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A REVIEW ON DEVELOPED AND VALIDATED METHOD FOR MONTELUKAST SODIUM AND BILASTINE FROM PURE AND IT'S PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Nowadays, many anti-allergic drugs are emerging in the market. One of them is combination of Montelukast Sodium and Bilastine. Both are different in their mode of action. Montelukast Sodium is a leukotriene receptor antagonist and Bilastine is a selective histamine H1 receptor antagonist. The aim of this article is to study the previously reported various analytical techniques for the determination of Montelukast Sodium and Bilastine. There are various techniques for estimation of drug such as RP-HPLC, UV spectroscopy, MS, etc. The RP-HPLC is the most accurate and easy method for estimation.

KEYWORDS: Montelukast Sodium, Bilastine, RP-HPLC, etc.

INTRODUCTION

Cysteinyl leukotriene and histamine are the potent inflammatory mediators which are involved in both the asthma and seasonal allergic rhinoconjunctis (SARC). A combination therapy of Montelukast Sodium and Bilastine may provide additive benefits. The combination therapy is superior to the Bilastine monotherpay in the reduction of the SARC symptoms and also improving the asthma quality of life over a longer period of time. Allergic rhinitis and asthma is a most common immunomediated diseases over the worldwide. Asthma is a chronic inflammatory disease of airway in which the obstruction to air flow. AR is the allergens induced disease which can causes the inflammation to the upper airway. Bilastine is a novel drug belonging to the oral second generation antihistamines. It is approved in India in February 2019 by DCGI. Bilastine is a non- sedating drug approved for the symptomatic treatment in patients with allergic disorders. Montelukast was firstly approved in USFDA in

1998 as a brand name Singulair. It shows its action by blocking the action of leukotriene D4 in the lungs that results in reducing the inflammation and relaxation of smooth muscle.

Drug profile

Montelukast sodium[1,5,19,23]

Montelukast Sodium is a monosodium salt which is a synthetic leukotriene receptor antagonist which is used as a anti-asthmatic agent. It is a selective and potent antagonist of cysteinyl leukotriene. It is used in the treatment of asthma as well as seasonal allergies in children and adults. Montelukast Sodium is a systemically active drug which can shows two mechanism of action i.e bronchodilator and anti-inflammatory.

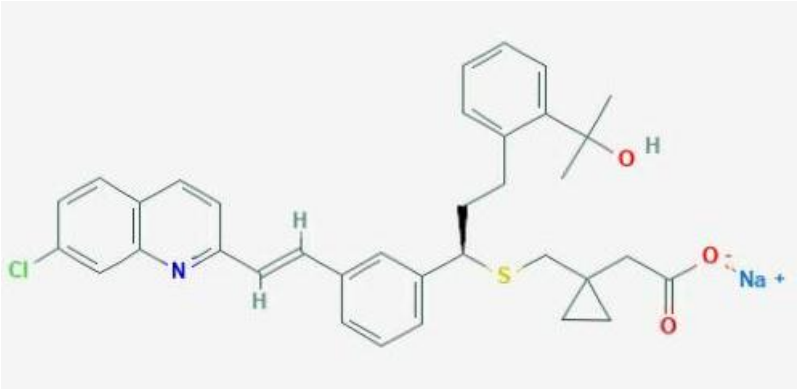

Fig. 1: Chemical structure of montelukast sodium.

Physicochemical properties[22,23,21]

Sr.no	Parameters	
1	Molecular formula	C35H35ClNNaO3S
2	Molecular weight	608.2 g/mol
3	IUPAC name	sodium;2-[1-[[(1*R*)-1-[3-[(*E*)-2-(7-chloroquinolin-2-yl)ethenyl]phenyl]-3-[2-(2-hydroxypropan-2-yl)phenyl]propyl]sulfanylmethyl]cyclopropyl]acetate
4	Appearance	White to off white in colour
5	Solubility	Methanol (freely soluble) Ethanol (Freely Soluble) Water (Freely Soluble)
6	Melting point	145°C to 148 °C
7	Class	Leukotriene receptor antagonist
8	CAS no	151767-02-01
9	Storage	Store at 25 °C
10	Brand name	Singulair

Mechanism of action[20,21,22]

Leukotriene LTC4, LTD4, LTE4 are collectively called as cysteinyl leukotriene. These are the peptide conjugated lipids. That are the product of activated eosinophils, basophils, macrophages and mast cell. CySLT's are the product or derivatives of arachidonic acid CySLT's are synthesized by immunocyte in respiratory mucosa in presence of allergens. And it is also released by the immunocyte. CySLT's can bind to CySLT's receptor. These receptors are mostly found in airway smooth muscle cells and airway macrophages. Montelukast Sodium can competitively block the binding of CySLT's to receptor that why they can inhibit the binding of inflammation mediator LTD4.

Pharmacokinetics[20,21,23]

Absorption

Orally administered Montelukast Sodium is rapidly absorbed. After orally administered 10 mg tablet reaching to the peak plasma concentrations is about 3 to 4 hours with bioavailability of 64 %. When 5 mg chewable tablets is administered then the Cmax is achieved 2 to 2.5 hours. When 4 mg chewable tablets are administered then the Cmax is achieved 2 hours.

Distribution

Most of the drug (more than 99 %) is bound to plasma proteins. The bounded drug is distributed across the blood brain barrier. About 8 to 11 liter, steady state volume of distribution of Montelukast Sodium**.**

Metabolism

It is extensively metabolised. Metabolism is generally occur in liver. The various enzyme like cytochrome P450 3A4 and 2CP are also involved in the metabolism of Montelukast.

Excretion

Generally, excretion occurs in bile with half life from 2.7 to 5.5 hours in healthy person.

Bilastine[8,18,23]

Bilastine is a novel drug which belongs to the class of anti-histamine. It is a second generation histamine H1 receptor antagonist which is used in the treatment of allergic reaction. It is also used in the treatment of chronic urticaria. Bilastine is work based on the blocking of histamine receptor. Bilastine is chemically similar to piperidinyl-benzimidazol.

Faes farma, Spain can developed the Bilastine. It is a safe and effective non-sedating H1-antihistamine approved for the treatment of rhinoconjunctis and urticaria.

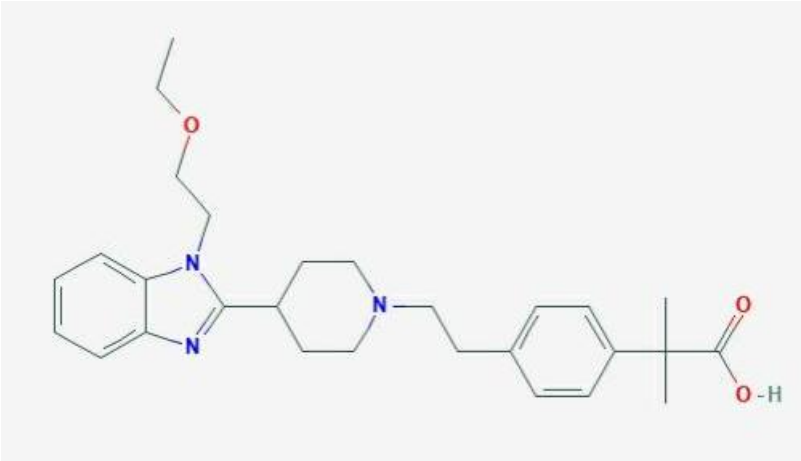

Fig. 2: Chemical structure of bilastine.

Physicochemical properties[17,22,23]

Sr. no	Parameters	
1	Molecular formula	C28H37N3O3
2	Molecular weight	463.6 g/mol
3	IUPAC name	2-[4-(2-(4-(1-(2-ethoxyethyl)-1H-benzimidazol-2-yl) piperidine-1-yl)ethyl)phenyl]-2-methylpropionic acid
4	Appearance	White crystalline powder
5	Solubility	Methanol (Soluble) Acetonitrile (Slightly Soluble) Water (Slightly Soluble)
6	Melting point	195°C
7	Class	Anti – histamine
8	CAS number	202189-78-4
9	Brand name	Billasi

Mechanism of action[17,18,22,23]

Bilastine is a selective histamine H1 receptor antagonist. Bilastine having the antagonist property towards the H receptor. They having higher affinity towards histamine H1 receptor with minimal effect of receptor for other mediator. Bilastine having 3 and 5 fold greater affinity than centirizine and fexofenadine respectively. During the allergic reaction mast cell undergoes denaturation which release the histamine and other substances. By binding and preventing to the activation of H1 receptor they reduces the effect of allergic reaction because of release of tissue cell.

Pharmacokinetics[17,18,22]

Absorption

Bilastine is rapidly absorbed after administring by oral route. The amount of absorption is proportional to the dose. The maximum plasma concentrations (Cmax) is around 1.3 hours. The oral bioavailability of drug is 61 %. When Bilastine is taken with grape juice Cmax is decreased by 30 %. When Bilastine is taken with low fat and high fat meal Cmax decreased 25 % and 33% as compared to fasted state. The anti-histaminic activity of drug shows within 30 min, and clinical effect persisting from 30 min. to 8 hours.

Distribution

About 84% to 90% of the Bilastine is bound to plasma proteins.

Metabolism

Bilastine does not interact as a inducer or as a inhibitors to the CYP450 isoenzymes. They does not show significant metabolism in human.

Excretion

After administration of the single dose of Bilastine 20 mg, approximately 95 % of Bilastine is excreated from body in the form of urine (28 %) and in faeces (67%) as a unchanged form of Bilastine. The elimination half-life of Bilastine is 14.5 hours in health volunteer.

Analytical method

This all method are use for the determination of Montelukast sodium and Bilastine. During the literature survey these all method were studied which are helpful to method development. The following are the previously reported analytical methods for estimation of the Montelukast Sodium and Bilastine Pharmaceutical dosage form and individual.

Previously reported analytical method

Sr. no	Title	Method	Description	References
1	Determination of Montelukast Sodium in Raw Material and Solid Dosage Form Using Reverse Phase HPLC	RP-HPLC	**Column:** Lichorosoval octylsilyl column **Dimensions:** 250 × 4.6 mm, 5 um **Mobile phase:** Acetonitrile: Sodium acetate buffer (80 : 20) **Flow rate:** 1 ml/ min **UV detection**	[1]

			wavelength: 350 nm	
2	RP-HPLC Method for the estimation of Montelukast Sodium in Pharmaceutical Dosage Form	RP-HPLC	**Column: Inertsil ODS C18 column** **Dimensions:** 250 × 4.6 mm, 5 um **Mobile phase:** Sodium phosphate buffer (0.02 M) : Methanol (85 : 15) **Flow rate:** 1 ml/min **Retention time:** 3.017 min. **UV detection:** 218vnm	[2]
3	Newly Developed and Validated Method of Montelukast Sodium Estimation in Tablet Dosage Form by Ultraviolet Spectroscopy and Reverse Phase High Performance Liquid Chromatography	RP-HPLC and UV spectroscopy	**Column:** Princeton SPHER C18 column **Dimensions:** 250 mm× 4.6 mm, 5u **Mobile phase:** Ammonium acetate: acetonitrile (25: 75 v/v)	[3]
4	Development and Validation of a RP-HPLC Method for Estimation of Montelukast Sodium in Bulk and in Tablet Dosage Form	RP-HPLC	**Column:** Octadecylsilane column **Mobile phase:** Sodium acetate: acetic acid (90:10 v/v) **Retention time:** 3.4 min **Detection:** 285 nm	[4]
5	Validated UV Spectroscopy Method for Estimation of Montelukast Sodium	UV Spectroscopy	**Absorbance Maxima:** 286.5 nm	[5]
6	Validated UV Spectroscopic Method for Estimation of Montelukast Sodium from Bulk and Tablet Formulation	UV Spectroscopy	**Absorbance Maxima:** 287 nm **Dilution media:** Phosphate buffer (pH 7.4) and Sodium laurel sulphate (0.5%)	[6]
7	Validated Spectrophotometric Methods for Determination of Montelukast Sodium in Pure and Dosage form using N-Bromimosuccinimide and dyed.	Spectrophotometry	N- Bromimosuccinimide as a oxidant Methylene blue, amaranth and indigo carmine are due. Absorbance: 664 nm, 520 nm and 610nm.	[7]
8	Development and validation of stability	UPLC	**Column:** Phenomenex C8	[8]

	indicating UPLC Method for the estimation of Bilastine in bulk and Pharmaceutical Dosage Form		**Dimensions:** Sodium phosphate buffer: Methanol: acetonitrile (60:30:10 v/v/v) **Flow rate:** 0.5 ml/min **Retention time:** 1.19 min **UV detection:**248 nm	
9	Method Development and Validation of New RP-HPLC Method for Estimation of Bilastine in Pharmaceutical Dosage Form	RP-HPLC	**Column:** Inertsil ODS C18 **Dimensions:** 250mm×4.6mm,5 u **Mobile phase:** Methanol: Acetonitrile (60:40) **Flow rate:** 1.2 ml/min **Retention time:** 2.8 min **Run time:** 6 min	[9]
10	Application of Analytical Quality by Design concept for Bilastine and it's degradation impurities determination by hydrophilic interaction liquid chromatographic method	HILIC	**Column:** Luna HILIC **Dimensions:** 100mm×4.6mm, 5 um **Mobile phase:** Acetonitrile: glacial acetic acid (90.5:9.5) **Flow rate:** 1 ml/min **Detection wavelength:** 275 nm	[10]
11	Method Development and Validation of Bilastine by HPLC	HPLC	**Column**: Phenomenex C18 **Dimensions:** 150mm× 4.6 mm, 5um **Mobile phase:** Buffer : Acetonitrile: Methanol (45:25:30) **Flow rate:** 1 ml/ min **Run time:** 10 min Detection wavelength: 254 nm	[11]
12	Stability indicating Method Development and Validation For the Determination of Bilastine and it's Impurities by UPLC Method	UPLC	**Column:** CSH Phenyl-hexyl column **Dimensions:** 2.1 mm× 150 mm, 1.7 u **Mobile phase:** 0.05% TFA + Water and 0.05% TFA + acetonitrile **Flow rate:** 0.10 ml/min **Detection wavelength:** 275 nm	[12]
13	Analytical method development and	UV spectrophotometry	Wavelength Maxima for Bilastine is 214 nm and	[13]

	validation for simultaneous estimation of Bilastine and Montelukast Sodium by UV spectrophotometry.		for Montelukast Sodium is 218 nm in methanol.	
14	A new stability indicating RP-HPLC method for determination of Bilastine in bulk and Pharmaceutical formulation	RP-HPLC	**Column:** Phenomenex Gemini C18 column **Dimensions:** 150 × 4.60 mm , 5 um **Mobile phase:** Formic acid : Methanol (50:50) **Flow rate:** 0.8 ml / min **Detection wavelength:** 282 nm **Retention time:** 2.167 nm	[14]
15	Degradation kinetics of Bilastine determined by RP-HPLC method and identification of it's degradation products in oxidative condition	RP-HPLC	**Column:** water symmetry C18 column **Dimensions:** 250×4.6 mm, 5um **Mobile phase:** Acetonitrile: Phosphate buffer (30: 70)	[15]
16	Development and validation of RP-HPLC method for estimation of the Bilastine from Bulk and formulation	RP-HPLC	**Column:** C18 column **Dimensions:** 250×4.6 mm **Mobile phase:** Methanol: Orthophospharic acid buffer (70:30) **Flow rate:** 0.8 ml/min **Detection wavelength:** 280 nm **Retention time:** 3.280 min **Run time:** 40 min	[16]

CONCLUSION

In this article, we review the information about the previously reported analytical methods for analysis of Montelukast sodium and Bilastine in their bulk and Pharmaceutical dosage form. Most of techniques having the flow rate is 0.8- 1.2 min/ ml. Mainly this article gives the basic knowledge and information which is required for the development of new analytical methods for Montelukast Sodium and Bilastine.

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