INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Research Article

SIMULTANEOUS ESTIMATION OF FEXOFENADINE HYDROCHLORIDE AND MONTELUKAST SODIUM IN BULK DRUG AND MARKETED FORMULATION BY RP-HPLC METHOD

Ravisankar M, Subasini Uthirapathy*, Ananda Thangadurai, Jambulingam Munusamy and Kamalakannan Dhanapal
Swamy Vivekanandha College of Pharmacy, Tiruchengode-637 205, India

Article Received on: 02/03/12 Revised on: 04/04/12 Approved for publication: 10/04/12

*Dr. U.Subasini, M.pharm., Ph.D., Professor and Head, Dept.of pharmacognosy, Swamy Vivekananadha College of Pharmacy, Tiruchengode, Namakkal (Dt) Tamil Nadu, India-637 205

ABSTRACT
A new simple and precise accurate RP-HPLC method has been developed and validated for simultaneous estimation of Montelukast Sodium and Fexofenadine in tablet formulations. The chromatographic separation was performed in Water symmetry C8 (150X4.6mm 5µm) and mobile phase 0.05 m potassium di hydrogen ortho phosphate: acetonitrile in the ratio of 35:65 and the pH – 6 adjusted by triethylamine.The flow rate was 1.0ml/min and the wavelength selected for the quantization was 226 nm. The retention time was found to be 2.127 min for Fexofenadine and 5.650 min for Montelukast sodium .The linearity were found to be in the range of 4.8 - 28.8 µg/ml and 0.4 – 2.4 µg/ml for Fexofenadine and Montelukast respectively with the correlation co efficient of 0.999.The mean recoveries for Fexofenadine and Montelukast were 99.85 % and 100.19 % respectively, and relative standard deviation was less than 2%. Precision were performed as per ICH guidelines with the result shows relative standard deviation not more than 2%.The assay value for Fexofenadine and Montelukast were found to be 100.55 % and 100.40 % respectively.

KEYWORDS: Fexofenadine, Montelukast sodium, High performance liquid chromatography, Validation, Simultaneous estimation, ICH guidelines.

INTRODUCTION

Fexofenadine hydrochloride is an antihistaminic drug used in the treatment of hay fever and similar allergy symptoms. Fexofenadine like other second and third generation antihistamines, does not readily pass through the blood brain barrier, and so causes less drowsiness than first generation histamine receptor antagonists. It inhibits antigen – induced bronchospasm in sensitized guinea pigs and histamine release from peritoneal mast cells in rats.

Fexofenadine hydrochloride (±)-4-[1nylmethyl)-1-piperidinyl]-butyl]-α,α-dimethylhydroxy-4-benzeneaceticacid hydrochloride. It is a white to off-white crystalline powder .It is freely soluble in methanol and ethanol, slightly soluble in chloroform and water and in soluble in hexane.

Montelukast sodium is a antiasthmatic agent, leukotriene modifier. It inhibits physiologic actions of LTD4 at the CysLT1 receptors, without any agonist activity.

Montelukast sodium 2-[1-({[(1R)-1-{3-[(E)-2-(7-chloroquinolin-2-yl)ethenyl]phenyl}-3-[2-(2-hydroxypropan-2-yl)phenyl]propyl]sulfanyl}methyl)cyclopropyl]acetic acid sodium salt.

Montelukast sodium is hygroscopic and optically active white to off white powder. It is freely soluble in methanol, ethanol and water. Literature surveys shows that Spectrophotometeric method for Fexofenadine has been developed and validated[1, 2, 3] and spectrophotometeric method for Fexofenadine with Montelukast also has been reported[4]. The RP- HPLC method for Fexofenadine with other drugs were performed [5] and RP-HPLC method for Montelukast with other drugs shown in literature[6,7].The spectrophotometeric method for Montelukast and Levocitirizine by area under curve method was indicated[8]. Literature survey revealed that the stability indicating HPLC method for the determination of motelukast in human plasma also has been reported [9] and Simultaneous determination of fexofenadine and its related compounds by HPLC also reported[10]. The aim of the present work to develop the simple, economical, accurate, reliable reverse phase HPLC method for the estimation of Montelukast sodium and Fexofenadine in bulk and combined dosage form. This method was validated as per the ICH guidelines[11]. Suitable statistical tests were performed on validation report.

MATERIALS AND METHODS

Chemicals and reagents

Acetonitrile of HPLC grade were purchased from Merck. Potassium dihydrogen ortho phosphate and Tri ethyl amine were purchased from SD fine chem., Mumbai, India. The working standard was generously donated by Kausikh Therapeutics and Private Ltd, Chennai.

Chromatography conditions

Analysis was performed with a Shimazdu chromatograph equipped with an LC-20 AT solvent delivery system and SPD 20 UV detector set as 226 nm. The equipment was controlled by Spin chrom software. Compounds were separated on a 250x4.6 mm 5 µ particles, Water symmetry C 8 column. The mobile phase was 0.05M Potassium dihydrogen ortho phosphate P^h-6 with Triethyl amine: Acetonitrile (35:65).The flow rate was 1 mL /minute. Before analysis both the mobile phase and sample solutions were degassed by use of sonicator. The identity of compounds established by comparing the retention times of compounds in the sample solutions with those in standard solution. Chromatography was performed in an air-conditioned room at ambient temperature.

Preparation of standard solutions

Accurately weighed Fexofenadine (24 mg) and Montelukast (2 mg) were transferred to two separate 100 ml volumetric flask, dissolved in methanol and diluted to the mark with mobile phase.From stock solution 1 ml was pippeted in to 10 ml volumetric flask to obtain final concentration 24 µg/ml of Fexofenadine and 2 µg/ml of Montelukast. Sample solution prepared by equivalent to standard concentration. Then it was sonicated for 10 minutes.

Preparation of sample solutions

Ten tablets were accurately weighed, each containing 120 mg of Fexofenadine and 10 mg of Montelukast were triturated and finely powdered. A quantity of powder equivalent to 120 mg and of Fexofenadine and 10 mg of Montelukast was weighed and transferred to 50 ml volumetric flask, dissolved in methanol and diluted with mobile phase. From this final concentration of 24 µg/ml of Fexofenadine and 2 µg/ml of Montelukast were prepared. The chromatograms for sample and standard indicated in (Fig 3 and 4).

Assay

The assays performed by the Marketed formulation of Fexofenadine and Montelukast sodium (Montair – FX).The prepared standard and sample solutions were injected in HPLC. Results for assay showed in Table 1.

METHOD VALIDATION

Accuracy studies

Accuracy studies were performed by standard addition method. Known amount of standard added with different concentration range (80 %, 100%, and 120%) of sample. Results showed in Table 2.

Precision

Precision was performed by six replicates of standard stock solution and area under curve (AUC) was recorded. It is evaluated by calculating standard deviation of resulting data. The results are showed in Table 3.

Linearity

Linearity was performed by six different concentration of a solutions were prepared and injected. The linearity range for Fexofenadine 4.8 - 28.8 µg/ml (Fig 5) and for Montelukast 0.4 – 2.4 µg/ml (Fig 6).The correlation co-efficient was found to be 0.99 for both Fexofenadine and Montelukast. The results are showed in Table 4 & 5.

System suitability

For chromatographic separation system suitability tests has been performed by injecting five replicates of standard solution. The system suitability parameters such as Theoretical plates, Resolution, Asymmetry values were found to be within standard limit. The results are showed in Table 6 and Table 7.

RESULT AND DISCUSSION

The proposed method was developed and validated as per ICH guidelines. This method shows the good precise, accurate and linear. All the RSD value was found to be not more than two. Linearity were found to be in the range of 4.8 - 28.8 µg/ml for Fexofenadine and Montelukast 0.4 – 2.4 µg/ml with the correlation co-efficient 0.999 for both drugs. It indicated the developed method having a good linearity. All the system suitability parameters were found within the standard limit. The rapid reproducible method RP-HPLC method developed for estimation of Fexofenadine and Montelukast sodium in bulk dosage forms and in marketed formulation is accuracy, precise, linear, satisfactory results were obtained from the validation of the method. The advantages occur in this method, low cost, less running time and high percentage of recovery. So this method can be used for routine analysis of Fexofenadine and Montelukast sodium in bulk and the combined dosage form.

ACKNOWLEDGEMENT

This work was supported by the kausikh therapeutics and private limited from the department of quality control. The authors are grateful to Mr.Karthikeyan QC chemist to giving this opportunity. We are also thankful to Mr. Chandra sekhar and Mr.Ramaiah for technical assistance.

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Table 1: Results for assay

Drug	Lable claim	% assay	Amount present
Fexofenadine	120 mg	100.55 %	120.65 mg
Montelukast sodium	10 mg	100.40 %	10.04 mg

Table 2: Results for accuracy

Drug	Concentration	Amount added (µg/ml)	Amount present (µg/ml)	Recovery (%)	RSD (%)
FEF	80 %	20.6	20.71	100.51	0.34
	100 %	26.4	26.26	99.47	0.36
	120 %	31.2	31.06	99.54	0.41
MKT	80 %	1.8	1.80	100.27	0.68
	100 %	2.2	2.23	101.22	1.79
	120 %	2.6	2.58	99.08	1.08

Table 3: Results for Precision

	Fexofenadine		Montelukast	
S. no	**Retention time**	**Peak area**	**Retention time**	**Peak area**
1	2.127	154.714	5.45	93.837
2	2.12	153.48	5.423	93.676
3	2.127	155.046	5.423	93.694
4	2.12	154.558	5.43	94.723
5	2.13	154.233	5.413	93.441
6	2.13	153.939	5.413	93.348
Average	2.125667	154.3283	5.425333	93.7865
S.D	0.00459	0.565132	0.01375	0.492342
% RSD	0.22	0.37	0.25	0.52

Table 4: Linearity for Fexofenadine

Concentration µg/ml	**Area**
0.4	24.287
0.8	40.598
1.2	57.9
1.6	75.093
2	93.186
2.4	110.266

Table 5: Linearity for Montelukast

Concentration µg/ml	**Area**
4.8	38.992
9.6	68.726
14.4	97.098
19.2	123.074
24	152.782
28.8	180.437

Table 6: System suitability report

	Fexofenadine		Montelukast sodium	
S.no	**Retention time**	**Peak area**	**Retention time**	**Peak area**
1	2.123	153.216	5.432	95.134
2	2.127	154.225	5.4332	94.804
3	2.123	151.261	5.507	94.406
4	2.127	152.826	5.45	94.874
5	2.123	151.726	5.42	95.303
AVG	2.1246	152.6508	5.44844	94.9042
STD	0.002191	1.184804	0.034435	0.343149
% RSD	0.10	0.78	0.63	0.36

Table 7: System suitability parameters

Drug	**Fexofenadine**	**Montelukast**	**Standard limit**
Theoretical plates	3325	8994	NLT 2000
Resolution	-	18.092	NLT 2
Asymmetry	1.114	1.474	NMT2

Figure 1: Chemical Structure of Fexofenadine Hydrochloride

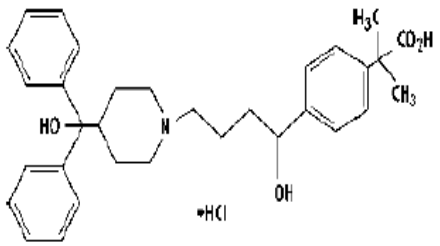

Figure 2: chemical structure of montelukast sodium

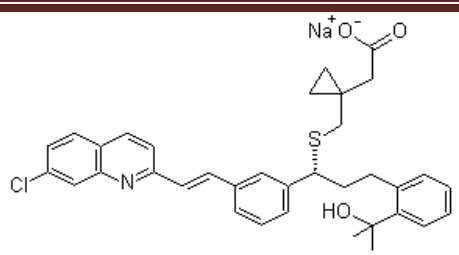

Figure 3: chromatogram for sample

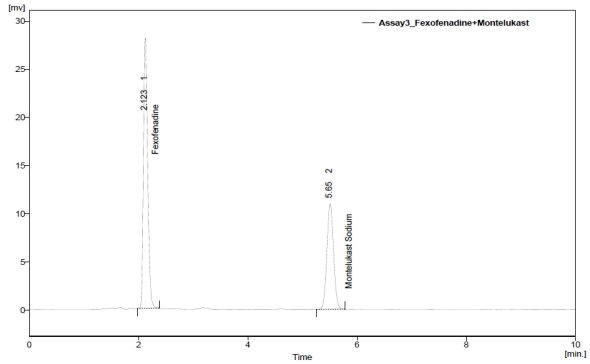

Figure 4: chromatogram for standard

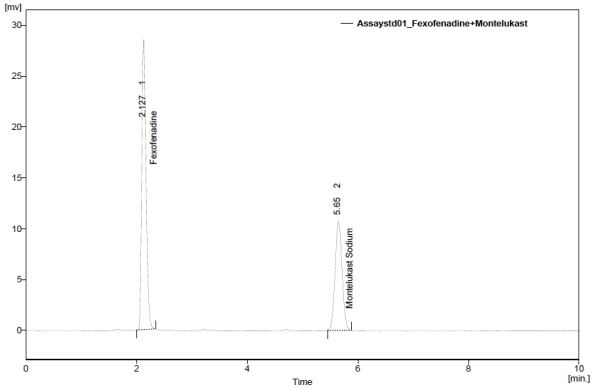

Figure 5: Linearity for Fexofenadine

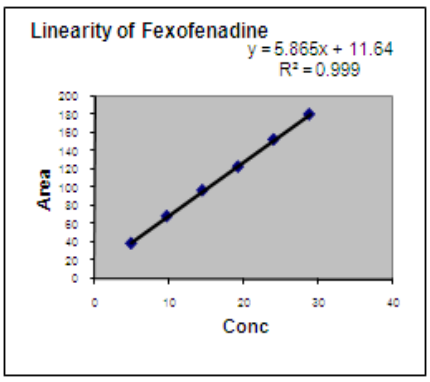

Figure 6: Linearity for Montelukast