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FORCED DEGRADATION STUDIES OF COMBINATION OF LEVOCETRIZINE, AMBROXOL AND MONTELEUKAST BY VALIDATED RP-HPLC METHOD

D Chaithanya Sudha Penta, Prof. Dannana Gowri Sankar

A.U.College of Pharmaceutical Sciences, Andhra University, Visakhapatnam-530003, A.P, India.

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ABSTRACT

A new selective rapid reverse phase high performance liquid chromatographic stability indicating method had been developed and validated for simultaneous quantitative determination of Levocetrizine, Ambroxol and monteleukast in bulk and pharmaceutical dosage form. The chromatographic separations are carried out with Kromasil C-18, (250×4.6 mm) and 5µm particle size column. The mobile phase consists of phosphate buffer: Acetonitrile (40:60 %v/v), to this add 1 ml of triethylamine and adjust the mobile phase pH 4.0 with o-phosphoric acid. The flow rate was 1.0 mL/min and eluents were detected at 225 nm using UV detector. The retention times of Levocetrizine, Ambroxol and Monteleukast were found to be 2.185, 2.622 and 3.931 min respectively. The percentage recoveries were found to be in the range of 99 -101%. The calibration curve was constructed between peak area vs concentration and demonstrated which are in the range of 500µg/ml Levocetrizine, 50 µg/ml Ambroxol and 100 µg/ml Monteleukast. Degradation studies were studied for Levocetrizine, Ambroxol and monteleukast under various stress conditions such as acid hydrolysis, base hydrolysis, oxidation, thermal, photochemical and UV. All the degradation peaks were resolved effectively using developed method with different retention times. The developed method was validated according to ICH guidelines. As the method could effectively separates the degradation products from active ingredient, it can be used for routine analysis of drug both in bulk and pharmaceutical dosage form.

Corresponding author

D Chaithanya Sudha Penta

A.U.College of Pharmaceutical Sciences,
Andhra University,
Visakhapatnam-530003, A.P, India.
chaithumpharm@gmail.com

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INTRODUCTION

Levocetrizine Hydrochloride is non-sedating antihistamine. It is used in relieving the pain and spasm of the smooth muscles. It has a chemical name of (R)[2-[4-[(4-chlorophenyl) phenylmethyl]-1-piperazinyl] ethoxy] acetic acid. The chemical formula of Levocetrizine Hydrochloride is $C_{21}H_{25}ClN_2O$ and molecular weight is 388.88 g/mol.

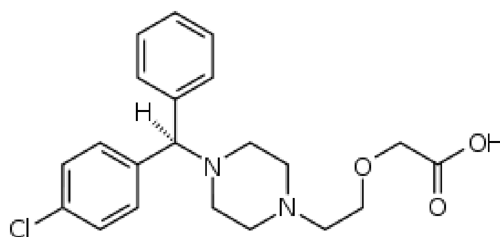


Figure.1 Chemical structure of levocetrizine.

Ambroxol is a secretolytic agent used in the treatment of respiratory diseases associated with viscid or excessive mucus. It has a chemical name of 4-[(2-amino-3,5-dibromophenyl)methylamino]cyclohexan-1-ol hydrochloride. The chemical formula is $C_{13}H_{18}Br_2N_2O$ and molecular weight is 378.10 g/mol.

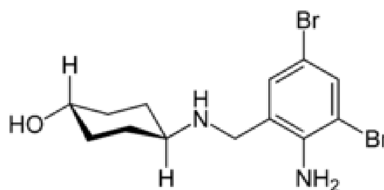


Figure.2 Chemical structure of Ambroxol.

Monteleukast is a leukotriene receptor antagonist. It has a chemical name of {1-[({(1R)-1-{3-[(E)-2-(7-Chloro-2-quinolinyl)vinyl]phenyl}-3-[2-(2-hydroxy-propanyl)phenyl]propyl}sulfanyl)methyl]cyclopropyl}acetic acid. The chemical formula of $C_{35}H_{35}ClNO_3S$ and the molecular weight is 586.184g/mol.

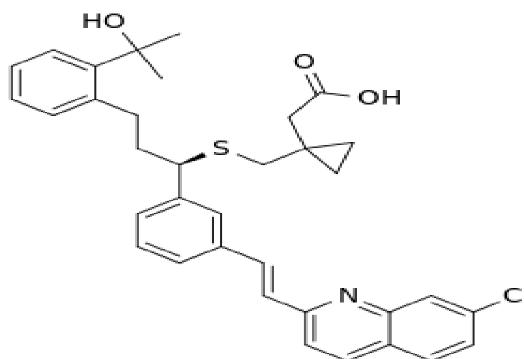


Figure.3 Chemical structure of Monteleukast.

The combination of Levocetrizine, Ambroxol and monteleukast shows significant effect on symptom relief when compared to individual drugs used in the rhinititis treatment. However no references have been found for simultaneous determination of Levocetrizine, Ambroxol and monteleukast in pharmaceutical formulations.

MATERIALS AND METHODS

Chemicals and solvents

Levocetrizine, Ambroxol and monteleukast were obtained as gift samples from Eris life sciences Pvt.Ltd, India. The commercial Pharmaceutical Preparation containing 5mg of Levocetrizine and 75mg of Ambroxol and 10mg of Montelukast respectively were procured from local pharmacy. Ortho phosphoric acid, Acetonitrile, and water used are of HPLC grade.

Instrumentation

The chromatographic separations were performed using HPLC-Waters alliance (Model-2695) consisting of an in-built auto sampler, a column oven and UV detector. The data was acquired through Empower-2-software. The column used was Kromasil C18 (250×4.6mm i.d, 5µm particle size). Meltronics sonicator was used for enhancing dissolution of the compounds. Elico pH meter was used for adjusting the pH of buffer solution. All weighing was done on Sarotorious balance (model AE-160).

Chromatographic conditions

The mobile phase consists of buffer : Acetonitrile in the ratio of 40:60v/v%. The mobile phase was pumped from solvent reservoir in the ratio of 40:60 %v/v to the column in the flow rate of 1.0 ml/min whereas run time set was 8 min. The separation was performed on Kromasil C18 column and the column was maintained the temperature of 25°C and the volume of each injection was 10 µL. Prior to injection, the column was equilibrated for at least 30 min with mobile phase flowing through the system. The eluents were monitored at 225 nm.

Table 1. Optimized Chromatographic conditions and system suitability parameters for proposed HPLC method for Levocetrizine, Ambroxol and monteleukast.

Parameter	Chromatographic conditions
Instrument :	Waters 2695, High performance Liquid Chromatography
Flow rate :	1 ml/min
Column :	Kromasil C18, 250 x 4.6 mm, 5µ.
Detector wave length :	225nm
Column temperature :	25°C
Injection volume :	10µL
Run time :	6 min
Diluent :	Water : Acetonitrile (50:50)
Mode of separation :	Isocratic mode

Preparation of buffer solution: (PH:4.0):

1ml of Ortho phosphoric acid solution in a 1000ml of volumetric flask add about 100ml of milli-Q water and final volume make up to 1000 ml with milli-Q water and degas to sonicate and finally make up the volume with water then added 1ml of Triethylamine then pH adjusted to 4.0 with dil. Orthophosphoric acid solution.

Preparation of mobile phase:

Buffer and Acetonitrile are in the ratio 40:60 %v/v, filtered through 0.45 µ filter under vacuum.

Preparation of standard solution:

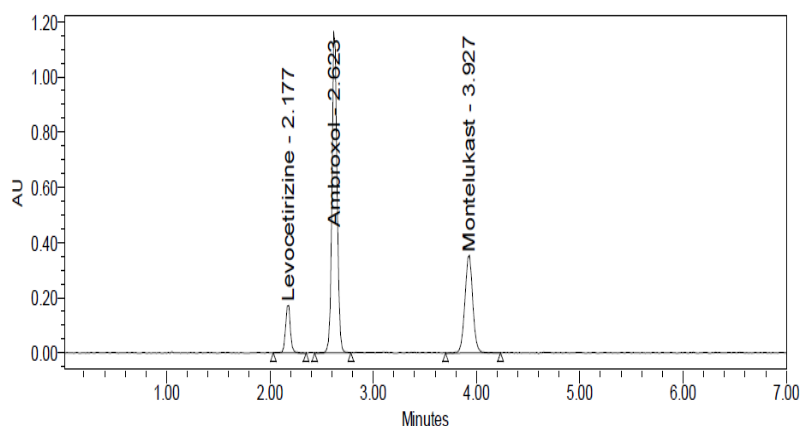
Accurately Weighed and transferred 5mg of Levocetrizine and 75mg of Ambroxol and 10mg of Montelukast working Standards into a 25ml clean dry volumetric flask, add 3/4th volume of diluent, sonicated for 15 minutes and make up to the final volume with diluents. 1ml from the above two stock solutions was taken into a 10ml volumetric flask and made up to 10ml with diluents(Water and Acetonitrile (50:50)).

Preparation of sample solution:

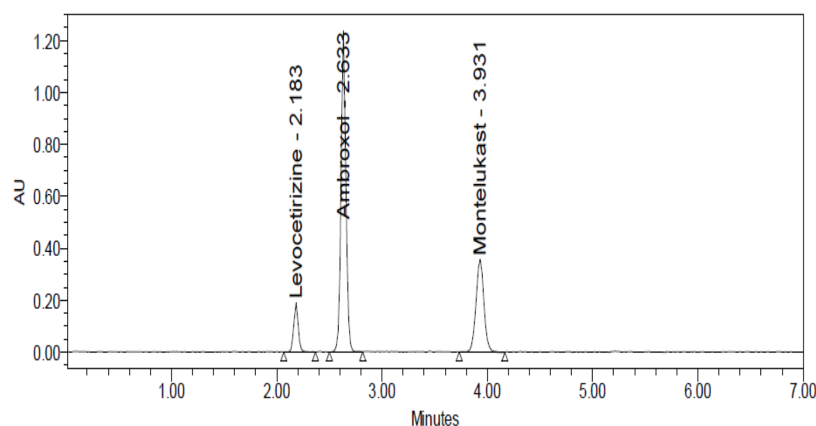
1capsule was weighed, powdered (equivalent to 5mg of Levocetrizine and 75mg of Ambroxol and10 mg of Montelukast) was transferred into a 100mL volumetric flask, 50mL of diluent added and sonicated for 25 min, further the volume made up with diluent and filtered. From the filtered solution 1ml was pipeted out into a 10 ml volumetric flask and made upto 10ml with diluent.

Label Claim:

5mg of Levocetrizine and 75mg of Ambroxol and10 mg of Montelukast.



Standard chromatogram



HPLC chromatogram of sample

Validation of Proposed method:

The developed method was validated as per the ICH (International Conference on Harmonization) guidelines with respect to System suitability, Precision, Specificity, Forced degradation studies, Linearity, Accuracy, Limit of detection and Limit of quantification.

Linearity:

Aliquots of 0.25, 0.5, 0.75, 1.0, 1.25 and 1.5 ml were taken from stock solution of concentration 50µg/ml of Levocetrizine, 750 µg/ml Ambroxol and 100 µg/ml Montelukast and then diluted up to mark with diluent. Such that the final concentrations were in the range 5-30 ppm of Levocetrizine, 75 – 450 ppm of Ambroxol and 10-60 ppm of Montelukast. Volume of 10µl of each sample was injected in five times for each concentration level and calibration curve was constructed by plotting the peak area versus drug concentration. A linear relationship between peak area vs. concentration was observed in the range of study. The observations and calibration curve were shown in figures 4, 5 and 6 .

Table.2 linearity.

S.NO	Conc. Of Levocetrizine in ppm	Levocetrizine peakArea	Conc. of Ambroxol in ppm	Ambroxol Peakarea	Conc. of Montelukast in ppm	Montelukast PeakArea
1	5	152199	75	1106642	10	485033
2	10	276727	150	1958600	20	925598
3	15	416420	225	2857505	30	1320284
4	20	562221	300	3911394	40	1814650
5	25	683537	375	4772457	50	2222829
6	30	817482	450	5687965	60	26188891

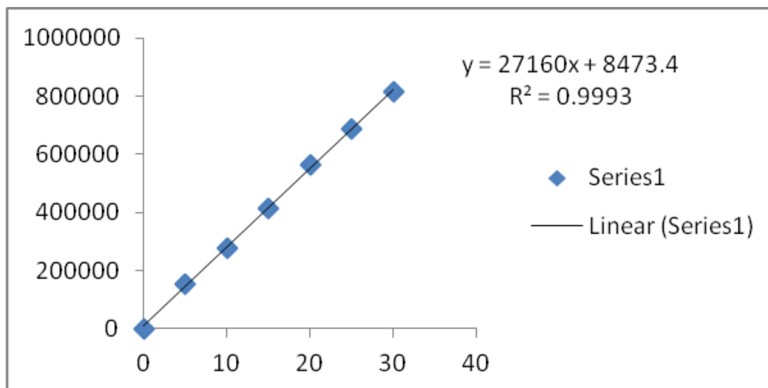


Figure.4 Linearity of Levocetrizine.

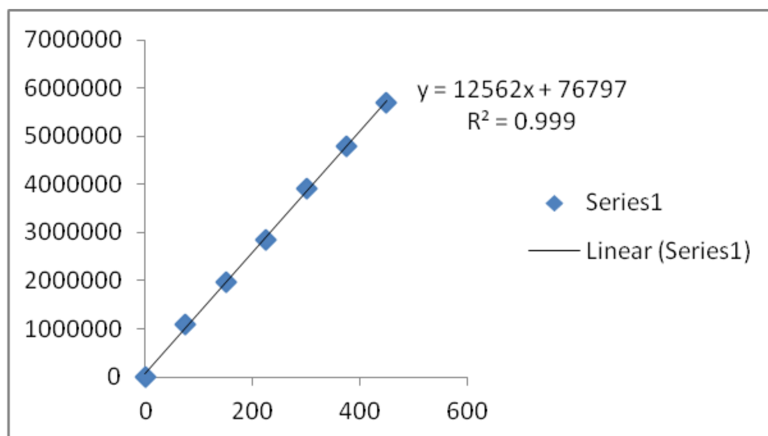


Figure.5 Linearity of Ambroxol.

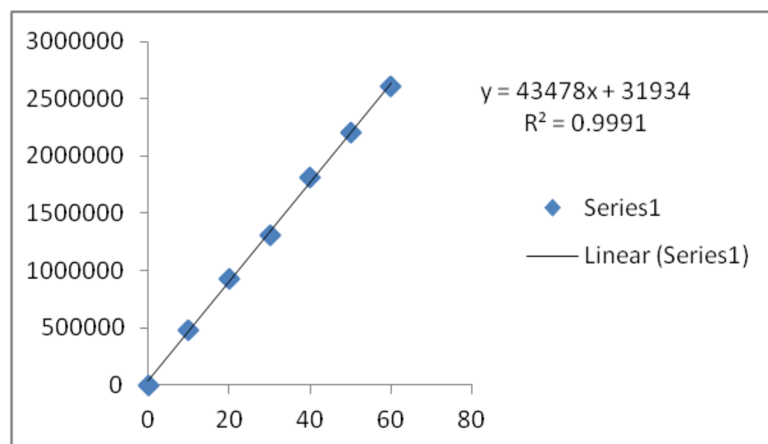


Figure.6 Linearity of Montelukast.

System precision:

Precision is the measure of closeness of the data values to each other for a number of measurements under the same analytical conditions. Standard solution of 50µg/ml of Levocetrizine and 750 µg/ml of Ambroxol and 100 µg/ml of Montelukast were prepared as per test method and injected for 6 times. Results are shown in Table-3.

Table.3 System precision.

Injections S.No	Peak Areas		
	Levocetrizine	Ambroxol	Montelukast
1	557404	3882016	1849061
2	550196	3982251	1813601
3	571923	3822974	1878273
4	563786	3929453	1841012
5	570723	3941477	1870517
6	558126	3900311	1825778
AVG	561951	3909747	1846374
SD	8313.2	54844.4	25038.6
%RSD	1.5	1.4	1.4

Precision

Intraday and interday precision study of Levocetrizine and Ambroxol and Montelukast were carried out by estimating corresponding responses for 6 times on the same day and on consecutive days for the concentration of 50µg/ml of Levocetrizine and 750 µg/ml of Ambroxol and 100 µg/ml of Montelukast. The percent relative standard deviation (%RSD) was calculated which was within the acceptable criteria of not more than 2. The results were shown in tables 4 and 5.

Table.4 Intra-day precision.

Samples	%Assay		
	Levocetrizine	Ambroxol	Montelukast
1	99.79	99.75	99.03
2	100.41	100.83	99.87
3	100.77	100.35	100.71
4	99.61	99.47	98.43
5	99.64	100.58	101.99
6	100.16	100.17	98.48
AVG	100.06	100.19	99.75
SD	0.467	0.51	1.4
%RSD	0.47	0.51	1.4

Table.5 Inter-day precision.

Samples	%Assay		
	Levocetrizine	Ambroxol	Montelukast
1	103.8	97.2	92.5
2	102.8	95.5	92
3	101.6	97.4	92
4	104.6	95.9	93
5	102.4	94.8	94.9
6	103.9	97.8	92.9
AVG	103.18	96.4	92.8
SD	1.1	1.2	1.07
%RSD	1.08	1.25	1.16

Accuracy (Recovery studies)

To determine the accuracy in sample preparation, method of standard additions was made for measuring the recovery of the drugs. A fixed amount of sample was taken and standard drug was added at 50, 100 and 150% levels. The results were analyzed and the results were found to be within the limits. The accuracy was expressed as the percentage of the analytes recovery. The results were shown in table 6.

Table.6 (a) .Accuracy Levocetrizine.

Accuracy %	Concentration in ppm	Peak area	% Recovery
50	10	821421	99.19
100	20	1092246	99.68
150	30	1370214	100.41
AVG	99.91		
SD	0.61		
%RSD	0.6		

Table. 6 (b). Accuracy Ambroxol.

Accuracy %	Concentration in ppm	Peak area	% Recovery
50	150	5733613	100.97
100	300	7646933	100.8
150	450	9478635	99.84
AVG		100.53	
SD		0.7	
%RSD		0.64	

Table. 6 (c). Accuracy Montelukast.

Accuracy %	Concentration in ppm	Peak area	% Recovery
50	20	2649249	99.8
100	40	3538829	100.8
150	60	4390208	99.76
AVG		100.17	
SD		0.8	
%RSD		0.79	

Specificity

The specificity of the method was performed by injecting blank solution (without any sample) and then a drug solution of 10µl injected into the column, under Optimized chromatographic conditions, to demonstrate the separation of the molecules Levocetrizine, Ambroxol and monteleukast from any of the impurities, if present. As there was no interference of impurities and also no change in the retention time, the method was found to be specific.

Limit of Detection and Limit of Quantification

LOD and LOQ were calculated using the following formula LOD = 3.3(SD)/S and LOQ = 10 (SD)/S, where SD = standard deviation of response (peak area) and S= slope of the calibration curve. Limit of Detection and Limit of Quantification were found to be 0.02 µg/ml and 0.06 µg/ml for Levocetrizine & 0.23 µg/ml and 0.69 µg/ml for Ambroxol, 0.08 µg/ml and 0.25 µg/ml for Montelukast respectively as per ICH guidelines. The results were shown in table7.

Table .7 LOD and LOQ.

Drug	S.D	Slope	LOD(ppm)	LOQ(ppm)
Levocetrizine	151.1	27147	0.02	0.06
Ambroxol	8674	12547	0.23	0.69
Montelukast	1099.5	43647	0.08	0.25

Robustness

Robustness was carried by varying three parameters from the optimized chromatographic conditions such as making small changes in flow rate (±0.1ml/min), mobile phase composition (±5%) and column temperature (±5ºC). It was observed that the small changes in these operational parameters did not lead to changes of retention time of the peak of interest and the %RSD was not more than 2. The degree of reproducibility of the results proven that the method is robust. The results were shown in the table 8.

Table.8 Robustness.

Drug name	Parameter	Optimized condition	Used condition	Peak area	Retention Time	Plate Count	Tailing factor
Levocetrizine	Flow rate	1ml/min	0.9ml/min	575241	2.403	10129	1.1
	(±0.1ml/min)		1ml/min	558126	2.184	10470	1.1
			1.1ml/min	563706	2.419	10531	1.06
	Column temp.	25^0c	20^0c	579626	2.197	9591	1.0
	(±5^0c)		25^0c	558126	2.184	10470	1.1
			30^0c	587175	2.210	10711	0.98
	Mobile phase	40:60	35:65	583103	2.41	9439	1.07
	Composition		40:60	558126	2.184	10470	1.1
	(5%v/v)		45:55	573243	2.419	9827	1.09
Ambroxol	Flow rate	1ml/min	0.9ml/min	3822645	2.866	13908	1.02
	(±0.1ml/min)		1ml/min	3882016	2.623	14574	1.07
			1.1ml/min	3939473	2.881	13738	1.02
	Column temp.	30^0c	20^0c	3850084	2.622	11709	1.07
	(±5^0c)		25^0c	3882016	2.623	14574	1.07
			30^0c	3805234	2.623	10126	1.06
	Mobile phase	40:60	35:65	3905905	2.867	14036	1.02
	Composition		40:60	3882016	2.623	14574	1.07
	(5%v/v)		45:55	3866289	2.879	14356	1.02
Montelukast	Flow rate	1ml/min	0.9ml/min	1884972	4.315	14290	0.97
	(±0.1ml/min)		1ml/min	1870517	3.937	12931	1.03
			1.1ml/min	1921641	4.331	14648	0.96
	Column temp.	30^0c	20^0c	1885689	3.947	14206	0.95
	(±5^0c)		25^0c	1870517	3.937	12931	1.03
			30^0c	1895249	3.956	14328	0.97
	Mobile phase	40:60	35:65	1908122	4.321	14905	0.97
	Composition		40:60	1870517	3.937	12931	1.03
	(5%v/v)		45:55	1898837	4.316	14426	0.97

System suitability

The system suitability was determined by making six replicate injections from freshly prepared standard solutions. The observed RSD values were well within usually accepted limits (≤2%). Theoretical plates, tailing factor of Levocetrizine, Ambroxol and monteleukast were determined. The results are all within acceptable limits summarized in Tables 4,5,6.

Forced degradation studies

Forced degradation studies were performed to demonstrate the optimized method is stability indicating. To prove the method which can be able to measure accurately active pharmaceutical ingredient in presence of degradants which are expected to be formed during different types of degradations applied to the drug sample.

For forced degradation analysis, aliquots of stock (2mg/ml, 3mg/ml and 2.5mg/ml) were separately treated with 1ml of 2N HCl (Acid stability), 1ml of 2N NaOH (Alkaline stability), 1ml of 20% H_2O_2 (Oxidative degradation), exposure of standard drug solution at 105ºC for 6 hrs (dry heat degradation), photo stability degradation (exposure of drug at 200 watt/m2) and neutral degradation (refluxing with water at 60ºC for 6 hours. Stability of these samples was compared with fresh sample on the day of analysis. The HPLC chromatograms of degraded products show no interference at the analyte peaks, hence the method was specific and stability indicating. The chromatograms were shown in figures and the results were shown in table 8. The detailed degradation for each condition is as follows:

Oxidation:

To 1 ml of stock solution of Levocetrizine, Ambroxol and monteleukast, 1 ml of 20% hydrogen peroxide (H_2O_2) was added separately. The solutions were kept for 30 min at 600c. For HPLC study, the resultant solution was diluted to obtain 500µg/ml of Levocetrizine , 50 µg/ml Ambroxol and 100 µg/ml Fenpiverinium were injected into the system and the chromatograms were recorded to assess the stability of sample.

Acid Degradation Studies:

To 1 ml of stock solution Levocetrizine, Ambroxol and monteleukast, 1ml of 2N Hydrochloric acid was added and refluxed for 30mins at 600c .The resultant solution was diluted to obtain 500µg/ml of Levocetrizine , 50 µg/ml Ambroxol and 100 µg/ml monteleukast solutions were injected into the system and the chromatograms were recorded to assess the stability of sample.

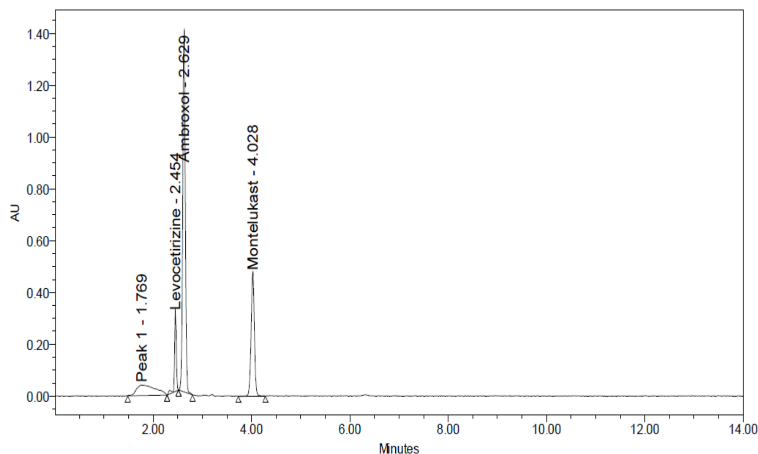


Figure.6 Acid degradation peak.

Alkali Degradation Studies:

To 1 ml of stock solution Levocetrizine, Ambroxol and monteleukast, 1 ml of 2 N sodium hydroxide was added and refluxed for 30mins at 600c. The resultant solution was diluted to obtain 500µg/ml of Levocetrizine, 50 µg/ml Ambroxol and 100 µg/ml monteleukast solution and 10 µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

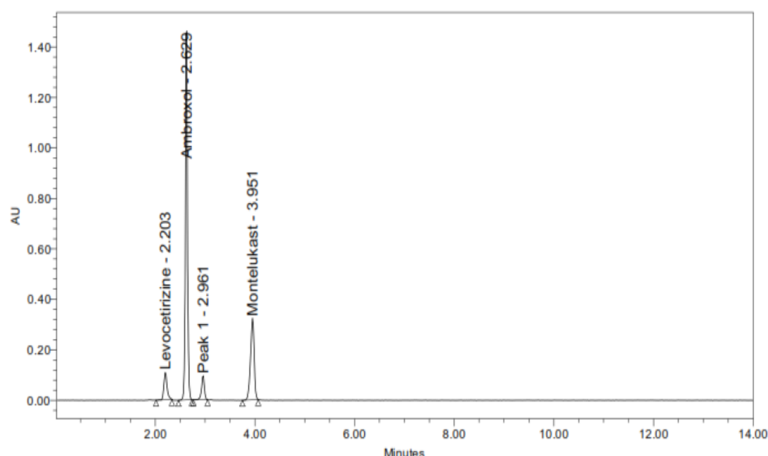


Figure.7 Base degradation peak.

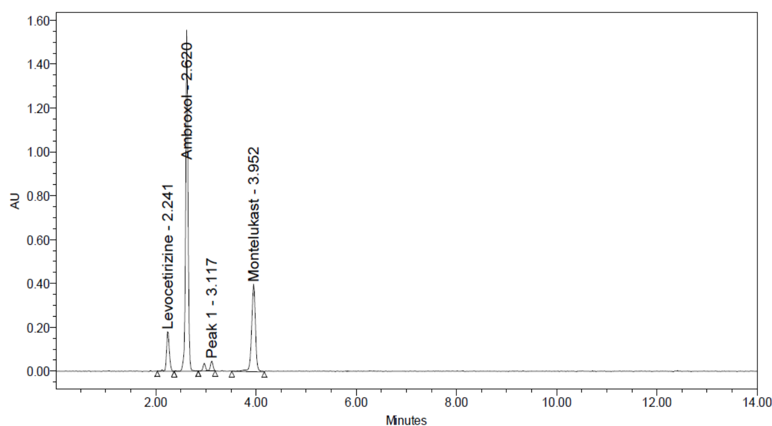


Figure.8 Peroxide degradation peak.

Dry Heat Degradation Studies:

The standard drug solution was placed in oven at 1050c for 6 h to study dry heat degradation. For HPLC study, the resultant solution was diluted to 500µg/ml of Levocetrizine , 50 µg/ml Ambroxol and 100 µg/ml monteleukast solution and 10µl were injected into the system and the chromatograms were recorded to assess the stability of the sample**.**

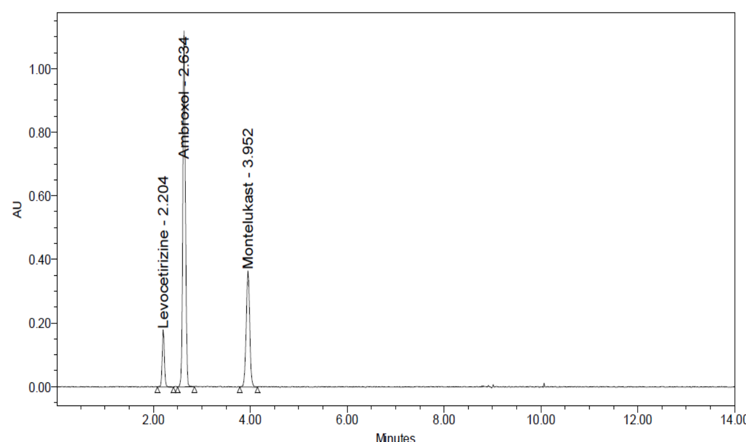


Figure.9 Thermal degradation peak.

Photo Stability studies:

The photochemical stability of the drug was also studied by exposing the 2mg/ml, 3mg/ml and 0.25mg/ml solution to UV Light by keeping the beaker in UV Chamber for 7days or 200 Watt hours/m2 in photo stability chamber. For HPLC study, the resultant solution was diluted to obtain 500µg/ml of Levocetrizine , 50 µg/ml Ambroxol and 100 µg/ml monteleukast and 10µl were injected into the system and the chromatograms were recorded to assess the stability of sample.

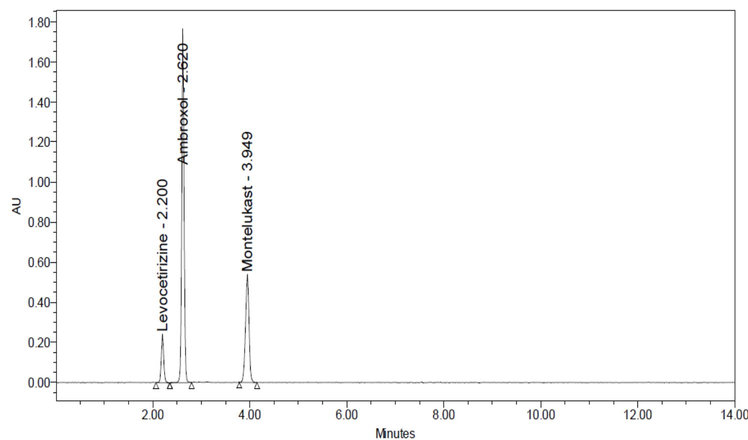


Figure.10 UV degradation peak.

Neutral Degradation Studies:

Stress testing under neutral conditions was studied by refluxing the drug in water for 6hrs at a temperature of 60º. For HPLC study, the resultant solution was diluted to 500µg/ml of Levocetrizine , 50 µg/ml Ambroxol and 100 µg/ml monteleukast were injected into the system and the chromatograms were recorded to assess the stability of the sample.

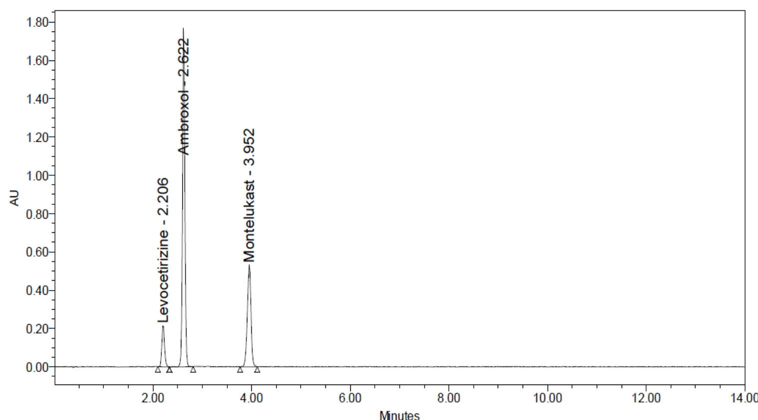


Figure.11 Water degradation peak.

Table.8 Degradation studies results.

Drug	Parameters	Acid degradation	Alkali Degradation	Peroxide degradation	Thermal Degradation	UV degradation	Water degradation
Levocetrizine	Peak area	545443	551196	557137	560266	560568	560938
	% Assay	96.87	97.89	98.94	99.5	99.5	99.6
	%degradation	2.937	1.91	0.856	2.998	0.246	0.180
	Purity angle	1.997	1.5	2.661	3.132	2.118	1.293
	Purity threshold	2.008	1.7	2.899	3.437	2.736	2.585
Ambroxol	Peak area	3780462	3813103	3861143	3886492	3904316	3908894
	% Assay	96.4	97.24	98.4	99.1	99.5	99.6
	%degradation	3.3	2.47	1.27	0.594	0.139	0.021
	Purity angle	10.995	13.1	12.396	3.220	12.013	25.024
	Purity threshold	25.025	24.9	25.384	4.502	9.276	25.354
Montelukast	Peak area	1793196	1799689	1817936	1839161	1841014	1842670
	% Assay	96.9	97.2	98.2	99.4	99.5	99.6
	%degradation	2.88	2.52	1.54	0.39	0.29	0.2
	Purity angle	0.741	0.34	0.258	0.761	0.624	0.614
	Purity threshold	0.843	0.53	1.018	0.878	0.748	0.751

Table.9 Characterstics of HPLC method.

Parameter	Drug name		
	Levocetrizine	Ambroxol	Montelukast
Linearity range (ppm)	5 – 30	75 - 450	10 - 60
Regression coefficient(r2)	0.999	0.999	0.999
Intercept	54353	76189	31614
Slope	27147	12547	43647
LOD (ppm)	0.02	0.23	0.08
LOQ (ppm)	0.06	0.69	0.25
Tailing factor	1.06	1.02	1.03
Plate count	12123	13091	12931

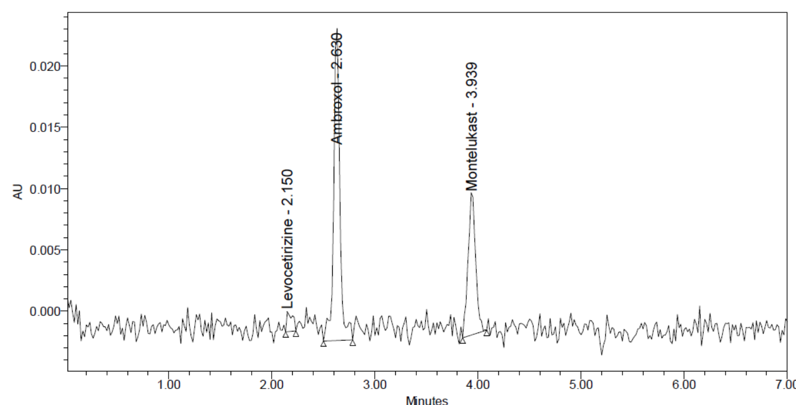


Figure.12 HPLC chromatogram of LOD.

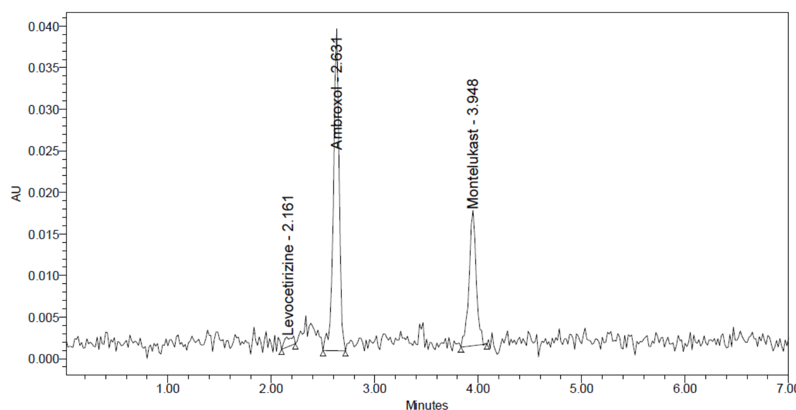


Figure.13 HPLC chromatogram of LOQ.

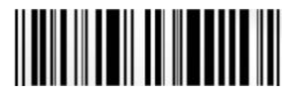
CONCLUSION

The developed method is accurate, simple, rapid and selective and proved to be stability indicating for the simultaneous estimation of Levocetrizine , Ambroxol and Montelukast in Bulk and pharmaceutical dosage form. The sample preparation is simple, the analysis time is short and the elution is by isocratic method. The retention time of Levocetrizine, Ambroxol and Montelukast were found to be 2.185, 2.622 and 3.931 mins respectively. The excipients of the commercial sample analyzed did not interfere in the analysis, which proved the specificity of the method for these drugs. Forced degradation studies of different conditions shows that all the degradants were well resolved from these main drug peaks and able to quantify the Levocetrizine, Ambroxol and Montelukast in presence of degradants and excepients proved that the method is found to be stability indicating. Hence the proposed method can be conveniently adopted for the routine quality control analysis in the bulk and combined formulations.

REFERENCES

1. Morita MR, Berton D, Boldin R, Barros FAP, Meurer EC, et al. (2008) Determination of levocetirizine in human plasma by liquid chromatography– electrospray tandem mass spectrometry: Application to a bioequivalence study. J Chromatogr B Analyt Technol Biomed Life Sci 862: 132-139.
2. Arayne MS, Sultana N, Nawaz M (2008) Simultaneous quantitation of cefpirome and cetirizine or levocetirizine in pharmaceutical formulations and human plasma by RP-HPLC. J Anal Chem 63: 881-887.
3. Selvan PS, Gopinath R, Saravanan VS, Gopal N (2006) Simultaneous Estimation of Levocetirizine, Ambroxol, Phenylpropanolamine and Paracetamol in Combined Dosage Forms by RP-HPLC Method. Asian J Chem 18: 2591- 2596.
4. Birajdar AS, Meyyanathan SN, Raja RB, Krishanaveni N, Suresh B (2008) Simultaneous analysis of ambroxol HCl with cetirizine HCl and of ambroxol HCl with levo-cetirizine dihydrochloride in solid dosage forms by RP-HPLC. Acta Chromatographica 20: 411-421.
5. Alsarra IA (2004) Development of a stability-indicating HPLC method for the determination of montelukast in tablets and human plasma and its applications to pharmacokinetic and stability studies. Saudi Pharm J 12: 136-143.
6. Sane RT, Menezes A, Mote M, Moghe A Gundi G (2004) HPTLC determination of montelukast sodium in bulk drugs and pharmaceutical preparations. J Planar Chromatogr 17: 75-78.
7. Radhakrishna T, Narasaraju A, Ramakrishna M, Satyanarayana A (2003) Simultaneous determination of montelukast and loratadine by HPLC and derivative spectrophotometric methods. J Pharm Biomed Anal 31: 359-368.
8. Ashokkumar S, Senthil Raja M, Perumal P (2009) RP-HPLC Method Development and Validation for Simultaneous Estimation of Montelukast Sodium and levocetirizine Dihydrochloride. International journal of pharmaceutical research 1: 8-12.

9. Smita Sharmaa MC, Sharma DV, Kohlib AD, Sharma C (2010) Development and validation of tlc-densitometry method for simultaneous quantifi cation of montelukast sodium and levocetirizine dihydrochloride pharmaceutical solid dosage form. Der Pharmacia Lettre 2: 489-494.
10. Ravisankar M, Subasini U, Jambulingam M and Kamalakannan D. Simultaneous estimation of fexofenadine hydrochloride and montelukast sodium in bulk drug and marketed formulation by RP-HPLC method. Int J Res Pharm Sci. 2012; 3(4): 356-359.
11. Ambadas RR and Vaishali SN. Determination of montelukast sodium and levocetirizine dihydrochloride in combined pharmaceutical dosage form by RP-HPLC. Lat Am J Pharm. 2010; 29(6): 1020-1023.
12. Sushma S and Pathak AK. Simultaneous estimation of levocetirizine dihydrochloride and montelukast sodium by RP-HPLC Method. Pharmacia. 2012; 1(3): 90-94.
13. Harika CH, Vijaykumar G and Harinadhbabu K. Development and validation of a RP-HPLC method for estimation of levocetirizine and montelukast in pharmaceutical dosage form. Int J Pharm. 2012; 2(3): 675-678.
14. Raghad H, Hind E and Samer H. Determination of levocetirizine configurational stability in tablets using chiral HPLC method. Int J Pharm Pharm Sci. 2011; 3(2): 103-107.
15. Anirudha RC, Vishnu PC, Swati CJ, Shialesh NS, Nilesh AB and Bharat DP. 2781–IJRPC 2012, 2(4) Laskhmana Rao et al ISSN: 2231 1063 Simultaneous estimation of montelukast sodium and fexofenadine HCl in pharmaceutical formulation by RPLCPDA. Int J Pharm Sci Res. 2012; 3(1): 241-248.
16. Sandeep Kumar BVV. Analytical method development and validation of levocetirizine hydrochloride and montelukast sodium in combined tablet dosage form by RP-HPLC. Int J Adv Pharm Res. 2011; 2(7): 380-396.
17. Alireza S, Afshin Z and Seyed MF. Rapid and sensitive determination of montelukast in human plasma by HPLC method using monolithic column application to pharmacokinetic studies. J Bioequi Availab 2010; 2(06): 135-138.
18. Chaitanya KK, Israel DS and Sankar DG. RP-HPLC method for the estimation of levocitrizine and its preservatives in oral solutions. Int J Pharm Res Dev. 2011; 3(1): 28-33.
19. Smitha P, Pore YV, Kuchekar BS, Khire VG. Determination of montelukast sodium and bambuterol hydrochloride tablets using RP-HPLC. Ind J Pharm Sci, 2009; 71(1): 58-61.
20. Shakalisava Y, Ragan F. Determination of montelukast sodium by capillary electrophoresis. J Sep Sci. 2008; 31(6- 7): 1137-1143.
21. International Conference on Harmonization. Q2(R1). Validation of analytical procedures: text and methodology. International Conference on Harmonization, IFPMA, Geneva, 2005.



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