INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Paper

A Novel and Validated RP-HPLC Method for the Simultaneous Determination of Fexofenadine Hydrochloride and Montelukast Sodium in Bulk Drug and Pharmaceutical Dosage Forms

Maheen Fathima*, Manju S. V., Chandanam Sreedhar

Department of Pharmaceutical Analysis, Karnataka College of Pharmacy, Bangalore, Karnataka-560064.

ARTICLE INFO

Published: 09 Sept 2026
Keywords:
Fexofenadine Hydrochloride, Montelukast Sodium, RP-HPLC, Method development, Validation,Simultaneous determination,Pharmaceutical dosage forms,Quality control,LOD, LOQ, ICH Guidelines
DOI:
10.5281/zenodo.22677626

ABSTRACT

A novel, sensitive, accurate, and robust reverse-phase high-performance liquid chromatography (RP-HPLC) method was developed and validated for the simultaneous determination of fexofenadine hydrochloride (FEX) and montelukast sodium (MON) in bulk drugs and pharmaceutical dosage forms. Chromatographic separation was achieved using an XBridge C18 column (250 × 4.5 mm, 5 µm) with a mobile phase consisting of trifluoroacetic acid buffer (pH 2.1) and methanol in a ratio of 70:30 (v/v). The analysis was performed at a flow rate of 1.0 mL/min with a 20 µL injection volume, detection wavelength of 215 nm, and a total run time of 10 min. The method was validated according to ICH Q2 guidelines for linearity, precision, accuracy, robustness, limit of detection (LOD), and limit of quantification (LOQ). Good linearity was observed over 20–120 µg/mL for FEXOFENADINE and 10–60 µg/mL for MONTELUKAST, with correlation coefficients of 0.9965 and 0.9980, respectively. The method showed acceptable precision, accuracy, and robustness. LOD/LOQ values were 5.31/17.49 µg/mL for FEX and 2.88/9.50 µg/mL for MON. Retention times were 3.863 and 7.333 min, respectively. The method was successfully applied to tablet formulations and is suitable for routine quality control analysis

INTRODUCTION

Fexofenadine Hydrochloride is freely soluble in methanol and ethanol, slightly soluble in chloroform and water, and insoluble in hexane,chemically designated as 2-[4-[1-hydroxy-4-[4-[hydroxy(diphenyl)methyl]piperidin-1-yl]butyl]phenyl]-2-methylpropanoic acid Fexofenadine hydrochloride is a second-generation antihistamine, has minimal anticholinergic effects due to low affinity for cholinergic and α-adrenergic receptors. In addition

***Corresponding Author:** Maheen Fathima
Address: *Department of Pharmaceutical Analysis, Karnataka College of Pharmacy, Bangalore, Karnataka-560064.*
Email ✉: maheenfathima82@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

to H_1-receptor blockade, it exhibits anti-inflammatory activity by inhibiting leukotrienes, prostaglandins, COX-2, thromboxane, and iNOS-derived nitric oxide. It also downregulates cytokines and adhesion molecules (e.g., ICAM-1, VCAM-1, RANTES) and reduces eosinophil activation, contributing to its efficacy in allergic conditions [1,2]Montelukast,sodium chemically designated as2-[1-[[(1R)-1-[3-[(E)-2-(7-chloroquinolin-2-yl)ethenyl]yl)ethenyl]phenyl]-3-[2-(2-hydroxypropan-yl)phenyl]propyl]sulfanylmethyl] cyclopropyl]acetate is very soluble in methanol and in ethanol, and freely soluble in water is a potent and selective cysteinyl leukotriene receptor 1 (CysLT1) antagonist selectively binds to the CysLT1 receptor, inhibiting the binding of leukotrienes such as LTD4.This blockade prevents the downstream signaling effects typically induced by leukotriene receptor activation, by inhibiting the action of LTD_4, montelukast alleviates bronchoconstriction promoting bronchodilation and improving airflow in patients with asthma. It is primarily indicated for the prophylaxis and chronic treatment of asthma in adults and children, used in management of Chronic Urticaria.[3,4,5]

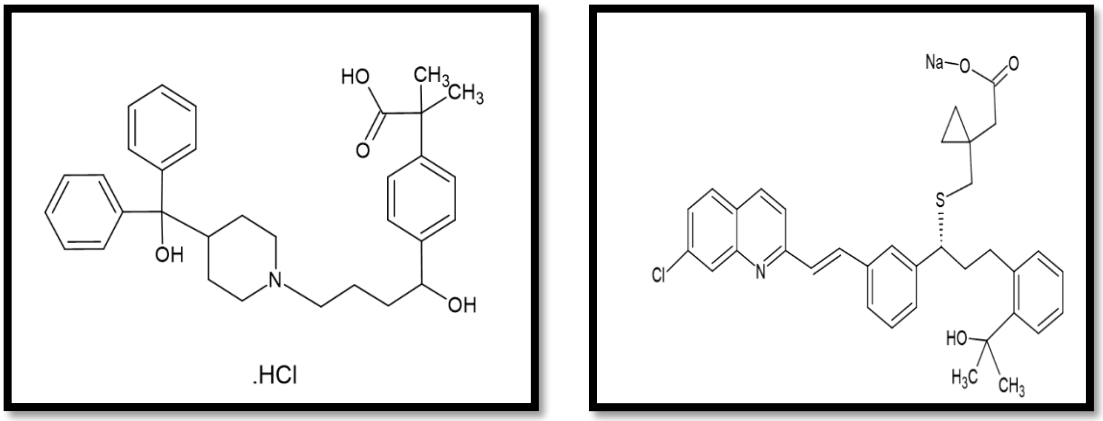


Figure 1: Structure of [a] Fexofenadine hydrochloride [b] Montelukast Sodium

There for the present research work aims to develop a simple, sensitive, accurate and reproducible method for simultaneous estimation of Montelukast Sodium and Fexofenadine hydrochloride in combined dosage form by RP-HPLC method.

2. MATERIALS AND METHODS

2.1. Chemicals and reagents

Active pharmaceutical ingredient of Montelukast Sodium and Fexofenadine hydrochloride was obtained as a gift sample from Anglo french Pharmaceutical Pvt. Ltd and Micro labs Pvt. Ltd, India.

2.2. Instrumentation and chromatographic conditions

The chromatographic analysis was performed using an Agilent 1120 Compact LC HPLC system equipped with a gradient pump, Rheodyne injector, UV–Visible variable-wavelength detector, and standard flow cell. Chromatographic separation was achieved on an X-Bridge C18 column (250 mm × 4.5 mm, 5 µm) maintained under ambient conditions. The mobile phase was optimized after evaluating different solvent combinations and ratios and consisted of trifluoroacetic acid buffer (pH 2.1) and methanol in a ratio of 70:30 (v/v). The system was operated at a flow rate of 1.0 mL/min with an injection volume of 20 µL and UV detection at 215 nm. The

total chromatographic run time was 10 min. Under the optimized conditions, well-resolved peaks were obtained with retention times of 3.863 min for fexofenadine hydrochloride and 7.333 min for montelukast sodium. Analytical weighing was performed using a Shimadzu AUX 220 balance, while an Equitron sonicator was used for sample and solvent preparation. A Super Fit vacuum pump and Tarsons filtration assembly with 0.45 µm nylon membrane filters (Merck Millipore) were used for filtration. A Shimadzu UV-1800 double-beam UV–Visible spectrophotometer was used for wavelength selection and spectral analysis. Chromatographic data acquisition, evaluation, and storage were performed using EZChrome Elite software.

2.3 Preparation of mobile phase:

The buffer solution was prepared by dissolving 1g of 0.1% of Trifluoroacetic acid buffer in 1000 ml HPLC grade water (20 mM). The pH of the resulting solution was adjusted to 2.1 by using HPLC grade Triethylamine. HPLC experiments were carried out using a binary pump, pump A containing Methanol and pump B containing Trifluoroacetic acid buffer.

2.4 Standard solutions preparation of Fexofenadine Hydrochloride and Montelukast Sodium

The standard stock solution of Fexofenadine Hydrochloride and Montelukast Sodium was prepared by dissolving 50 mg of the drug into 50 ml of the volumetric flask in Methanol (HPLC grade), volume was made up to the mark with the same solvent. This gave the concentration of 1000 µg/ml for both Fexofenadine Hydrochloride and Montelukast Sodium (Stock-1). Further dilution of 10 ml in 100 ml volumetric flask makes up the volume with Methanol gives 100 µg ml-1(stock-2). From stock solution-2, 6 dilutions were prepared between 120 µg/ml for Fexofenadine Hydrochloride and 60 µg/ml .Montelukast Sodium from the above dilutions of working concentration made up by using Methanol in the ratio of 70:30 Trifluoroacetic acid buffer: Methanol.

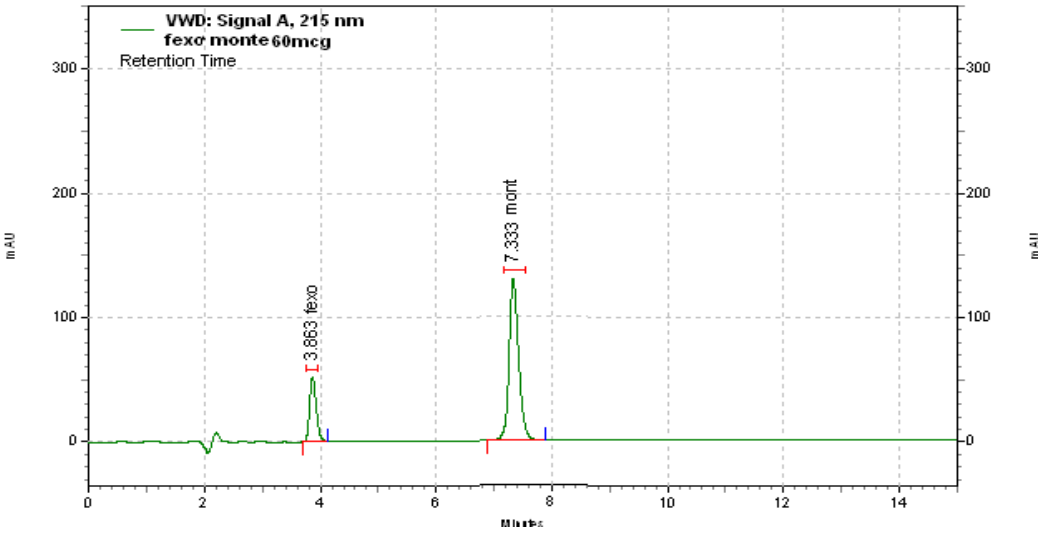


Figure 2: Chromatogram for Fexofenadine Hydrochloride and Montelukast Sodium

1. RESULTS AND DISCUSSION

3.1 Validation of analytical method

1.Linearity and range:

By using the working standard, aliquots of 10-120µg/ml,of Fexofenadine hydrochloride and

montelukast sodium, were prepared with methanol. Six dilutions of each of the above-mentioned concentrations were prepared separately and from these six dilutions, 20µl of each concentration was injected into the HPLC system. Then their chromatogram was recorded. Peak areas were recorded for all the peaks and a standard calibration curve of peak area against concentration was plotted.

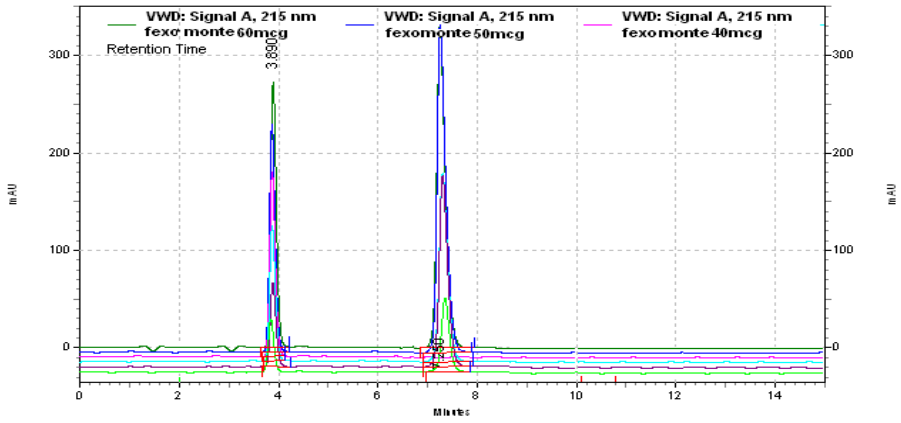


Figure 3: Linearity Chromatogram for Fexofenadine Hydrochloride and Montelukast Sodium 40-60µg/ml

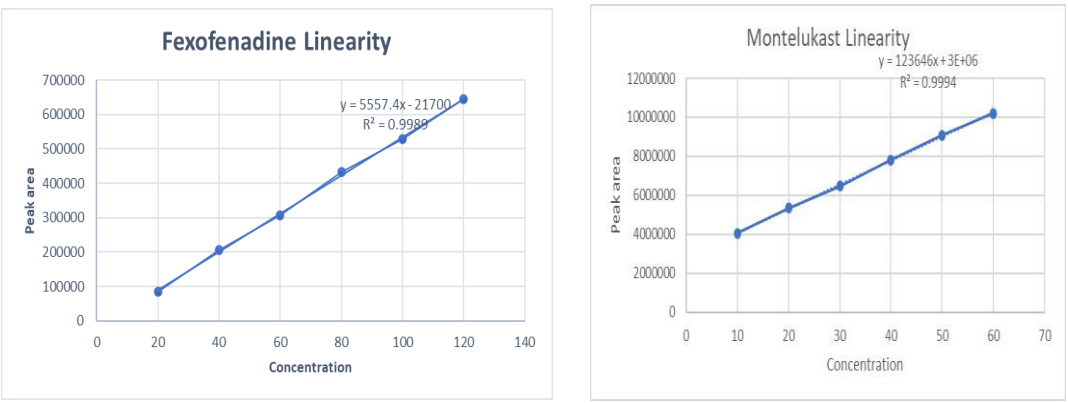


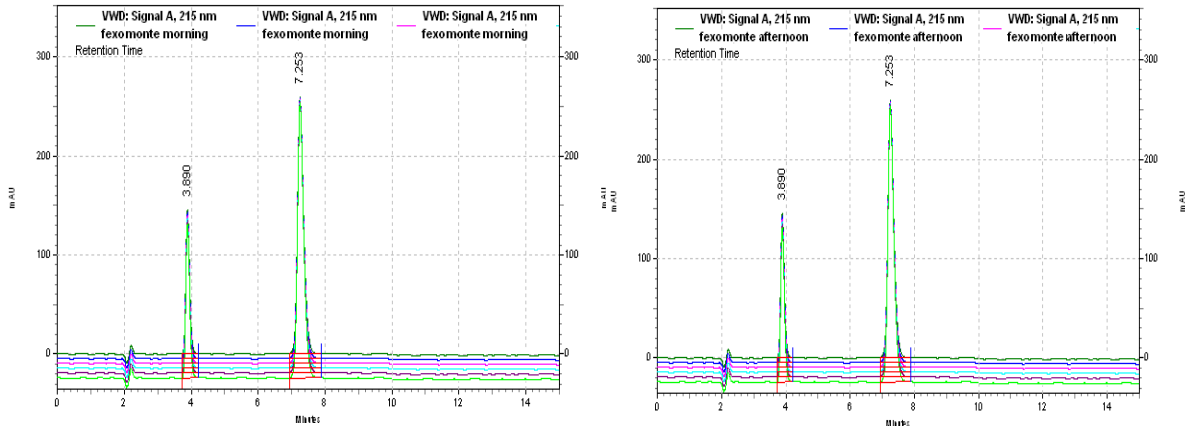
Figure 4: Linearity graph of Fexofenadine Hydrochloride and Montelukast sodium

Table 1: Linearity data for Fexofenadine Hydrochloride and Montelukast Sodium Specfication r2 = 1

S.NO	Fexofenadine Hydrochloride		Montelukast Sodium	
	Concentration (µg/ml)	Area	Concentration (µg/ml)	Area
1.	20	84666	10	4055927
2.	40	176483	20	7651946
3.	60	206566	30	7759156
4.	80	433708	40	7810011
5.	100	8838303	50	9079415
6.	120	9714180	60	9704527

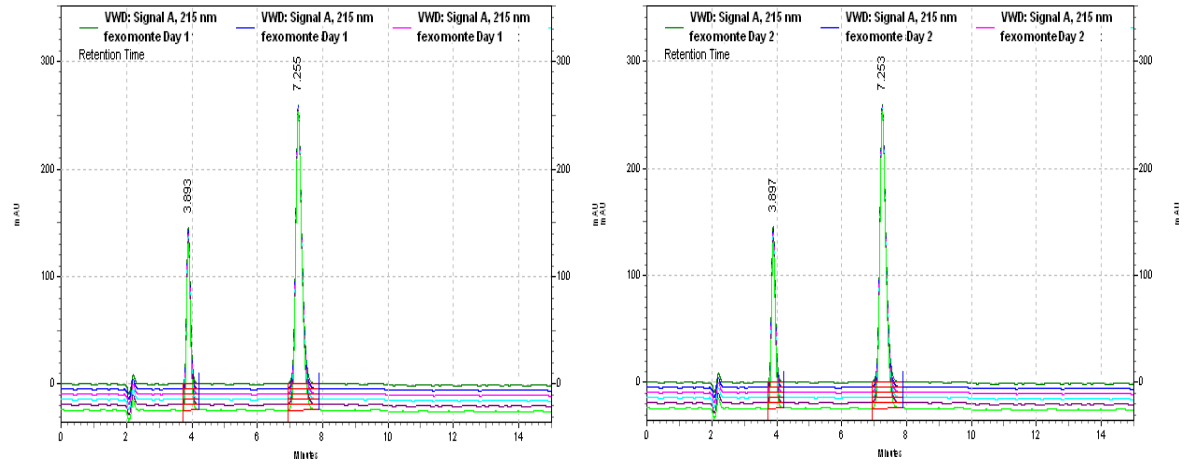
2.Precision

The precision of the assay was determined in terms of intra-day and inter-day variation in the peak area for a set of drug solutions 50-50µg/ml, assayed six times on the same day and on different 2 days.



a b

Figure 5: Intraday Chromatogram for Fexofenadine Hydrochloride and Montelukast Sodium a) Morning b) Afternoon



a b

Figure 6: Intraday Chromatogram for Fexofenadine Hydrochloride and Montelukast Sodium a) Day 1& b) Day 2

1. Accuracy

2. The accuracy was carried out for both **Fexofenadine Hydrochloride and Montelukast Sodium**drugs at 80%, 100%, and 120% levels. % recovery was determined.

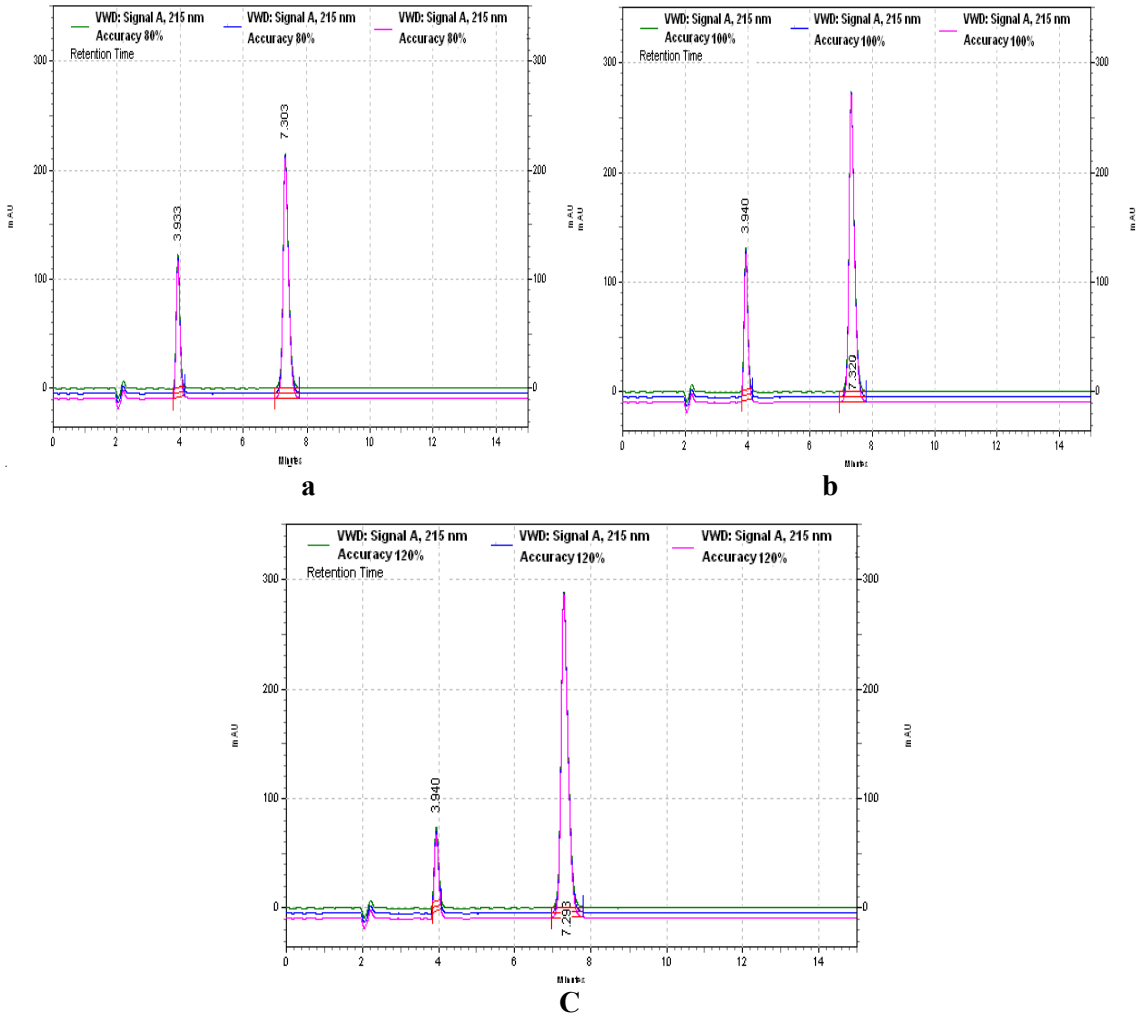


Figure 7: Chromatogram for accuracy of a) 80%, b) 100% , c) 120%

4.Limit of detection and limit of quantification

LOD and LOQ were calculated according to ICH recommendations where the approach is based on the signal-to-noise ratio. Chromatogram signals obtained with known low concentrations of analytes were compared with the signals of the blank samples. A signal–to–noise ratio of 3:1 and 10:1 was considered for calculating LOD and LOQ respectively.

Table 2: LOD and LOQ for simultaneous estimation of Fexofenadine Hydrochloride and Montelukast Sodium

Name of the drug	LOD µg/ml	LOQ µg/ml
Fexofenadine Hydrochloride	5.31	17.49
Montelukast Sodium	2.88	9.50

5.System Suitability

The resolution, number of theoretical plates, Capacity Factor, S/N (6 Sigma) and peak asymmetry were calculated for the standard solutions.

Table 3: Optimum conditions in RP-HPLC method for simultaneous estimation of Fexofenadine Hydrochloride and Montelukast Sodium

Parameter	Method		Acceptance Criteria
	Fexofenadine Hydrochloride	Montelukast Sodium	
λ max (nm)	215nm	215nm	-
Linear Range(µg/ml)	20-120 µg/ml	10 -60µg/ml	-
Correlation Coefficient(r^2)	0.9965	0.998	NMT 1
Precision (RSD)	0.2824-0.4946	0.0737-0.3868	NMT 2
Accuracy (% Recovery)	100 to 101%	100 to 102%	Between 100-102%
Limit of Detection (µg/ml)	5.31 µg/ml	17.49 µg/ml	-
Limit of Quantification(µg/ml)	2.88µg/ml	9.50 µg/ml	-
Number of Theoretical Plates per meter	3281	3569	NLT 2000
Tailing Factor	0.9281	0.8254	NMT 2

CONCLUSION

In conclusion, a simple, sensitive, precise, and accurate reverse-phase high-performance liquid chromatography (RP-HPLC) method was successfully developed and validated for the simultaneous estimation of Fexofenadine Hydrochloride and Montelukast sodium in both bulk and pharmaceutical dosage forms. In the method employed a mobile phase consisting of Trifluoroacetic acid buffer pH 2.1: Acetonitrile (70:30 v/v), with separation achieved using an X bridge C-18 column (250 mm x 4.5 mm, 5µ). The retention times were minutes for Fexofenadine Hydrochloride and minutes for Montelukast sodium, with a total run time of 10 minutes. The method demonstrated excellent precision with %RSD values below 2% and exhibited good linearity over a concentration range of 20 µg/ml to 120 µg/ml. Accuracy was confirmed through recovery studies, with results ranging between 100-102%. The limits of detection (LOD) and quantification (LOQ) were determined for both compounds. The method adhered to ICH guidelines for analytical method validation, demonstrating its reliability. Overall, this RP-HPLC method is rapid, economical, and well-suited for routine analysis of Fexofenadine Hydrochloride and Montelukast sodium in both bulk and pharmaceutical formulations.The proposed method is novel, validated, and suitable for regular quality control testing in pharmaceutical laboratories

REFERENCES

1. Arefin P, Habib Ms, Ahmed Nu, Rahim Ma, Ibrahim M, Bhattacharjee Sc, Chakraborty D, Das S, Karmakar D,Bhowmik D, Islam S. Allergic rhinitis and importance of Fexofenadine hcl Sustained release microsphere as its treatment approach. Int J App Pharm. 2022;14(1):13-7.
2. Ansotegui IJ, Bousquet J, Canonica GW, Demoly P, Gómez RM, Meltzer EO, Murrieta-Aguttes M, Naclerio RM, Rosario Filho N, Scadding GK. Why fexofenadine is considered as a truly non-sedating antihistamine with no brain penetration: a systematic review. Current Medical Research and Opinion. 2024 Aug 2;40(8):1297-309.
3. Ahmed SA, Shinde VP. Development and Validation of a RP-HPLC Method for

Simultaneous Quantification of Montelukast and Fexofenadine in Pharmaceutical Formulations. Journal of Pharma Insights and Research. 2025 Jun 5;3(3):326-32.

4. Vekaria H, Limbasiya V, Patel P. Development and validation of RP-HPLC method for simultaneous estimation of montelukast sodium and fexofenadine hydrochloride in combined dosage form. Journal of Pharmacy Research. 2013 Jan 1;6(1):134-9
5. Mhaske MP, Gawali PS, Bhalerao PS, Kolhe MH, Bhor RJ, Shinde GS, Kakad SB. Method Development and Validation of Fexofenadine and Montelukast in Pure and Pharmaceutical Formulation. Research Journal of Pharmacy and Technology. 2025;18(8):3468-72.

HOW TO CITE: Maheen Fathima, Manju S. V., Chandanam Sreedhar, A Novel and Validated RP-HPLC Method for the Simultaneous Determination of Fexofenadine Hydrochloride and Montelukast Sodium in Bulk Drug and Pharmaceutical Dosage Forms, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 9, 942-949, https://doi.org/10.5281/zenodo.22677626