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Research Article

Simultaneous Estimation of Acebrophylline, Montelukast Sodium and Levocetirizine by RP-UPLC Method in Combined Dosage Forms

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Abstract

A new simple, precise method was developed for Acebrophylline, Montelukast sodium and Levocetirizine by using UPLC for Simultaneous Estimation. Acebrophylline is combination of Theophylline and Ambroxol. The compounds were separated by using column C- 18 BEH 2.1 x 50 mm (1.7 µm) at ambient temperature. Flow rate was 0.6 ml/min; wavelength of 230 nm, Mobile phase was methanol:acetonitrile: Buffer (30:40:30) potassium dihydrogen phosphate buffer was used with pH 6.0. The injection volume was 2 µl and Run time 4.5 min. The retention time of Acebrophylline (Theophylline and Ambroxol), Montelukast sodium and Levocetirizine 0.87,1.34, 2.01, 3.20 mins respectively. The percentage purity was found to be 99.72, 99.96 and 99.81 respectively. The validation parameters Specificity, Accuracy, linearity, LOD, LOQ and Robustness were studied. The linearity of was Acebrophylline 40 - 320 µg/ml, for Montelukast sodium 2 - 16 µg/ml and for Levocetirizine 1-8 µg/ml They have good linearity with Correlation coefficient Value of 0.996, 0.994, 0.994 respectively.

Keywords: *UPLC; Acebrophylline; Montelukast Sodium and Levocetirizine; Simultaneous Estimation*

Introduction

Acebrophylline is an effective bronchodilator medicine used to treat blockage, swelling, and irritation associated with bronchial asthma and chronic obstructive pulmonary disease (COPD) in adults. Acebrophylline is combination of Theophylline and Ambroxol. Several methods have been reported for the analysis of Acebrophylline in pharmaceutical dosage form as well as in the biological fluids and tissues. i.e. chromatographic methods ; HPLC [1,2]. Montelukast sodium (MS) a selective leukotriene antagonist of the cysteinyl leukotriene receptor, has been used in the treatment of asthma and allergic rhinitis. In this study, we evaluated the effect of MS on the early inflammatory phase (histological) of non-synovial tendon healing. On detailed literature survey, it was found that Montelukast sodium can be estimated by spectrophotometry HPLC [2-7] methods individually or in combination with other drug. Levocetirizine is an over-the-counter non sedating antihistaminic agent commonly used to treat allergic diseases. Numerous method was developed for Levocetirizine HPLC [2,4-6]. Clinically significant acute liver injury has been very rarely associated with its use. Since No RP-UPLC methods are reported for the simulta-

neous estimation of Acebrophylline, Montelukast sodium and Levocetirizine Sin combination, therefore an attempt has been made to estimate both these drugs simultaneous by a simple RP-UPLC method. The proposed method was optimized and validated as per ICH guidelines. The structure of are given in figure 1.

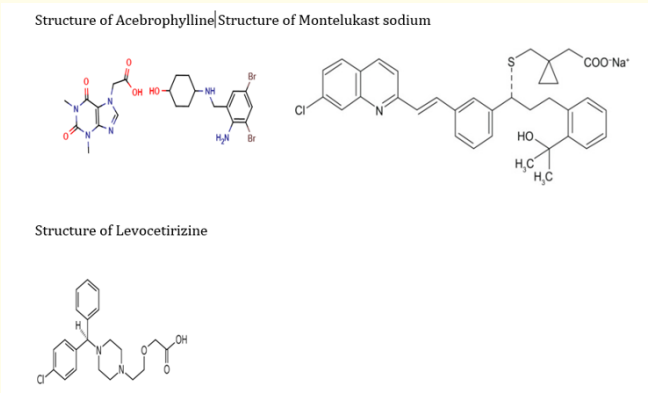

Figure 1

Materials and Methods

All solvents were HPLC grade and Reagents were Analytical Grade. Acetonitrile from RANCHEM, Potassium di hydrogen phosphate from Merck, Ortho phosphoric acid from Merck, Methanol from Merck Acebrophylline, Montelukast sodium and Levocetirizine, were procured from Apex Pharma Chennai. The method was developed in Waters UPLC Acquity system: C- 18 BEH column was used for the separation. The Mobile Phase consists of Methanol:acetonitrile: Buffer (30:40:30), Disodium hydrogen phosphate buffer was used with pH 6.0. The injection volume was 2 µl with flow rate of 0.6 ml per minute and wavelength was 230 nm. The analysis was performed at constant column temperature at 35°C. Mobile Phase was used as Diluent.

Results and Discussion

Method development

Selection of wavelength: Isobestic point Acebrophylline, Montelukast sodium and Levocetirizine was determined by dissolve it in Acetonitrile and scanned between 200 - 400 nm and the Isobestic Point was found to be 230nm.

Preparation of standard stock solution: Acebrophylline 200 mg was weighed accurately and dissolved in 100 ml, sonicate about 10 minutes, then 10 ml of the above solution diluted into 50 ml to get final concentration. Montelukast sodium 26.1 mg was weighed accurately and dissolved in 50 ml; sonicate about 10 minutes, then 1 ml of the above solution Pipette out into 50 ml to get final concentration. Levocetirizine 25 mg was weighed accurately and dissolved in 100ml; sonicate about 10 minutes, then 5 ml of the above solution Pipette out into 50 ml to get final concentration.

Preparation of sample

Commercial available 10 tablets of Acebrofact LM were weighed and powdered, the powdered drug was weighed to about 600 mg dissolved into 50 ml Volumetric flask, dissolve it completely, add 5 ml of the above solution into 50 ml (Table 1 and figure 2).

Validation

This method was validate according to the ICH Guidelines, the following parameters were studied System Suitability, Specificity, Linearity and Range, Accuracy, Robustness Limit of Detection and Limit of Quantitation.

System suitability

System suitability studies were performed by injecting 5 replicate of injections of Acebrophylline, Montelukast sodium and Levocetirizine It was performed to determine the resolution, theoretical plates, tailing factor, repeatability of retention time etc. All parameters were within the range.

Commercial Formulation	Drug	Standard area	Sample Area	Label Claim (mg)	Amount Present (mg)	% Purity
Acebrofact LM	Acebrophylline	7369309	7372569	200	199.4	99.72
	Montelukast sodium	599383	588103	10	9.99	99.96
	Levocetirizine	192199	188598	5	4.9	99.81

Table 1: Assay of acebrophylline, montelukast sodium and levocetirizine.

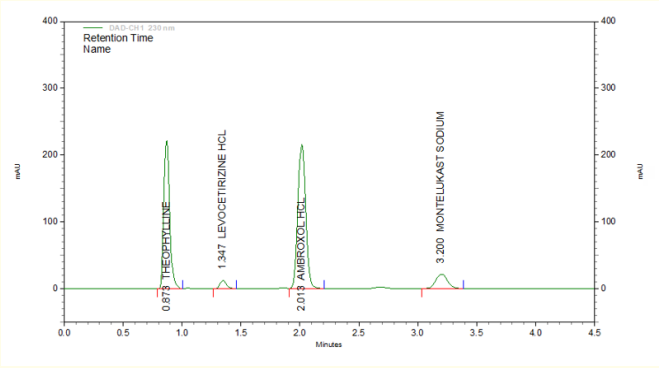

Figure 2: Chromatogram of acebrophylline, montelukast sodium and levocetirizine.

S.no	Acebrophylline		Montelukast sodium	
	Conc (mcg/mL)	Mean area	Conc (mcg/mL)	Mean area
1	40	937990	2	74372
2	80	2311259	4	184637
3	120	3892325	6	308995
4	160	5205682	8	415064
5	200	6776304	10	550290
6	240	8207452	12	655016
7	280	9627185	14	782290
8	320	11054114	16	913149

S.no	Levocetirizine	
	Conc (mcg/mL)	Mean area
1	1	23748
2	2	58993
3	3	96546
4	4	134127
5	5	176097
6	6	212452
7	7	253550
8	8	289620

Table 2: Linearity and range.

Specificity

Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. It was performed to identify the any impurity may present; it was done by using standard, sample, placebo dilutions of both of the drugs. It was observed there is no interference.

Calibration curve (Linearity)

Linearity of Acebrophylline, was found to be 16 µgm/ml to 320 µgm/ml, with R^2 Value of 0.9996. Linearity of Montelukast sodium was found to be 2 µgm/ml to 16 µgm/ml, with R^2 Value of 0.9994. and Linearity of Levocetirizine was found to be 1 µgm/ml to 8 µgm/ml, with R^2 Value of 0.9994 (Table 2).

Accuracy

Accuracy is closeness of agreement between true value and Value to be found. For Accuracy studies three levels were selected 80%, 100% and 120% for Acebrophylline, Montelukast sodium and Levocetirizine. Recovery was found with Average value of 99.81%, 99.78% and 99.64% respectively (Table 3).

Robustness

Robustness study was done by changing the pH, wavelength, flow rate in both the drug. % RSD was within the limit as per ICH guidelines.

Limit of detection

For Limit of detection the S/N Ratio should be ≥ 3 and ≤ 9. Limit of detection of Acebrophylline, was 0.4 ppm and signal to Noise Ratio was 3.79. Limit of detection of Montelukast sodium was 0.2 ppm and signal to Noise Ratio was 3.23, and Levocetirizine was 0.25 ppm and signal to Noise Ratio was 3.67 respectively.

Limit of quantitation

For Limit of Quantitation the S/N Ratio should be ≥ 10 and ≤ 30 Acebrophylline, Montelukast sodium and Levocetirizine were within the limit.

% Conc	Acebrophylline				Montelukast			
	mg/tab	Area		% Assay	mg/tab	Area		% Assay
		STD	Sample			STD	Sample	
80%	199.32	7190251	6274185	99.66	9.97	592654	507937	99.78
100%	199.82	7190251	7216778	99.91	9.93	592654	580410	99.37
120%	199.62	7190251	8133611	99.81	9.93	592654	654906	99.39

% Conc	Levocetirizine			
	mg/tab	Area		% Assay
		STD	Sample	
80%	4.96	189828	163418	99.35
100%	4.98	189828	188151	99.68
120%	4.98	189828	212190	99.64

Table 3: Accuracy.

Conclusion

It was concluded that the developed Method was simple, Accurate, Rapid and sensitive, it can be used in quality control laboratories for routine analysis. The method provides economically feasibility due to the lesser consumption of sample run time.

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