumentation and chromatographic conditions:
Chromatographic separation of drug was performed on precoated silica gel aluminium plate 60 F254 (20 ×10) with 250 µm thickness (E. MERCK, Darmstadt, Germany) using a CAMAG Linomat 5 sample applicator (Switzerland). Samples were applied on the plate as a band with 8 mm width using Camag 100 µL sample syringe (Hamilton, Switzerland).

CONCLUSION

Stability indicating HPTLC-Densitometric method for simultaneous estimation of LEVO and MONT as bulk drugs and in tablet dosage form has been developed and validated as per ICH guidelines. The standard deviation, % RSD calculated for the method are low, indicating a high degree of precision of the method. The results of the recovery studies performed indicated that the method is accurate for estimation of drugs in tablet dosage form. The results of the stress studies indicated the specificity of the method. The method can be used to determine the purity of the drugs available from various sources by detecting the related impurities.

UV-SPECTROSCOPY MATERIALS AND METHODS

Instrument A double beam UV/Visible spectrophotometer (Shimadzu 1cm matched quartz cells, and UV probe 2.10 software was used. Calibrated analytical balance was used for weighing purpose. Bath so nicator (Enertech solutions). All statistical calculations were carried out using Microsoft Excel Der Pharmacia Litter, 2014, 6 (3):

A double beam UV/Visible spectrophotometer (Shimadzu ® 1700 Pharmaspec) with wavelength accuracy (±0.5 1cm matched quartz cells, and UV probe 2.10 software was used. Calibrated analytical balance Bath sonicated (Enertech® Electronics Pvt. Ltd., Mumbai) was used for sonication of All statistical calculations were carried out using Microsoft Excel® 2007 analytical tool. Montelukast sodium was obtained as gift sample from More pen Lab. Ltd. Solan, India. Levocetirizine dihydrochloride was obtained as gift sample from Symed Lab. Ltd. Hyderabad, India. Sodium lauryl sulphate was purchased from Loba Chemie Pvt. Mumbai, India. All were prepared in distilled water. Montelukast sodium and Levocetirizine dihydrochloride combination tablet (Telekast-L®, Lupin Lab. Ltd. India) was purchased from local market. A 0.5% w/v sodium lauryl sulphate (SLS) in distilled water was used as a medium for analytical method development.
Limit of detection (LOD) and limit of quantification: ICH guidelines describe several approaches to determine limit of detection and limit of quantification. These include visual inspection, signal to-noise ratio, and the use of standard deviation of the response and the slope of the calibration curve. The value of LOD and LOQ were calculated according to 3.3/S and 10/S criteria respectively, where the standard deviation of the intercepts of the regression lines and S is the slope of the calibration curve.

CONCLUSION:

The developed derivative UV spectrophotometric method is a new, simple, precise, accurate and economical for simultaneous quantitative estimation of MONT and LEVO. The method was validated (as per ICH guidelines) for various parameters, viz., linearity, accuracy, precision, limits of detection (LOD) and limit of quantification (LOQ). It could serve as an alternative method for determination of MONT and LEVO simultaneously in marketed products and therefore, may be used for routine quality control analysis of MONT and LEVO in multidrug products.

LEVOCETIRIZINE DIHYDROCHLORIDE + AMBROXOL HYDROCHLORIDE

HPLC method

Unadulterated trials of LEVO and AMB were generously provided by Orchidaceous plant Chemicals and Pharmaceutical Ltd. located in Chennai, India. The diluters used in the study were of HPLC and analytical mark and remained obtained from Merck in Mumbai, India. Three different brands of capsules, namely A iritis Plus (Brand 1; Nicholas Piramal India Ltd, Mumbai, India), Lavetta – A (Brand 2; Alembic Ltd, Vadodara, India), and Levocet – Plus (Brand 3; Hetero Health Care Ltd, Hyderabad, India), were obtained from the inhabitant market for evaluation.

HPLC conditions

For investigation, the arranged examples practiced isocratic HPLC by means of the following device: an LC-10AT system (Shimadzu Corporation, Kyoto, Japan), a Hamilton Rheodyne hypodermic (Hamilton Bonaldis AG, Switzerland) with a volume of 20 µl for model vaccination, and a hypodermic load sample injector (Model 7725i,

Rheodyne LP, CA, USA). A Luna C18 post with sizes of 250 x 4.6 mm i.d. (Phenomenex, USA) was utilized. The mobile phase consisted of a mixture of acetonitrile and buffer (composed of 10mM diammonium atomic number 1 o-phosphate with pH adjusted to 7.0 using sodium hydroxide) in a ratio of 60:40 v/v. Prior to analysis, the movable phase was aired using an accelerated bath (Model Sonorex, Bandelin Electronic, Germany). The HPLC study was showed at room temperature, through a flow rate of 1 ml/min, using a semiconductor diode array detector (Shimadzu SPD M10Avp model, Shimadzu Corporation, Kyoto, Japan). Finding happened at a wavelength of 230 nm. Data study was completed by means of the Class M10 package (Shimadzu Corporation, Kyoto, Japan).

CONCLUSION

The HPLC method created for the accurate, precise, quick, and selective determination of AMB and LEVO in capsules. Therefore, it may be utilised quickly and easily for routine quality control analysis, especially when there are a lot of samples involved. The created approach was discovered to be specific since there was no excipient interference, which is supported by the lack of additional peaks.

LEVOCETIRIZINE + PHENYLEPHRINE RP-HPLC Materials & Methods

Substance and Samples: Methanol of HPLC grade and ortho-phosphoric acid of AR grade, along with pure standards of Levocetirizine dihydrochloride (99.26%) and Phenylephrine (99.89%), were active in the study. Water was disinfected using the Milli-Q Millipore system. Prior to use, all solvents and solutions were filtered through a 0.45 µm pore size membrane filter (Millipore Millex® FH filter units, Dura pore-PVDF, Polyethylene) and exposed to degassing.

Instrumentation and Materials: Analysis was achieved on Waters Younglings HPLC separation module within built UV detector. Chromatographic software Empower 2 was used for data collection and processing. The analytical column was Phenomenex Gemini C 18 (5 m, 250 mm 4.6 mm).

Conclusion

A extremely consistent and effective method for determining the quantities of LEVO and PHE in both bulk and tablet dosage forms has been effectively developed using RP-HPLC. The numerical analysis of the method demonstrated outstanding linearity, reproducibility, and validation across various parameters, indicating its accuracy and precision. These discoveries powerfully care the pertinence of the method for the rapid and reliable resolve of LEVO and PHE.

UV-SPECTROSCOPY

Elements and Reagents: Pure LEVO and PHE were provided as free samples for analysis by Baroque Pharmaceuticals, Khambhat, Gujarat, India. A local pharmacy sold LEVO and PHE tablets, levocet D+ manufactured by Hetero Healthcare Ltd., Hyderabad, India, and Rinostat-L manufactured by RPG Life Sciences Ltd.,
Maharashtra, India.

Instruments: Shimadzu UV-Visible 1700 double beam spectrophotometer, 1 cm matched quartz cells, and UV probe 2.34 software were utilised. Analytical balance calibration Weighing was accomplish with a Shimadzu BP211D (Sartorius Gottingen AG, Germany). The Microsoft Excel 2007 analytical tool was used to achieve all statistical controls.

Conclusion: A highly reliable measurable examination method, using the first-order imitative approach, takes remained planned for the concurrent purpose of LEVO and PHE in combination tablet dose forms. This technique offers a straightforward and correct method with high specificity. To confirm its strength and dependability, the technique was carefully verified in agreement with the ICH standards, cover aspects such as linearity, accuracy, precision, limits of discovery (LOD) and quantification (LOQ), and repeatability. The results found from these approximations funding the appropriateness of the planned method for repetitive analysis and excellence control calculations of LEVO and PHE in mixture dose forms.

LEVOCETIRIZINE + MONTELUKAST+ AMBROXOL HYDROCHLORIDE RP-HPLC method

Device: Chromatographical quantities were carried out utilizing a Shimadzu model system, which comprised an LC10AD and LC10ADvp in the black delivery module, an SPD10A UV-Visible indicator, a Rheodyne injector regulator prepared through a 20 µl loop, and a UV detector (SPD10A). The system was controlled by a system controller (SCL-10A) and a personal computer running Shimadzu chromatographic software program (LC Solution, Release 1.11SP1). To degas the mobile phase, a Branson sonicated was employed. Optical

density spectra were recorded using a UV-Visible spectrophotometer and a quartz cell with a path length of 1.00 cm.

Chemicals and reagents: Ambroxol (AMB), Montelukast (MLS), Levocetirizine (LEVO), and Probenecid (IS) working standards. MeCN and MeOH were HPLC grade, while dipotassium hydrogen inorganic phosphate and orthophosphoric acid were analytical-reagent rating.

Conclusion: An isocratic RP-HPLC-UV method for parallel size of AMB, LEVO, and MLS in human plasm samples was advanced and improved in this study. The time of analysis and determination were optimized at the same time using chemometrics methods such as CCD and Derringer's desirability function. The education's results demonstration the price of by means of this technique to regulate the best conditions for causal medications in plasma samples. The entire period for chromatographical analysis per sample was about 8.665 minutes. The justification research confirmed the examine surroundings by positive that it was exact, accurate, linear, exact, and robust. The method was discovered to be easy and sensitive, and it may be effectively active in routine investigation for the quantity of AMB, LEVO, and MLS in organic materials.

Drug combination	Method and instrument	Parameters	Detector used	LOD and LOQ	Concentration range	Reference
1.Levocetirizine dihydrochloride and Montelukast sodium	UV-Spectroscopy Double beam UV- Vis spectrophotometer Shimadzu 1700	Mobile phase-Toluene:Ethyl acetate: Methanol (2.5:5:2.5) v/v/v UV detection at240nm.	UV detector	LEVO LOD-44.4ng/band LOQ-134.66ng/band MONT LOD-29.12ng/band LOQ-88.24ng/band	% RSD of peak not more than 2%	10
2.Levocetirizine dihydrochloride and Montelukast sodium	RP- HPLC WatersHPLC	Pumps- 515 Auto sampler-2960 Column used- C18 (4.68×150mm×5µm) Mobile phase-Acetonitrile: Ammonium acetate buffer (65:35) UV detection at230nm	UV detector 2998	LEVO LOD-0.05µg/ml LOQ-0.17µg/ml MONT LOD-0.10µg/ml LOQ-0.33µg/ml	% RSD not more than 2%	11

3.Levocetirizine dihydrochloride and Montelukast sodium	RP-HPLC LC- Waters	Pumps-600 Auto sampler-717 Column used- C18 (4.68×150mm×5µm) Mobile phase-Methanol: Water(75:25) v/v Detection wavelength at 235nm	Photodiode Array detector	LEVO LOD- 0.42ng/ml LOQ- 0.36ng/ml MONT LOD- 0.16ng/ml LOQ- 0.12ng/ml	% RSD not more than 2%	12
4.Levocetirizine dihydrochloride and Montelukast sodium	HPTLC	Sampler-Camag 100 microlitre sample syringe Slit dimension-5mm×0.45mm Mobile phase-Toluene: Ethyl acetate: Methanol: ammonia (2.5:7:2.5:1)	UV detector	LEVO LOD- 90ng/spot LOQ- 200ng/spot MONT LOD- 50ng/spot LOQ-110ng/spot	RSD Value LEVO-0.42% MONT-0.20%	13
5.Levocetirizine dihydrochloride and Ambroxol hydrochloride	RP-HPLC (Shimadzu corporation)	Pump- LC-10AT Injecting sampler-Hamilton Rheodyne syringe. Column used- C18 L Mobile phase-Acetonitrile: Buffer (60:40) v/v Detection wavelength at 230nm	Photodiode Array detector	LEVO LOD-0.1µg/ml LOQ-0.3µg/ml AMB LOD-1.5µg/ml LOQ-4.5µg/ml	Less than 6% for LEVO Less than 6% for AMB	14

6.Levocetirizine dihydrochloride and Phenylephrine hydrochloride	RP-HPLC Waters Younglin system	Pump- Gradient Column used- C18 Phenomenex Gemini Mobile phase – Methanol: Water (70:30) v/v Detection wavelength at 230nm	UV detector	LEVO LOD- 0.19 µg/ml LOQ- 0.57 µg/ml PHE LOD- 2.9 µg/ml LOQ- 8.17 µg/ml	% RSD not more than 2%	15
7.Levocetirizine dihydrochloride and Phenylpropanolamine hydrochloride	RP-HPLC	Pump- Binary gradient pump Sampler- Rheodyne injector Hamilton syringe Column used- C18 Phenomenex Luca Mobile phase- Acetonitrile: Triethylamine (70:30)	Multiple Wavelength detector		% RSD not more than 2%	16
8.Levocetirizine dihydrochloride, Montelukast sodium and Ambroxol hydrochloride	HPLC	Pump- LC10 AD Sampler- Rheodyne Injector Column used- C18 Phenomenex column Mobile phase- Acetonitrile: Methanol: K2HPO4 (32.7:30:37.3) v/v/v	UV-Vis detector		% RSD not more than 2%	17
9. Levocetirizine dihydrochloride, Montelukast sodium and Ambroxol hydrochloride	RP-HPLC	Pump-LC10 AD and LC10 ADVP Sampler- Rheodyne injector Mobile phase- Acetonitrile: Methanol: K2HPO4 (40:30:30) v/v/v	SPD 10A UV-Vis detector	LEVO LOD- 0.23 ng/ml LOQ- 0.58 ng/ml MONT LOD- 0.3 ng/ml LOQ- 1.12 ng/ml AMB LOD-0.16 ng/ml LOQ- 0.47ng/ml	% RSD not more than 2%	18

10.Levocetirizine dihydrochloride, Montelukast sodium and Acebrophylline	RP-HPLC	Column used-C18 Hypersil Mobile phase-Methanol: acetonitrile: ammonium acetate buffer (60:30:10)		LEVO LOD-0.21µg/ml LOQ-0.63µg/ml MONT LOD-0.35µg/ml LOQ-1.07µg/ml THP LOD-3.24µg/ml LOQ-9.08µg/ml AMB LOD-4.11µg/ml LOQ-	% RSD less than 2%	19
11. Levocetirizine dihydrochloride, Montelukast sodium and Acebrophylline	UV-Spectroscopy UV-Vis double beam spectrophotometer Perkin Elmer		UV-Vis Detector	LEVO LOD-0.29µg/ml LOQ-0.6µg/ml	% RSD not more than 2%	20
12. Levocetirizine dihydrochloride, Montelukast sodium and Acebrophylline	HPLC Waters HPLC	Pump-515 Column used Macherey Nagel column (4.6×250mm) Mobile phase-Ammonium phosphate buffer: Methanol (15:85) v/v	Photodiode Array detector		% RSD not more than 2%	21
13.Levocetirizine dihydrochloride and Pseudoephedrine	RP-HPLC	Pump-LC 10A TVP PUMP Sampler-Rheodyne injector Column used-Hypersil C18 (250×4.5mm), 0.5µ, column	SPD 10A UV detector		% RSD not more than 2%	22

		Detection wavelength-257nm				
14.Levocetirizine dihydrochloride, Ambroxol hydrochloride and Pseudoephedrine	HPTLC	Mobile phase-Ethyl acetate: Methanol: Ammonia (8:1:0.5) v/v/v	UV detector	LEVO LOD-25ng/spot LOQ-60ng/spot PSEUDO LOD-40ng/spot LOQ-87ng/spot AMB LOD-35ng/spot LOQ-71ng/spot	% RSD not more than 2%	23
15.Levocetirizine dihydrochloride, Phenylephrine hydrochloride, paracetamol and Ambroxol hydrochloride	RP-HPLC	Column used-Nucleosil C18 Flow rate: 1ml/min Detection wavelength-230nm Mobile phase-Methanol: Sodium phosphate dibasic anhydrous (65:35) v/v	UV detector		% RSD not more than 2%	24
16.Levocetirizine dihydrochloride and Dextromethorphan hydrobromide	RP-HPLC	Pump-LC 20AT double reciprocating pump Column used: Phenomenox C18 analytical column. Mobile phase: Potassium dihydrogen phosphate buffer: Acetonitrile: Tetrahydrofuran (70:25:5) v/v/v	SDP- 20A UV-Vis detector		% RSD for LEVO-0.05% % RSD for DEXO-0.27%	25

		Detection wavelength: 232nm				
17. Levocetirizine dihydrochloride and Diethylcarbamazine	RP-HPLC Wters1515	Pump- LC 20 AT pump Rheodyne 7725 injector Column used: Hypersil BDS C18 column Mobile phase: Potassium orthophosphate buffer: Acetonitrile (20:80) v/v	Photodiode Array detector	LEVO LOD-0.08ppm LOQ-0.2ppm DIET LOD-2.42ppm LOQ-7.42ppm	%RSD for LEVO- 0.5 %RSD for DIET- 0.3	26
18.Levocetirizine dihydrochloride and Fexofenadine hydrochloride	RP-HPLC LA Chrom ELITE	Pump- L 2130 Auto sampler-L 2200 Column oven-C 2300 Column used-C18 analytical column. (150×4.6mm) Mobile phase-Potassium dihydrogen phosphate buffer: Acetonitrile (68:32) v/v	Photodiode Array detector	LEVO LOD-6.8µg/ml LOQ-22.7µg/ml FEXO LOD-9.0µg/ml LOQ-30µg/ml	%RSD less than 2%	27
19. Levocetirizine dihydrochloride, Salbutamol sulphate And Ambroxol hydrochloride	UV-Spectroscopy Double beam UV-Vis spectrophotometer Shimadzu 1800 Japan	Detection wavelength range-200-400nm	UV-Vis detector	LEVO LOD-0.457µg/ml LOQ-1.386µg/ml SAL LOD-0.523µg/ml LOQ-1.372µg/ml AMB LOD-0.450µg/ml LOQ-1.424µg/ml	%RSD less than 2%	28

20. Levocetirizine dihydrochloride, Fexofenadine, Buclizine and Gliquidone	RP-HPLC method	Pump-LC10AT pumps Rheodyne manual injector Column used: STAR RP18 End capped column. Mobile phase-Methanol: Water (80:20) v/v Detection wavelength-230nm	SDP 10AV UV Detector	LEVO LOD-0.16µg/ml LOQ-0.55µg/ml FEXO LOD-0.19µg/ml LOQ-5.0µg/ml BUCL LOD-0.09µg/ml LOQ-0.32µg/ml GLI LOD-0.10µg/ml LOQ-0.33µg/ml	%RSD less than 2%	29

CONCLUSION

This comprehensive review article provides an overview of the investigative systems stated for the synchronized estimate of levocetirizine dihydrochloride in mixture with other drugs in bulk dosage forms obtainable in the marketplace. New progressions have led to the growth of numerous investigative systems for measurable approximation of drugs in joint dosage forms, with a concentration on chromatographical and spectroscopical methods. The appraisal places of interest that RP-HPLC is the most commonly working technique associated to additional chromatographical and spectroscopic methods due to its greater determination skills, predominantly after joined with a PDA (Photodiode Array) indicator. RP-HPLC with PDA discovery also suggestions fast study. However, chromatographical methods have positive limits, counting difficulty, time ingesting, high set/ up costs, and the essential for expert operatives. In difference, spectrophotometric devices are reasonable, forthright, and validate high accuracy and precision. It is remarkable that both spectrophotometric and chromatographical methods can be used efficiently for immediate approximation of levocetirizine dihydrochloride and other mixture drugs in bulk and shared pharmacological dose forms. All advanced systems followed to ICH rules and efficaciously encountered the getting measures upon justification.

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