Research Article

Available Online at: www.ijphr.com

International Journal of Pharmaceuticals and Health care Research

ISSN: - 2306 – 6091

ESTIMATION OF MONTELUKAST SODIUM AND FEXOFENADINE HYDROCHLORIDE IN BULK AND TABLET DOSAGE FORM BY Q-ABSORBANCE METHOD

[1]Ravisankar M, [2]Subasini U, [*1]Ananda Thangadurai S, [1]Jothimanivannan C, [1]Sundaraganapathy R, [1]Prudhvi T

[*1]Department of Pharmaceutical Analysis, Swamy Vivekanandha College of Pharmacy, Elayampalayam, Tamil Nadu, India - 637205.

[2]ASIA Metropolitan University, Medical campus, Bandar Seri Alalm, Johor Bahru 81750, Malaysia.

Abstract

A simple precise, accurate, cost effective method has been developed for the estimation of Montelukast sodium and Fexofenadine hydrochloride in combined tablet dosage form by Q-absorbance method. The isobestic point was found at 226 nm. The developed method showed linearity in the range of 5-25 µg/ml for both drugs. LOD and LOQ values were found to be 2.3 µg/ml and 3.45 µg/ml for Montelukast sodium and 2.67 µg/ml and 3.35 µg/ml for Fexofenadine hydrochloride respectively. The % RSD values were within the acceptable range. The developed method has been validated as per ICH guidelines.

Keywords: Fexofenadine hydrochloride, Montelukast sodium, Q-absorbance method.

Introduction

Fexofenadine hydrochloride is (*RS*)- 2-[4-[1-Hydroxy- 4-[4-(hydroxy- diphenyl- methyl) - 1-piperidyl]butyl]phenyl]- 2-methyl- propanoic acid. It is an antihistaminic drug used in the treatment of hay fever and similar allergy symptoms. Montelukast sodium is a antiasthmatic agent, leukotriene modifier. It inhibits physiologic actions of LTD4 at the Cys LT1 receptors, without any agonist activity. Montelukast sodium is an anti asthmatic agent, leukotriene modifier. It inhibits the physiological actions of LTD4 at the Cys LT1 receptors, without any antagonist[1, 2].

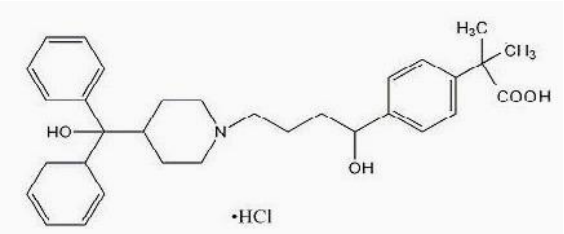

Fig. No. 01:
Structure of Fexofenadine hydrochloride

Montelukast sodium chemically it is an (R,E)-2-(1-((1-(3-(2-(7-chloroquinolin-2-yl) vinyl) phenyl)-3-(2-(2-hydroxypropan-2-yl) phenyl) propylthio) methyl) cyclopropyl) acetic acid monosodium salt.

Author for Correspondence:
Dr. Ananda Thangadurai S,
Department of Pharmaceutical Analysis,
Swamy Vivekanandha College of Pharmacy,
Elayampalayam, Tamil Nadu, India - 637205.
Email ID: anands17@rediffmail.com

It is used to treat the asthma and also it act as leukotriene modifier[3].

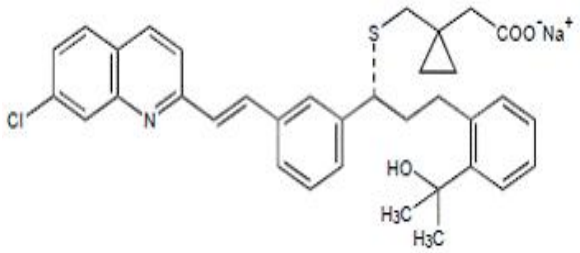

Fig. No. 02: Structure of Montelukast sodium

Literature survey revealed that very few analytical methods have been reported for the estimation of Montelukast sodium and Fexofenadine hydrochloride by HPTLC[4] and HPLC[5], but no work has been reported for the estimation of the same by UV spectrophotometry. Based on the above literature survey the simple, economical and accurate method was developed using UV spectrophotometry. The developed method has been validated as per ICH guidelines[6-7] in terms of Accuracy, Precision, Linearity, Robustness, LOD and LOQ.

Materials and methods

Reagents and chemicals

Pure samples of Montelukast sodium and Fexofenadine hydrochlorid were obtained as a gift sample. All the reagents were used analytical grade and all the glassware's were calibrated. Analytical grade methanol purchased form Merck, Mumbai India. Tablets of Fexofendine hydrochloride and Montelukast sodium in combined dosage form, MONTAIR-FX[8-9] with 10 mg Montelukast, 120 mg Fexofenadine as label claim manufactured by Cipla pharma Ltd.

Instrument

Perkin Elmer UV Lambda 25 double beam spectrophotometer was used for quantization, 1 cm quartz cell was used to record the spectra and absorbance. Shimadzu balance was used for weighing the samples.

Preparation of standard solutions

The standard stock solutions were prepared by 50 mg of Fexofenadine hydrochloride and Montelukast sodium were taken in 50 ml volumetric flask, dissolved in methanol and make up the volume with methanol (Stock solution A). From above solution 1 ml was pipette out into 100 ml volumetric flask make up the volume using methanol (Stock solution B). The final concentration of the solution containing 10 µg/ml of both drugs.

Preparation of sample solutions

10 tablets were weighed and average weight was calculated. The tablets were crushed by using mortor and pestle. Weigh the amount equivalent to 50mg was taken and dissolved in 50 ml volumetric flask using methanol. Sonicated for 10 min and diluted up to the mark with methanol. The final concentration of solution containing 10µg/ml of Fexofenadine hydrochloride and Montelukast sodium were prepared like standard.

Determination of isobestic point

By appropriate dilutions were made for both standard drugs and the λmax has been determined (Figure 3 & 4). The isobestic point was found at 226 nm and was shown in Figure 5.

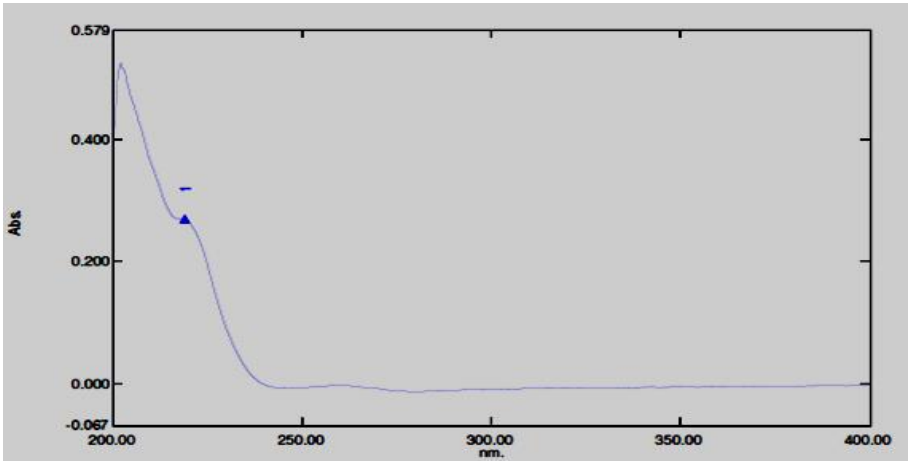

Fig. No. 03: λ max for Fexofenadine hydrochloride

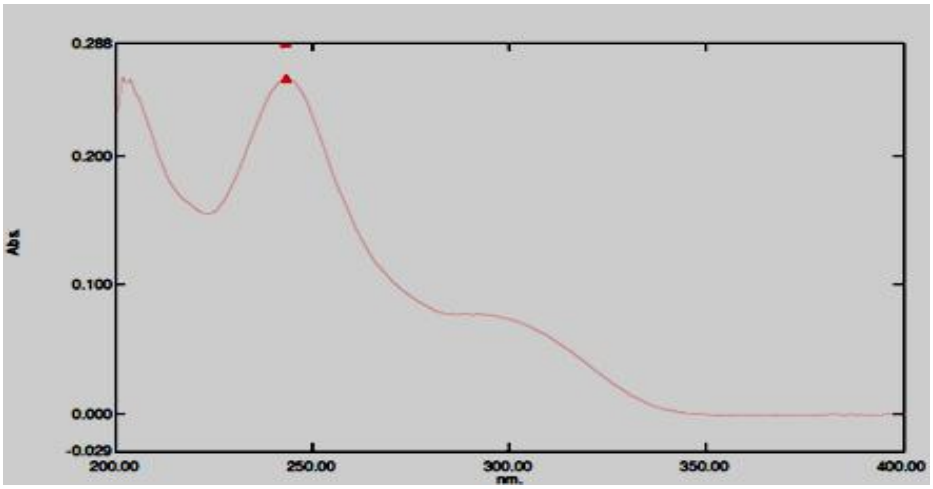

Fig. No. 04: λ max for Montelukast sodium

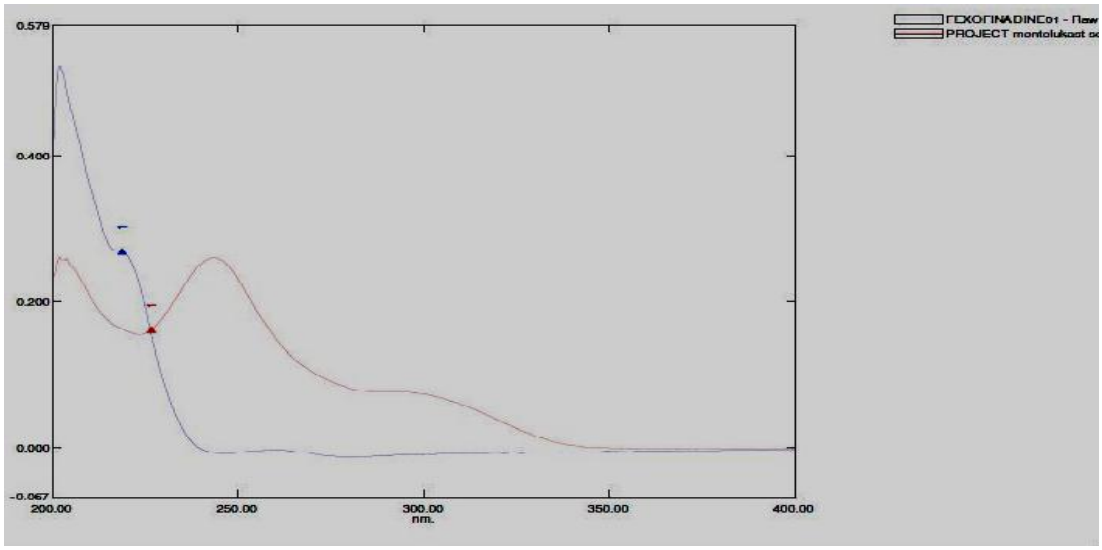

Fig. No. 05: Overlay spectra for Fexofenadine hydrochloride and Montelukast sodium

Estimation

Q-absorbance method uses the ratio of absorbances at two selected wavelengths, one at isobestic point and other being the λmax of one of the two compounds. From the standard stock solution solutions containing 10 µg/ml of Fexofenadine HCL and 10 µg/ml of Montelukast sodium were prepared by appropriate dilution and scanned in the UV region to find out the maximum absorbance (λmax) and isobestic point. Fexofenadine HCL and Montelukast sodium have λmax at 218 nm and at 243 nm respectively. Both the drugs were found to have same absorbance at 226 nm (isobestic point). The amounts present in the drugs were calculated using following formula. The results were shown in Table 1.

$$C_{Fexofenadine} = \frac{Qm - Qy}{Qx - Qy} \times \frac{A1}{ax1} \quad (1)$$

$$C_{Montelukast} = \frac{Qm - Qx}{Qy - Qx} \times \frac{A2}{ay1} \quad (2)$$

Where,
A1 and A2 are the absorbances of mixture at 226 nm and 218 nm and ax1, ax2 Absorptivity E (1%, 1 cm) of Fexofenadine and Montelukast at 218 nm,ax2 and ay2 Absorptivity of Fexofenadine and Montelukast at 226 nm and Qm = A2/A1, Qy = ay2/ay1 and Qx = ax2/ax1.

Method validation

Linearity

From standard stock solution A 1ml was pipette out and it was diluted in 10ml volumetric flask. From this solution containing 5-25 µg/ml of Montelukast and Fexofenadine were prepared. The absorbance was measured and the calibration curves were plotted. The results are shown in Table 2 and Figure 6, 7.

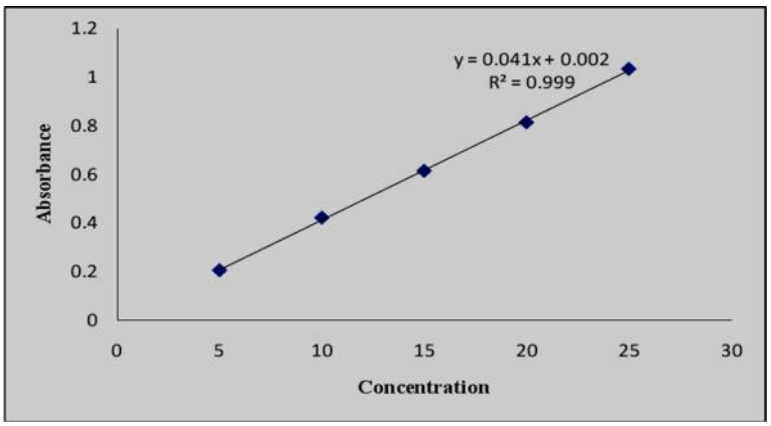

Fig. No. 06: Calibration curve for Fexofenadine hydrochloride

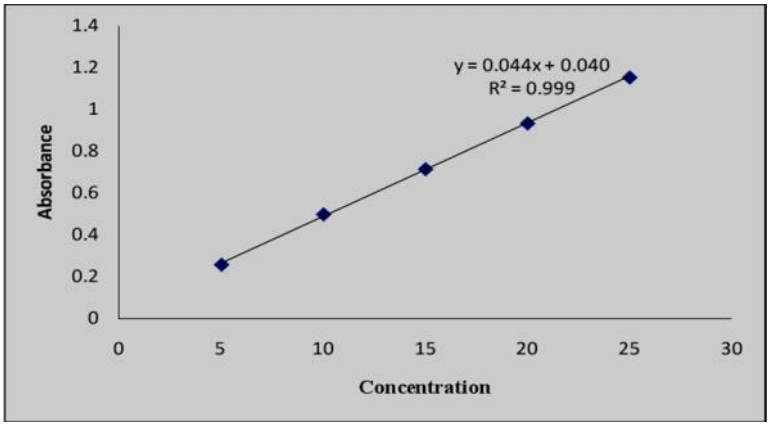

Fig. No. 07: Calibration curve for Montelukast sodium

Precision

The precision of the method was determined by the samples assayed for six times. The inter day and intraday precision were carried out and all the % RSD values were found within limit (Table 3).

Accuracy

The accuracy of the method was evaluated by 80 %, 100 %, 120 % of the sample was added with the known amount of standard and % Recovery of sample was calculated (Table 4).

Robustness

The robustness of the method was assessed by assay the samples with different instruments. The % RSD values were found within the limit (Table 5).

Ruggedness

The ruggedness of the method was determined by assaying the samples by three different analysts and the values were found within acceptance criteria (Table 6).

Limit of detection (LOD) & Limit of Quantification

The LOD and LOQ were calculated from the calibration curves. The LOD was calculated using following formula LOD = 3.3 x SD/ Slope and for LOQ =10 x SD/Slope (Table 2).

Results and discussion

Simple, precise and accurate spectrophotometric method was developed for the estimation of Fexofenadine hydrochloride and Montelukast sodium in Tablet dosage form. The λmax for Fexofenadine hydrochloride and Montelukast sodium were found to be 218 nm and 243 nm respectively and the isobestic point was found at 226 nm. The absorbance was measured at two wavelengths. The linearity regression data showed a good linear relationship over a concentration range 5-25 µg/ml for both drugs. The correlation coefficients for both drugs were found 0.9999. The % RSD for the precision was found within the acceptance criteria with low standard deviation values and it indicates the reproducibility and accuracy of the developed method.The recovery studies were also carried out to ensure the reproducibility and reliability of the method by adding known amount of standard with different concentrations of samples. The accuracy was found to be 99-100.10% for Fexofenadine hydrochloride and 99-99.91% for Montelukast sodium. The robustness of the method shows, the developed method remain unchanged by small variations and the % RSD values were found within limit. The ruggedness of the method has been evaluated by the assaying the samples with four different analyst and all the values were found within acceptance criteria.

Table No. 01: Results for Assay

Drug	Label claim	Amount recovered	% Amount found in drug
FEX	120 mg	119.4 mg	99.5 %
MKT	10 mg	9.91 mg	99.1%

Table No. 02: Results for Linearity

Parameters	FEX	MKT
Slope	0.041	0.044
Intercept	0.002	0.040
Correlation co-efficient	0.999	0.999
Linearity range	10-25 µg/ml	10-25 µg/ml
LOD	0.16 µg/ml	3 µg/ml
LOQ	0.48 µg/ml	9.09 µg/ml

Table No. 03: Results for Precision

Drug	Intraday	Interday		
	Precision (% RSD)	Precision (% RSD)		
		Day 1	Day 2	Day 3
FEX	0.64	0.44	0.36	1.01
MKT	0.45	0.54	0.84	0.78

Table No. 04: Results for Accuracy

% Amount added	% Mean recovery*		Standard deviation		% RSD	
	FEX	MKT	FEX	MKT	FEX	MKT
80	100.10	99.89	0.89	1.20	1.03	0.81
100	99.87	99.12	0.98	0.91	0.97	1.11
120	99.99	99.91	0.79	0.67	0.23	0.45

*Mean of three determinations for each concentrations

Table No. 05: Results for Robustness

Parameters	Standard Deviation		% RSD	
Different instruments	FEX	MKT	FEX	MKT
Shimadzu UV – 2600	0.87	0.78	0.99	0.45
Perkin Elmer lambda25	0.23	0.11	0.87	0.23

Table No. 06: Results for Ruggedness

Analyst	Standard Deviation		% RSD	
	FEX	MKT	FEX	MKT
Analyst-1	0.21	0.08	0.90	0.23
Analyst-2	0.77	0.62	0.60	1.38
Analyst-3	0.44	0.28	0.87	1.77

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