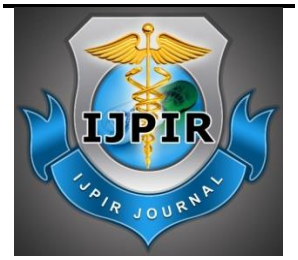
Research Article



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Stability indicating method development and validation for simultaneous estimation of ebastine and montelukast in pharmaceutical dosage form

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ABSTRACT

A rapid and sensitive method with UV detection (244nm) was developed for the simultaneous estimation of Ebastine and Montelukast in pharmaceutical dosage form. Using the column Discovery C8 250mm x 4.6 mm, 5µ with mobile phase containing buffer and acetonitrile taken in the ratio 62:38 was pumped through column at a flow rate of 1.2ml/min and temperature was maintained at 30^0c.Retention time of Ebastine and Montelukast were found 2.526 min and 3.249 min, %RSD were and found to be 0.5 and 0.8 respectively and %Assay was obtained as 98.89% and 99.40% respectively. LOD, LOQ values are obtained from regression equations of Ebastine and Montelukast were 0.04ppm, 0.13ppm and 0.29ppm, 0.88ppm respectively. Regression equation of Ebastine is y = 14905x+2045, and y = 12898x+24873 Of Montelukast.

Keywords: Ebastine, Montelukast, RP-HPLC, Validation, Stability

INTRODUCTION

High Performance Liquid Chromatography (HPLC) is the fastest growing analytical technique for analysis of drugs. Its simplicity, high specificity and wide range of sensitivity make it ideal for the analysis of many drugs in both dosage forms and biological fluids.

Ebastine is a second generation H1 receptor antagonist that is indicated mainly for allergic rhinitis and chronic idiopathic urticaria. It is available in 10 and 20 mg tablets and as fast dissolving tablets as well as in pediatric syrup. IUPAC name of Ebastine is1-(4-tert-butylphenyl)-4-[4-(diphenylmethoxy) piperidin-1-yl] butan-1-one.

Montelukast is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies. It is usually administered orally. IUPAC name of Montelukast is 2-[1-({[(1R)-1-{3-[(E)-2-(7-chloroquinolin-2-yl)ethenyl]phenyl}-3-[2-(2-hydroxypropan-2-

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yl)phenyl]propyl]sulfanyl}methyl)cyclopropyl]acet ic acid.

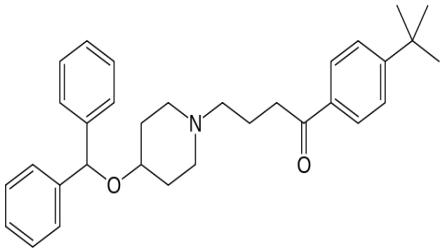

Fig.1 Ebastine

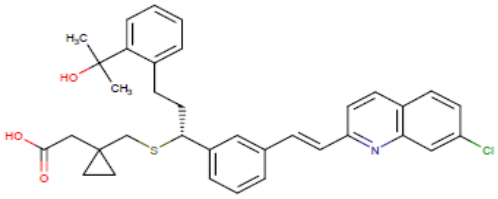

Fig.2 Montelukast

MATERIALS AND METHOD

Ebastine and montelukast, combination of Ebastine and Montelukast (EBAST M Tablets) are received from spectrum labs. Distilled water, acetonitrile, phosphate buffer, ammonium acetate buffer, methanol, potassium dihydrogen phosphate buffer, ortho phosphoric acid etc. HPLC instrument used was WATERS HPLC 2965 SYSTEM with Auto Injector and PDA 2996 Detector. Software used is Empower 2. UV-VIS spectrophotometer PG instruments T60 with special band width of 2mm and 10mm and matched quartz is used for measuring absorbance for Ebastine and Montelukast solutions.

Method

The method was developed by using the column Discovery C8 250 × 4.6 mm, 5µ with mobile phase composition 0.01N KH_2PO_4 and Acetonitrile in the ratio of 62:38 at a flow rate 1.2ml/min maintained at a temperature 30^0C and the wavelength obtained was 244 nm.

RESULTS AND DISCUSSION

Optimized method

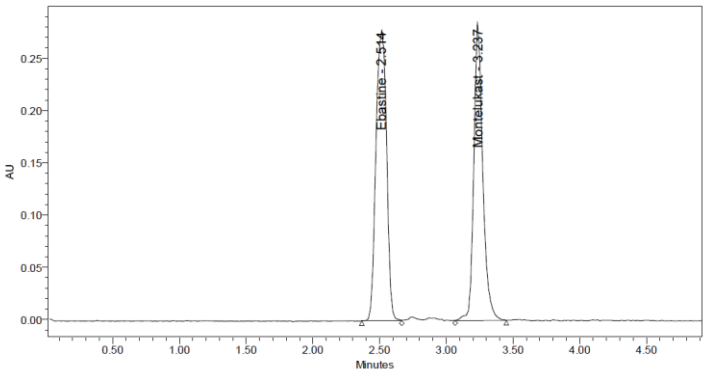

Fig.3. Optimized Chromatohram

Table: 1. System suitability studies of Ebastine and Montelukast method

Property	Ebastine	Montelukast
Retention time (t_R)	2.526 min	3.249 min
Theoretical plates(N)	9039 ± 63.48	11343 ± 63.48
Tailingfactor (T)	1.08± 0.117	1.26± 0.117

Linearity

Table: 2 Calibration data of Ebastine and Montelukast method.

S.no	Concentration Ebastine (µg/ml)	Response	Concentration Montelukast(µg/ml)	Response
1	0	0	0	0
2	25	386123	25	355552
3	50	753527	50	695452
4	75	1103490	75	1009580
5	100	1488247	100	1288016
6	125	1852769	125	1643376
7	150	2255060	150	1953362

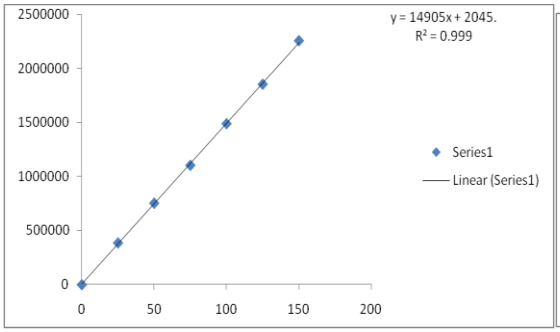

Fig: 4. Calibration curve of Ebastine

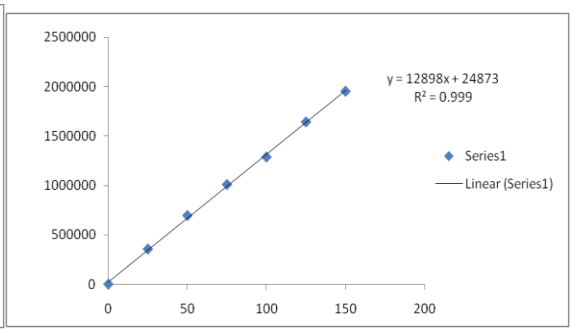

Fig: 5. Calibration curve of Montelukast

Precision

Intraday precision (Repeatability): Intraday Precision was performed and % RSD for Ebastine and Montelukast were found to be 0.5% and 0.8% respectively.

Table:3 Repeatability results for Ebastine and Montelukast.

Sr. No.	Ebastine	Montelukast
1	1440886	1232637
2	1437164	1226453
3	1435513	1245223
4	1449590	1221355
5	1429248	1246394
6	1448308	1233365
Mean	1440118	1234238
Std. Dev.	7816.3	9983.4
%RSD	0.5	0.8

Inter day precision

Inter day precision was performed with 24 hrs time lag and the %RSD Obtained for Ebastine and Montelukast were 0.4% and 0.6%.

Table:4 Inter day precision results forEbastine and Montelukast.

Sr. No.	Ebastine	Montelukast
1	1379942	1148512
2	1375065	1152014
3	1369918	1149532
4	1362990	1154467
5	1371533	1148618
6	1372624	1167365
Mean	1372012	1153418
Std. Dev.	5631.9	7208.3
%RSD	0.4	0.6

Accuracy

Three concentrations 50%, 100%, 150%, were injected in a triplicate manner and amount Recovered and % Recovery were displayed in Table: 5

Table: 5 Table of Accuracy

Sample	Concentration (%)	Recovery (%)	%RSD
Ebastine	50	99.64	0.96
	100	99.07	0.16
	150	99.60	0.13
Montelukast	50	98.90	0.66
	100	98.71	0.20
	150	99.62	0.06

LOD

Limit of detection was calculated by std deviation method Ebastine and Montelukast and LOD for Ebastine and Montelukast were found to be 0.04 and 0.29 respectively.

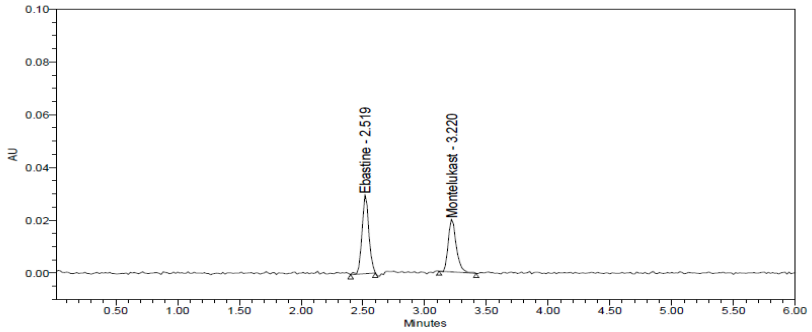

Fig : 6 LOD Chromatogram of Ebastine and Montelukast

LOQ

Limit of Quantification was calculated by std deviation method for Ebastine and Montelukast and LOQ for Ebastine and Montelukast were found to be0.13 and 0.88 respectively.

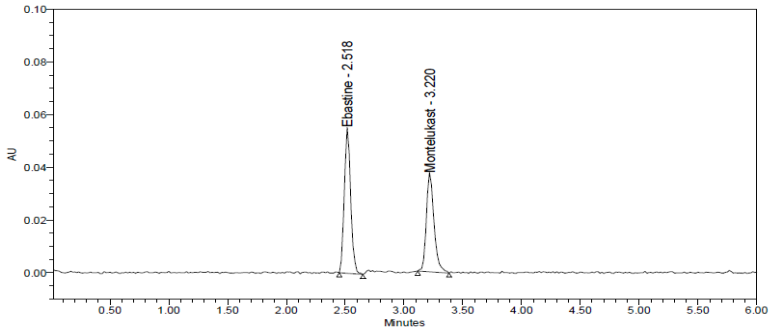

Fig: 6 LOQ Chromatogram of Ebastine and Montelukast

Robustness

Small deliberate changes in method like Flow rate, mobile phase ratio, and temperature are made but there were no recognized change in the result and are within range as per ICH Guide lines.

Table: 6 Robustness data of Ebastine and Montelukast

S.NO	Robustness condition	Ebastine %RSD	Montelukast %RSD
1	Flow minus(1ml/min)	0.8	0.9
2	Flow Plus(1.3ml/min)	0.2	0.3
3	Mobile phase minus(57:43)	0.2	0.3
4	Mobile phase Plus(67:33)	0.7	0.4
5	Temperature minus(25^{0c})	0.3	0.5
6	Temperature Plus(35^{0c})	0.9	0.6

Assay

Standard preparations are made from the API and sample preparations are from formulation(EBAST M TABLET). Both samples and standards are injected six homogeneous samples. Drug in the formulation was estimated by taking the standard as the reference. The Average %Assay was calculated and found to be 98.89 and 99.40 for ebastine and montelukast respectively.

Table: 7. Assay of Tablet

S. No.	Ebastine %Assay	Montelukast %Assay
1	98.94	99.27
2	98.68	98.77
3	98.57	100.28
4	99.54	98.36
5	98.14	100.37
6	99.45	99.33
AVG	98.89	99.40
STDEV	0.54	0.8040
%RSD	0.54	0.8

Degradation studies

Standards and degraded samples are injected and calculated the percentage of drug degraded in solution by applying different conditions like acid, alkali, and oxidative, photolytic, thermal and neutral analysis.

Table: 8 Degradation data

Type of degradation	Ebastine			Montelukast		
	AREA	% RECOVERED	% DEGRADED	AREA	% RECOVERED	% DEGRADED
Acid	1389478	95.41	4.59	1182120	95.20	4.80
Base	1415698	97.21	2.79	1209699	97.42	2.58
Peroxide	1434285	98.49	1.51	1223072	98.50	1.50
Thermal	1448462	99.46	0.54	1234984	99.46	0.54
Uv	1442012	99.02	0.98	1230069	99.06	0.94
Water	1442389	99.04	0.96	1233038	99.30	0.70

CONCLUSION

The proposed HPLC technique can be readily applied for the simultaneous determination of Ebastine and Montelukast in pharmaceutical dosage form. The optimized technique is specific with no interference from any of test compounds. This work is to report its stability studies with degraded product identification which helpful for identifying toxicity of degraded products and also to concern the storage conditions. So, the technique developed was precise, accurate, robust and economical that can be adopted in regular quality control test in industry and research laboratories.

Acknowledgement

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