WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 4, 665-678. Review Article ISSN 2277– 7105

# A REVIEW ON ANALYTICAL METHOD DEVELOPMENT FOR SIMULTANEOUS ESTIMATION AND VALIDATION OF MONTELUKAST SODIUM AND BILASTINE

**Krishna P. Vairagi* and Dr. Shuchi P. Desai**

Department of Pharmaceutical Quality Assurance, ROFEL Shri G.M. Bilakhia College of Pharmacy, Vapi, Gujarat, India.

Article Received on
06 February 2021,

Revised on 26 Feb. 2021,
Accepted on 16 March 2021

DOI: 10.20959/wjpr20214-20110

***Corresponding Author**
**Krishna P. Vairagi**
Department of Pharmaceutical Quality Assurance, ROFEL Shri G.M. Bilakhia College of Pharmacy, Vapi, Gujarat, India.

## ABSTRACT

Bilastine is a selective histamine H1 receptor antagonist. It binds to and prevents the activation of the H1 receptor, reduces the development of allergic symptoms due to the release of histamine from mast cells. So, it acts as antiallergenic and acts to reduce allergic symptoms such as nasal congestion and urticaria. Montelukast Sodium is a leukotriene receptor antagonist that binds with CysLT type 1 receptor, which consequently assists in inhibiting any physiological actions of CysLTs like LTC4, LTD4, and LTE4 at the receptor that may facilitate asthma or allergic rhinitis. And hence it's mainly used to control and prevent symptoms caused by asthma (such as wheezing and shortness of breath) and in allergic rhinitis. Both drugs in combination are used in treatment of allergic rhinitis and mild to moderate asthma. In this review, there is involvement of analytical methods on Bilastine and Montelukast Sodium. However, there are no any methods available for combination of Bilastine and Montelukast Sodium. There are UV, HPLC, HPTLC and UPLC method on Bilastine and Montelukast Sodim either individually or along with other drugs. This review can be used for further analytical method development.

**KEYWORDS:** Allergic rhinitis, Bilastine, Montelukast sodium, RP-HPLC, HPTLC.

## INTRODUCTION

Allergic rhinitis (AR) is a chronic inflammatory disease. AR is an immunoglobulin E–mediated inflammatory reaction in the nasal mucosa caused by inhaled allergens, such as pollen, mold, or animal dander. Allergic Rhinitis is part of a systemic inflammatory process

and is associated with other inflammatory disorders, including asthma, rhinosinusitis, and allergic conjunctivitis.

Asthma is a disease that affects your lungs. It is one of the most common long term diseases of children, but adults can have asthma, too. Asthma causes wheezing, breathlessness, chest tightness, and coughing at night or early in the morning. Allergic rhinitis or asthma can be associated with chronic sinusitis.[1,2]

When AR patients are exposed to allergens, allergic reactions develop in 2 different patterns according to time sequence. One is the early reaction, in which sneezing and rhinorrhea develops in 30 minutes and disappears. The other is the late reaction, which shows nasal obstruction approximately 6 hours after exposure to allergens and subsides slowly. The early reaction is the response of mast cells to offending allergens (type I hypersensitivity). Stimulated mast cells induce nasal symptoms by secreting chemical mediators such as histamine, prostaglandins and leukotrienes. In contrast to the early reaction, eosinophils chemotaxis is the main mechanism in the late reaction, which is caused by chemical mediators produced in the early reaction. Several inflammatory cells, eosinophils, mast cells and T cells migrate to nasal mucosa, break up and remodel normal nasal tissue, and these processes result in nasal obstruction which is the main symptom of AR patients.

**Symptoms Of Allergic Rhinitis**: Sneezing, Runny nose, Itchy nose, Coughing, Itchy & Watery eyes, Sore or Scratchy throat, Frequent headaches, Eczema type symptoms- like having extremely dry itchy skin that can blister, Excessive fatigue.[3,4]

**Combined Dosage Form**: Drug Combination Bilastine and Montelukast Sodium was approved by CDSCO on 11th of March, 2020. Drug Combination Bilastine and Montelukast Sodium used for the treatment of allergic rhinitis and mild to moderate asthma. Bilastine is an antiallergenic and acts to reduce allergic symptoms such as nasal congestion and urticaria. Montelukast Sodium is used to control and prevent symptoms caused by asthma and in allergic rhinitis.[5]

**Physical and Chemical Properties**

**1. Montelukast Sodium**

Montelukast sodium is white to pale yellow powder. It's chemical name is Monosodium salt of 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1- methy

lethyl) phenyl] propyl]thio]methyl]cyclopropane aceticacid. It's molecular formula $C_{35}H_{35}ClNNaO_3S$. It's molecular weight is 608.2 g/mol. Freely soluble in ethanol, methanol, and water and practically insoluble in acetonitrile. Its melting point is 110-115 °C. The LogP (Partition coefficient) 8.49. It is official in Indian Pharmacopoeia 2018, Japan Pharmacopoeia 2016.[6]

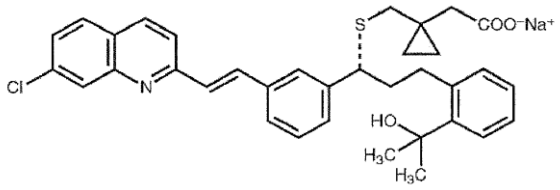


**Fig. 1: Chemical Structure of Montelukast Sodium.**

**2. Bilastine**

It is white crystalline powder. It's chemical name 2-[4-[2-[4-[1-(2-ethoxyethyl)benzimidazol-2-yl]piperidin-1-yl]ethyl]phenyl]-2-methylpropanoic acid. The molecular formula $C_{28}H_{37}N_3O_3$. The molecular weight is 463.6 g/mol. Soluble in DMSO (Dimethyl Sulfoxide), ethanol and water. It's melting point is 197.5-199.8 °C. LogP (Partition coefficient) value is 5.06. It is not official in any Pharmacopoeia.[7]

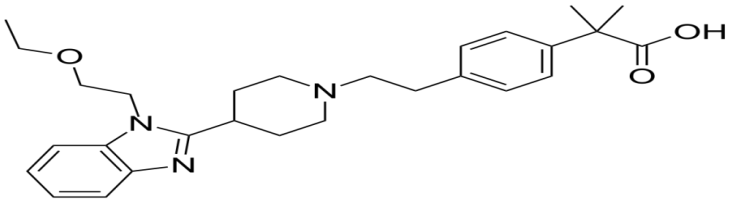


**Fig. 2: Chemical Structure of Bilastine.**

**Analytical Methods**

Analytical chemistry is defined as the science and art for determining the composition of material with concerned to elements and compounds present in it. It is divided into two branches namely quantitative and qualitative. We can find both qualitative as well as quantitative results. A qualitative method yields information of the chemical identity of the species in the sample. A quantitative method provides numerical information regarding the relative amounts of one or more of the analytes in the sample. Method development is a process of proving that an analytical method is acceptable for use to measure the concentration of an API in a specific compounded dosage form. The analytical method development and validation is essential for analytical method development and tested

extensively. Validation of an analytical method which is used during drug development and drug manufacturing is required to demonstrate that the methods are fit for their intended purpose. The validation parameters which are tested include specificity, linearity, accuracy, precision, range, detection limit, quantization limit, and robustness. There is introduction of number of drugs in market every year. These drugs may be either new entities or structural modification of the existing drug. Under these conditions, analytical procedures and standard methods for these drugs may not be available in the pharmacopoeias. So it is necessary to develop newer analytical methods for such drugs.[8,9]

The methods like UV, HPLC have been reported for Bilastine individually and along with other drugs. For estimation of Montelukast Sodium, methods like UV, HPLC, HPTLC were reported either individually or in combination with other drugs. However, there is no any method on combination of Bilastine and Montelukast sodium till date has been reported.

**Literature Review of Bilastine**

- **Official method for estimation for Bilastine**

There is no official method for Bilastine in any Pharmacopoeia.

**Table 1: Reported methods for estimation of Bilastine.**

| Sr. No. | Method | Description | Ref. No. |
|---|---|---|---|
| 1. | **UV Spectrophotometric** method for quantitative determination of **Bilastine** using experimental design for robustness. | **Model**: Lambda 35<br>**Solvent**: 0.1 mol $L^{-1}$ HCl.<br>**Wavelength**: 210nm<br>**Linearity**: 3- 20µg/ml | [10] |
| 2. | Method Development And Validation Of New **RP-HPLC Method** For The Estimation Of **Bilastine** In Pharmaceutical Dosage Form | **Column**: Inertsil ODS C18 (250mmx4.6mm, 5µm)<br>**Wavelength**: 254nm<br>**Mobile phase**: Methanol : Acetonitrile 60:40(v/v)<br>**Flow rate**: 1.2ml/min<br>**Retention time:** 2.8min<br>**Linearity**: 10-250µg/ml | [11] |
| 3. | **Degradation kinetics of Bilastine** determined by **RP-HPLC** method and identification of its degradation product in oxidative condition | **Column**: Water symmetry C18 column (250 mm×4.6 mm , 5µm)<br>**Mobile phase**: Acetonitrile : Phosphate buffer 30:70(v/v)<br>**Wavelength**: 275nm<br>**Flow rate**: 1ml/min<br>**Retention time**: 8.5min<br>**Linearity**: 10–240µg/ml | [12] |

<table>
<tr>
<td>4.</td>
<td>Stability Indicating Method Development And Validation For The Determination Of Bilastine And Its Impurities By UPLC</td>
<td>Column: Water RP-UPLC Acquity (2.1 mm × 150 mm, 1.7µm)<br>Wavelength: 275nm<br>Mobile phase: 0.05% TFA in water and 0.05%TFA in Acetonitrile<br>Flow rate: 0.1ml/min<br>Retention time:7.54min<br>Stability results
<table>
<tr><th>Stress Conditions</th><th>%Drug remained</th></tr>
<tr><td>Acidic (1N HCl 60°C, 2 hr)</td><td>99.5</td></tr>
<tr><td>Basic (1 N NaOH 60°C, 2 hr)</td><td>95.0</td></tr>
<tr><td>Peroxide (3% H2O2, 6hr)</td><td>99.4</td></tr>
<tr><td>Thermal (105 °C , 48 hr)</td><td>99.7</td></tr>
<tr><td>Photolytic stability</td><td>99.9</td></tr>
</table>
</td>
<td>[13]</td>
</tr>
<tr>
<td>5.</td>
<td>Analytical Method Development And Validation For The Estimation Of Bilastine In Bulk And Pharmaceutical Dosage Form By UPLC</td>
<td>Column: Phenomenex C8 column (50 mm × 2.1 mm, 1.7µm)<br>Mobile phase: pH 3.5 Sodium Phosphate 10mM Buffer : Methanol : Acetonitrile 60 : 30 : 10 (v/v/v)<br>Wavelength: 248nm<br>Flow rate: 0.5 ml/min<br>Retention time: 1.190 min<br>Linearity: 50-50µg/ml</td>
<td>[14]</td>
</tr>
</table>

## LITERATURE REVIEW OF MONTELUKAST SODIUM

**Table 2: Official methods for Montelukast Sodium.**

| Sr. No. | Official In | Method | Description | Ref. No. |
|---|---|---|---|---|
| 1. | IP 2018 | Chromatographic methods | **Column:** Hypersil ODS Octadecylsilane (15cm×4.6 mm, 5µm)<br>**Mobile phase**: Dissolve 3.85g of ammonium acetate in 1oooml of water, add 1ml of triethylamine, adjusted to pH 5.5 with glacial acetic acid, Methanol<br>**Wavelength:** 240nm<br>**Flowrate:** 1ml/min<br>**Injection volume:** 20µl | 15] |

**Table 3: Reported methods for Montelukast Sodium.**

| Sr. No. | Method | Description | Ref. No. |
|---|---|---|---|
| 1. | **UV Spectrophotometric Method** Development And Validation For Simultaneous Determination Of **Fexofenadine Hydrochloride** And **Montelukast Sodium** In Tablets | **Model:** Shimadzu 1800<br>**Solvent:** 0.1N NaOH<br>**Simultaneous Equation Method:**<br>**Wavelength:**<br>**FEX-** 259nm<br>**MKT**- 344.5nm<br>**Linearity:**<br>**FEX:** 50 - 180µg/ml<br>**MKT:** 1 - 35µg/ml | [16] |
| 2. | **Spectrophotometric Method** Development and Validation for **Montelukast Sodium** and **Simvastatin** in Bulk and Tablet Dosage Form Using **Absorption Ratio Method** | **Model:** Labindia UV 3000+<br>**Solvent:** 0.1 M NaOH<br>**Absorption Ratio Method:**<br>**Iso-absorptive point**- 244nm<br>λmax of MKT- 295nm<br>**Linearity:**<br>Both drugs: 2 - 10µg/ml | [17] |
| 3. | Simultaneous **UV Spectrophotometric Method** For Estimation Of Ebastine And **Montelukast Sodium** In Tablet Dosage Form By **Q-Ratio Method** | **Model:** Labindia UV 3000+<br>**Solvent:** 0.1 M NaOH<br>**Q-Ratio Method:**<br>**Iso-absorptive point**- 261.34nm<br>Λmax of EBS- 253nm<br>**Linearity:**<br>Both drugs: 5 - 45µg/ml | [18] |
| 4. | Validated **Uv Spectroscopic Method** For Estimation Of **Montelukast Sodium** From Bulk And Tablet Formulations | **Model:** Systronics 2203<br>**Solvent:** 7.4 pH Phosphate buffer+ 0.5% Sodium Lauryl Sulphate<br>**Wavelength:** 287.3nm<br>**Linearity:** 2 - 100µg/ml | [19] |
| 5. | Simultaneous Determination Of **Montelukast Sodium** And **Bambuterol Hydrochloride** In Tablet Dosage Form By **Ultraviolet Spectrophotometry** | **Model:** Systronics 2202<br>**Solvent:** Water<br>**Simultaneous Equation Method:**<br>**Wavelength:**<br>MKT- 322nm<br>BAM- 266nm<br>**Linearity:**<br>MKT: 1 - 10µg/ml<br>BAM**:** 5 - 40µg/ml | [20] |
| 6. | Simultaneous Determination of **Montelukast Sodium** and **Levocetirizine Dihydrochloride** in Pharmaceutical Preparations by **Ratio Derivative Spectroscopy** | **Model:** Varian Cary 100<br>**Solvent:** Methanol<br>**Ratio Derivative Spectroscopy:**<br>**Wavelength:**<br>MKT- 250.4nm<br>LEV- 238.4nm<br>**Linearity:**<br>MKT: 4 - 12µg/ml<br>LEV: 2 - 6µg/ml | [21] |

| | | | |
|---|---|---|---|
| 7. | Newly Developed and Validated Method of **Montelukast Sodium** Estimation in Tablet Dosage Form by **Ultraviolet Spectroscopy** and **Reverse Phase-High Performance Liquid Chromatography** | **UV Spectroscopy:**<br>**Model:** Beckman CoulterDU800<br>**Solvent:** Water : Methanol 1:1 (v/v)<br>**Wavelength**: 280nm<br>**Linearity:** 1- 10µg/ml<br>**RP-HPLC:**<br>**Column:** C18 column (250 mm×4.6 mm, 5µm)<br>**Mobile phase:** Ammonium acetate : Acetonitrile 25:75 (v/v)<br>**Retention time:** 3.7min<br>**Linearity:** 150 - 500ng/ml | [22] |
| 8. | Method Development and Validation for Simultaneous Estimation of **Montelukast Sodium** and **Desloratadine** by **RP-HPLC** | **Column:** Hypersil BDS C18 column (250 mm × 4.6 mm, 5µm)<br>**Mobile phase:** Orthophosphoric acid : Water 20:80 (v/v)<br>**Wavelength:** Both drugs: 280nm<br>**Flow rate:** 1ml/min<br>**Retention time:**<br>MKT: 2.929min<br>DES: 4.439min<br>**Linearity:**<br>MKT: 10 - 30µg/ml<br>DES: 5 - 15µg/ml | [23] |
| 9. | **RP-HPLC** Method Development And Validation Of **Montelukast Sodium** In Bulk Drug And Dosage Form | **Column:** Zobrax Eclipse XDB-C18 column (4.6mm×150mm, 5µm)<br>**Mobile phase:** Methanol:Acetonitrile:Water 60:30:10 (v/v/v)<br>**Wavelength:** 344nm<br>**Flow rate:** 1ml/min<br>**Retention time:** 3.582min<br>**Linearity:** 5 - 30µg/ml | [24] |
| 10. | Determination of **Montelukast Sodium** in Raw Material and Solid Dosage Form Using **Reverse Phase HPLC** | **Column:** Octylsilyl C8 (250 mm × 4.6 mm, 5µm)<br>**Mobile phase:** Acetonitrile : Sodium acetate buffer 80:20 (v/v)<br>**Wavelength:** 350nm<br>**Flow rate:** 1ml/min<br>**Retention time:** 8.214min<br>**Linearity:** 0.00008 - 0.2mg/mL | [25] |
| 11. | Simultaneous Estimation Of **Levocetirizine Dihydrochloride** And **Montelukast Sodium** By **RP-HPLC Method** | **Column:** Supelcosiltm LC-8 column (15cm x 4.6mm, 5µm)<br>**Mobile phase:** 0.02M Potassium dihydrogen phosphate buffer solution: Methanol 40:60 (v/v)<br>**Wavelength:** 218nm<br>**Flow rate:** 1ml/min<br>**Retention time**:<br>LEV: 4.46min<br>MKT: 7.34min | [26] |

<table>
<tr><td></td><td></td><td>Linearity:<br>LEV: 5 - 20µg/ml<br>MKT: 10 - 40µg/ml</td><td></td></tr>
<tr><td>12.</td><td>Novel LC Method Development and Validation for Simultaneous Determination of Montelukast and Doxofylline in Bulk and Pharmaceutical Dosage Forms</td><td>Column: C18 (150mm × 4.6mm, 5µm)<br>Mobile phase: Methanol and Phosphate buffer at pH 4.5<br>Wavelength: 280nm<br>Flow rate: 1ml/min<br>Retention time:<br>MKT: 4.7min<br>DOX: 1.9min<br>Linearity:<br>MKT: 0.005 – 0.015mg/ml<br>DOX: 0.2 – 0.6mg/ml</td><td>[27]</td></tr>
<tr><td>13.</td><td>HPLC method for the simultaneous determination of Levocetirizine, Ambroxol and Montelukast in human Plasma employing response Surface Methodology</td><td>Column: Phenomenex® C18 analytical column (150mm×4.6mm, 5µm)<br>Mobile phase: MeOH-MeCNdipotassium hydrogen phosphate buffer (pH 7.0), adjusted with 10% phosphoric acid<br>Wavelength: 230nm<br>Flow rate: 0.8-1.2 ml/min.</td><td>[28]</td></tr>
<tr><td>14.</td><td>Stability Indicating Assay Method for Montelukast Sodium in Pharmaceutical Formulations by RP-HPLC</td><td>Column: Zorbax SB Phenyl (50mm×4.6 mm, 1.8µm)<br>Mobile phase: A) 0.15% trifluro acetic acid in milli-Q grade water<br>B) 0.15% trifluro acetic acid in acetonitrile<br>Wavelength: 238nm<br>Flow rate: 1.2ml/min<br>Retention time: 8.9min<br>Linearity: 5 - 15µg/ml<br><br>Stability results:
<table>
<tr><th>Stress conditions</th><th>%drug degraded</th></tr>
<tr><td>Acidic (1N HCL, 2hrs)</td><td>2.2</td></tr>
<tr><td>Basic (1N NaOH 60°C, 2hrs)</td><td>15.2</td></tr>
<tr><td>Peroxide (1% H2O2, 1hr)</td><td>13.8</td></tr>
<tr><td>Water (60°C, 5hrs)</td><td>8.2</td></tr>
<tr><td>UV (200 W/m2/hrs)</td><td>1.2</td></tr>
<tr><td>Photolight (200 million Lux hrs)</td><td>5.5</td></tr>
<tr><td>Thermal (105°C, 7days)</td><td>5.2</td></tr>
<tr><td>Humidity (90% 25°C, 7days)</td><td>3.8</td></tr>
</table></td><td>[29]</td></tr>
<tr><td>15.</td><td>High performance liquid chromatographic method development for simultaneous analysis of Doxofylline and Montelukast sodium in a</td><td>Column: Inertsil C8 column (4.6mm×250mm, 5µm)<br>Mobile phase: Methanol : Sodium Phosphate buffer 75:25 (v/v)<br>Wavelength: 230nm</td><td>[30]</td></tr>
</table>

| | | | |
|---|---|---|---|
| | combined form | **Flow rate:** 1ml/min<br>**Retention time:**<br>DOX: 3.4min<br>MKT: 5.5min<br>**Linearity:**<br>DOX: 1.6 – 4.87mg/ml<br>MKT: 0.51 – 1.55mg/ml | |
| 16. | Development and validation of a **HPLC method** for the determination of **montelukast** and its degradation products in pharmaceutical formulation using an experimental design | **Column:** Inertsil C18 Column (250mm×4.6mm, 5µm)<br>**Mobile phase:** Acetonitrile : 0.01M Potassium dihydrogen phosphate buffer 7:3 ( v/v)<br>**Wavelength:** 355nm<br>**Flow rate:** 1ml/min<br>**Linearity:** 50 – 300mg/ml | [31] |
| 17. | Analytical Method Development and Validation of **Montelukast Sodium** and **Bambuterol Hydrochloride** in Combined Dosage Form by **RP-HPLC** | **Column:** Phenomenex C18 (250mm x 4.6mm, 5µm )<br>**Mobile phase:** Methanol :Aacetonitrile : 1% Trichloroacetic 80:10:10 (v/v/v)<br>**Wavelength:** 220nm<br>**Flow rate:** 1ml/min<br>**Retention time:**<br>MKT: 3.17min<br>BAM: 2.35min<br>**Linearity:** Both drugs: 0.5 - 10µg/ml | [32] |
| 18. | Development of Validated **HPLC** and **HPTLC Methods** for Simultaneous Determination of **Levocetirizine Dihydrochloride** and **Montelukast Sodium** in Bulk Drug and Pharmaceutical Dosage Form | **HPTLC:**<br>**Stationary phase:** Precoated aluminum plate 60 F254 (20×10 cm, 250µm) thickness<br>**Mobile Phase:** Toluene : Ethyl acetate: Methanol : Ammonia 2.5:7:2.5:1 (v/v/v/v)<br>**Linearity:**<br>LEV: 500 - 2500ngspot-1<br>MKT: 1000 - 5000ngspot-1<br>**HPLC:**<br>**Column:** BDS Hypersil C18 analytical column<br>**Mobile phase:** Sodium dihydrogen phosphate buffer (0.02 M) : Methanol 25:75 (v/v) pH 7<br>**Wavelength:** 231nm<br>**Flow rate:** 1ml/min<br>**Retention time:**<br>LEV: 3.55min<br>MKT: 7.45min<br>**Linearity:**<br>LEV: 1 – 10µg/ml<br>MKT: 2 – 20µg/ml | [33] |
| 19. | Method Development and Validation for the Simultaneous Determination of **Fexofenadine Hydrochloride** and **Montelukast Sodium** in Drug | **Stationary phase:** aluminum plate 60 F254 (20 ×10 cm, 250 µm)<br>**Mobile phase:** Toluene : Ethyl acetate: Methanol : Ammonia (30%) 0.5:7:2:0.5 (v/v/v/v)<br>**Wavelength:** 220nm | [34] |

<table>
<tr><td></td><td>Formulation Using Normal Phase High-Performance Thin-Layer Chromatography</td><td>Flow rate: 1ml/min<br>Rf values:<br>FEX: 0.21<br>MKT: 0.59<br>Linearity:<br>FEX: 2400 – 10800ngspot-1<br>MKT: 200 – 900ngspot-1</td><td></td></tr>
<tr><td>20.</td><td>RP-UPLC method development and validation for the simultaneous estimation of Montelukast and Ebastine in bulk and pharmaceutical dosage form</td><td>Column: Waters C18 (150mmx 3mm, 2µm)<br>Mobile phase: 0.1% Ortho phosphoric acid : Acetonitrile 60:40 (v/v)<br>Wavelength: 244nm<br>Flow rate: 0.3ml/min<br>Retention time:<br>MKT: 1.298min<br>EBA: 1.636min<br>Degradation data:
<table>
<tr><th rowspan="2">Condition</th><th colspan="2">%drug degraded</th></tr>
<tr><th>MKT</th><th>BAM</th></tr>
<tr><td>Acidic</td><td>4.29</td><td>5.66</td></tr>
<tr><td>Alkali</td><td>5.43</td><td>5.56</td></tr>
<tr><td>Oxidation</td><td>2.37</td><td>4.21</td></tr>
<tr><td>Thermal</td><td>1.15</td><td>4.40</td></tr>
<tr><td>UV</td><td>2.46</td><td>2.50</td></tr>
<tr><td>Water</td><td>0.31</td><td>0.56</td></tr>
</table></td><td>[35]</td></tr>
</table>

## CONCLUSION

From this literature review, it can be concluded that there is no any method on combination of Bilastine and Montelukast Sodium till date has been reported. However there are methods like, UV, HPLC, UPLC and HPTLC have been reported for Bilastine individually and along with other drugs. For estimation of Montelukast Sodium, methods like UV, HPLC, HPTLC were reported either individually or in combination with other drugs. This paper deals with all methods available on Bilastine and Montelukast Sodium currently. It will be helpful for further research on both of this drug and their combination for future analytical studies. This can be used as reference for further method development and validation in future.

## REFERENCES

1. Russell May J, William K. Dolen. Management of Allergic Rhinitis: A Review for the Community Pharmacist. Clinical Therapeutics, 2017; 1(1): 1-10.
2. Allergic Rhinitis. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2846743/.
3. Allergic Rhinitis. https://pharmaceutical-journal.com/article/research/allergic-rhinitis-impact-diagnosis-treatment-and-management

4. Bousquet J, Schunemann HJ, Samolinski B et. al. Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. J. Allergy Clin Immunol, 2012; 130(5): 1049-1062.
5. Drug Information, CDSCO approval, December 2020. https://cdsco.gov.in /opencms/opencms/system/modules/CDSCO.WEB/elements/d ownload_file_division. jsp?num_id=NjYwMA==
6. Drug profile, Montelukast sodium, December 2020. https://pubchem.ncbi.nlm.nih.gov/compound/Montelukast-sodium
7. Drug profile, Bilastine, December 2020. https://pubchem.ncbi.nlm.nih.gov /compound/Bilastine.
8. Beckett AH, Stenlake JB. Practical Pharmaceutical Chemistry. 4th ed., New Delhi; CBS publisher and distributors: 2002, pp. 279-300.
9. Chatwal GR, Anand SK. Instrumental methods of chemical analysis. 5th ed., Mumbai; Himalaya publishing house: 2002, pp. 2149-2184.
10. Andressa Tassinari da Silva, Gabriela Rossi Brabo, Isadora Dias Marques a, Lisiane Bajerski, Marcelo Donadel Malesuik, Clésio Soldateli Paim. UV Spectrophotometric method for quantitative determination of Bilastine using experimental design for robustness. Drug Anal Res., 2017; 01: 38-43.
11. V. Amarendra Chowdary, Anusha Kota, Syed Muneer. Method Development And Validation Of New Rp-Hplc Method For the Estimation of Bilastine in Pharmaceutical Dosage Form. World J. Pharm. Pharm. Sci., 2017; 6(8): 2297-2315.
12. Radia Ouarezki, Saliha Guermouche, Moulay-Hassane Guermouche, Degradation kinetics of Bilastine determined by RP-HPLC method and identifcation of its degradation product in oxidative condition. Slovak Academy of Sciences, 2019.
13. Rambabu Katta, N. N. V. V. S. S. Narayana Murty, Ramasrinivas, G. N. Rao. Stability Indicating Method Development and Validation for the Determination of Bilastine And its impurities by Uplc Method. IJPSR, 2020; 11(3): 1312-1321.
14. Shaista Firdous, S. H. Rizwan. Analytical Method Development And Validation For The Estimation Of Bilastine In Bulk And Pharmaceutical Dosage Form By Uplc. WJPLS, 2020; 6(10): 138-143.
15. The Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare; 7th ed., The Indian Pharmacopeia commission, Ghaziabad, 2018; II: 2681-2683.

16. Sowjanya G., Trideva Sastri K. UV Spectrophotometric Method Development And Validation For Simultaneous Determination Of Fexofenadine Hydrochloride And Montelukast Sodium In Tablets. W. J. Pharm. Pharma Sci.**,** 2017; 6(10): 780-789.
17. Kumar Sathis S., Lps. Nainesha Allada, Narayudu Y. Spectrophotometric Method Development and Validation for Montelukast Sodium and Simvastatin in Bulk and Tablet Dosage Form Using Absorption Ratio Method. Pharm. Innov. J., 2014; 3(5): 54-59.
18. Savsani Jyoti J., Goti Pratik P., Patel Parula B. Simultaneous UV Spectrophotometric Method For Estimation Of Ebastine And Montelukast Sodium In Tablet Dosage Form By Q-Ratio Method. Int. J. Chemtech Res., 2013; 1(5): 47-55.
19. Pallavi K., Srinivasa Babu P. Validated UV Spectroscopic Method For Estimation Of Montelukast Sodium From Bulk And Tablet Formulations. Int. J. Pharm. Sci., 2012**;** 1(2): 104-111.
20. Latha Pushpa E., Abiram L. Simultaneous Determination of Montelukast Sodium And Bambuterol Hydrochloride In Tablet Dosage Form By Ultraviolet Spectrophotometry. Int. Res. J. Pharm. App Sci., 2011; 1(1): 1-8.
21. 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): 4-9.
22. Selvadurai Muralidharan, Low Jia Qi, Lai Ting Yi, Kaur Narvinder, Kumar Subramani Parasuraman, Jayaraja, Venugopal Vijayan, Palanimuthu Vasanth Raj. Newly Developed and Validated Method of Montelukast Sodium Estimation in Tablet Dsosage Form by Ultraviolet Spectroscopy and Reverse Phase-High Performance Liquid Chromatography. PTB Reports, 2016; 2(2): 27-30.
23. Gandhi Bonthu Mohan, Rao Atmakuri Lakshmana, Rao Jangala Venkateswara. Method Development and Validation for Simultaneous Estimation of Montelukast Sodium and Desloratadine by RP-HPLC. Am J. Analyt Chem, 2015**;** 6: 651-658.
24. Gholve Sachin, Thonte Sanjay, Bhusnure Omprakash. Rp-Hplc Method Development and Validation Of Montelukast Sodium In Bulk Drug And Dosage Form. Int. J. Pharm Bio Sci., 2015; 6(2): 354 – 360.
25. Syed Saeed-Ul-Hassan1, Ahsan-Ul-Haq Ather, Muhammad Tayyab Ansari, Imran Tariq, Sabiha Karim. Determination of Montelukast Sodium in Raw Material and Solid Dosage Form Using Reverse Phase HPLC. Asian J. Chem., 2013; 25(13): 7481-7484.

26. Somkuwar Sushma, Pathak A.K. Simultaneous Estimation of Levocetirizine Dihydrochloride and Montelukast Sodium by Rp-Hplc Method. PHARMACIA, 2012**;** 1(3): 90-94.
27. Gadapa Nirupa, Kumar Siva A., Tripathi Upendra M. Novel LC Method Development and Validation for Simultaneous Determination of Montelukast and Doxofylline in Bulk and Pharmaceutical Dosage Forms. J. Chem., 2013; 1-7.
28. Ramalingam Suresh, Rajappan Manavalan, Kannappan Valliappan. HPLC method for the simultaneous determination of Levocetirizine, Ambroxol and Montelukast in human Plasma employing response Surface Methodology. Int. J. Drug Dev. & Res., 2012; 4(3): 173-185.
29. Mastanaiah Thummisetty, Dr. Jayapal Reddy Samaa, Rao Surya Narayana V., Reddannaa P. Stability Indicating Assay Method for Montelukast Sodium in Pharmaceutical Formulations by RP-HPLC. J. Pharm. Sci. & Res., 2011; 3(8): 1373-1377.
30. Revathi R., Ethiraj T., Thenmozhi P., Saravanan V.S., Ganesan V. High performance liquid chromatographic method development for simultaneous analysis of doxofylline and montelukast sodium in a combined form. Pharmaceutical Methods, 2011; 2(4): 223-228.
31. Ahmed B. Eldin, Abdalla A. Shalaby, Maha El-Tohamy. Development and validation of a HPLC method for the determination of montelukast and its degradation products in pharmaceutical formulation using an experimental design. Acta Pharmaceutica Sciencia**,** 2011; 53: 45- 56.
32. Patel S.A., Patel S. K., Patel D. J., Patel N. J. Analytical Method Development and Validation of Montelukast Sodium and Bambuterol Hydrochloride in Combined Dosage Form by RP-HPLC. Int. J. Pharmtech Res.**,** 2010; 2(3): 1767-1771.
33. Rathore Atul S., Sathiyanarayanan L., Mahadik K.R. Development of Validated HPLC and HPTLC Methods for Simultaneous Determination of Levocetirizine Dihydrochloride and Montelukast Sodium in Bulk Drug and Pharmaceutical Dosage Form. Pharmaceutica Analytica Acta, 2010; 1(1): 1-6.
34. Tandulwadkar Suparna S., More Snehal J., Rathore Atul S., Nikam, Lohidasan Sathiyanarayanan Ajinkya R., Mahadik Kakasaheb R. 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 Anal. Chem., 2019; 1-7.

35. Amaresha S, Jhat Rakesh K. RP-UPLC method development and validation for the simultaneous estimation of Montelukast and Ebastine in bulk and pharmaceutical dosage form. Int. J. Pharma. Anal. Res., 2018; 7(1): 96-105.