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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF FEXOFENADINE HYDROCHLORIDE AND MONTELUKAST SODIUM IN PHARMACEUTICAL DOSAGE FORM

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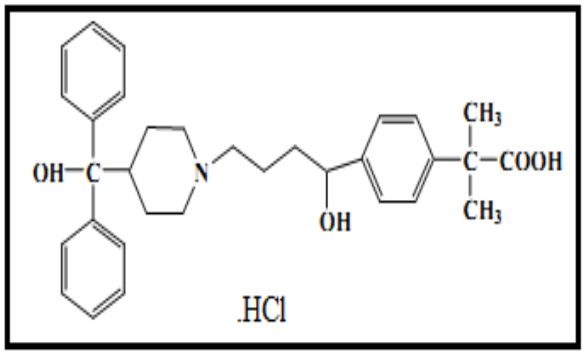
ABSTRACT

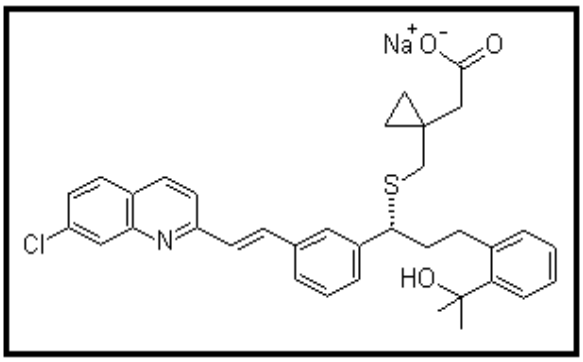
Two simple, accurate and reproducible spectrophotometric methods have been developed for the simultaneous estimation of Fexofenadine hydrochloride and Montelukast sodium in pharmaceutical dosage forms. The first method involves determination using the Simultaneous Equation Method while the second method is Multicomponent Mode Method. For both the methods sampling wavelengths selected were 259.0 nm and 282.0 nm over the concentration ranges of 24-144 µg/mL and 2-12 µg/mL for Fexofenadine hydrochloride and Montelukast sodium respectively. The results of the analysis were validated as per ICH guidelines & were found to be satisfactory to analyse the tablet dosage form.

INTRODUCTION

Fexofenadine hydrochloride (FEX), chemically, α, α-dimethyl-4-[1-hydroxy–4-[4-(hydroxydiphenyl - methyl) -1-piperidinyl] butyl]-benzene acetic acid hydrochloride salt is an antihistaminic drug used in the treatment of hay fever and similar allergy symptoms[1-2]. Literature survey reveals UV spectroscopic [3-4], HPLC[5-6] and HPTLC[7] methods for the estimation of FEX in combination with other drugs. Montelukast sodium (MTKT), chemically, 2-[1-[[1-[3-[2-[(7-Chloro-2-quinolyl)] vinyl] phenyl]-3-[2-(1-hydroxy-1-methyl-ethyl)phenyl] propyl] sulfanylmethyl] cyclo propyl] acetic acid sodium salt is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies[8-9]. Literature survey reveals several spectroscopic[10-11], HPLC[12-13] and HPTLC[14] methods for the estimation of MTKT in combination with other drugs.



Fexofenadine hydrochloride



Montelukast sodium

FEX and MTKT are available in combined pharmaceutical dosage form for the treatment of allergic rhinitis. A need was felt to develop UV methods to analyze the drugs simultaneously. This paper describes two simple, rapid, accurate, reproducible and economical methods for the simultaneous determination of FEX and MTKT in tablet formulations using Simultaneous Equation Method and Multicomponent Mode Method.

Experimental:-

Instrumentation:-

A Shimadzu UV/Visible spectrophotometer, model 1700 (Japan) was employed with spectral bandwidth of 2 nm and wavelength accuracy of ± 0.5 nm, with automatic wavelength correction was employed. A Denver electronic analytical balance was used for weighing the samples.

Reagents and Chemicals:-

Analytical pure samples of FEX (Emcure Pharmaceuticals Ltd., Pune, India) and MTKT (Zydus Pharmaceutical Ltd., Ahmedabad, India) were used in the study. The pharmaceutical dosage form used in this study was MONTAIR FX (Cipla Ltd., Solan, India) labelled to contain 120 mg FEX and 10 mg of MTKT.

Preparation of Standard Stock Solution:-

Standard stock solutions (200 µg/mL) of FEX and MTKT were prepared by dissolving accurately about 20 mg of each drug separately in methanol in 100 ml volumetric flask. The working standard solutions of these drugs were obtained by dilution of the respective stock solution with methanol.

Construction of Calibration Curve:-

Suitable dilutions of the standards solutions were scanned in the UV range and absorbances were determined. From absorption spectra of these drugs, absorbance maxima were obtained at wavelengths 220.0 nm and 259.0 nm for FEX & 282.0 nm for MTKT. As the combined dosage form is available in the ratio of 12:1, the working wavelength for both the methods selected were 259.0 for FEX and 282.0 nm for MTKT.

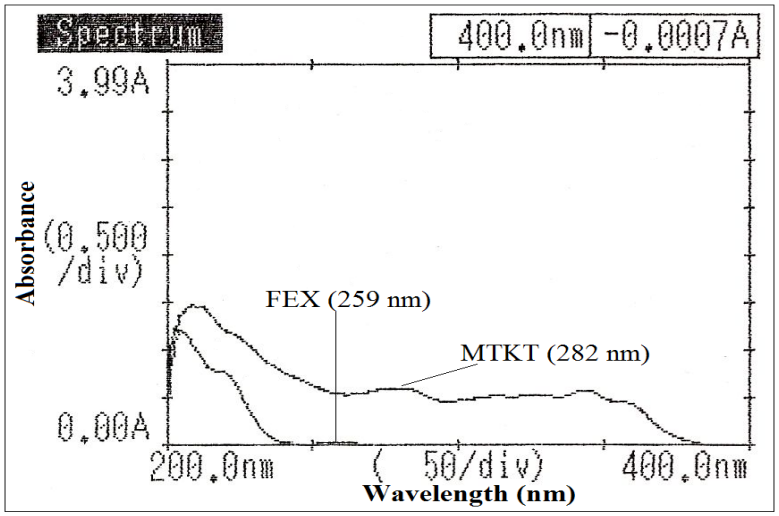


Fig.1: The overlain UV spectra of FEX and MTKT

FEX and MTKT exhibited linearity with absorbances in the range of 24-144 µg/mL and 2-12 µg/mL at their respective selected wavelengths. Co-efficient of correlation was found to be 0.997 and 0.999 for FEX and MTKT respectively. The optical characteristics and regression values for the calibration curves are presented in Table 1.

Method A:-

Simultaneous Equation Method:-

For simultaneous estimation of FEX and MTKT, mixed standards containing FEX and MTKT in a concentration ratio of 12:1 µg/mL each were prepared by appropriate dilution of the standard stock solutions with methanol. The absorbances of the mixed standard solutions were measured at the selected wavelengths. A set of two simultaneous equations were used for obtaining the concentrations of FEX and MTKT as follows;

$$C_{MTKT} = \frac{0.000132*A_2 - 0.00148A_1}{0.0332*0.000132 - 0.0475*0.00148} \quad \text{…….Eq. (i)}$$

$$C_{FEX} = \frac{0.0475*A_1 - 0.0332*A_2}{0.0332*0.000132 - 0.0475*0.00148} \quad \text{…….Eq. (ii)}$$

Where, A_1 and A_2 are absorbances of mixture at 282.0 nm and 259.0 nm respectively, absorptivities of MTKT at $\lambda_1$and λ_2 respectively and absorptivities of FEX at λ1 and λ2 respectively are calculated in terms of g/L. C_{MTKT} and C_{FEX} are concentrations of FEX and MTKT respectively. The concentration of FEX and MTKT in mixed standard and tablet formulation can be obtained by solving equation (i) and (ii).

Method B:-

Multicomponent Mode Method:-

For the analysis of FEX and MTKT by multicomponent method of analysis, the multicomponent mode of the UV visible spectrophotometer was used. Six mixed standards in ratio of 12:1 µg/mL showing linearity within the Beer's concentration range of FEX and MTKT were prepared. In multicomponent mode of the instrument, the mixed standards were scanned over the range of 200-400 nm at the selected working wavelengths. The overlain spectra of the six mixed standards were then employed to determine the concentration of the drugs in sample solutions. The total absorbance of a solution at a given wavelength is equal to the sum of absorbance of the individual component present. This relationship makes possible the quantitative determination of the individual constituent of a mixture even if their spectrum overlaps.

Assay of Tablet Formulation:-

Twenty tablets were accurately weighed and powdered. Powder equivalent to 30 mg of FEX and 2.5mg of MTKT was weighed and dissolved in 100 mL methanol with the aid of ultrasonication for 20 min. The solution was then filtered through Whatmann filter paper No.41 and diluted further to obtain final concentration of 72 µg/mL of FEX and 6 µg/mL of MTKT. The sample solutions were analyzed as per the procedure for mixed standards. The concentrations of each drug in sample solutions were calculated using equations (i) and (ii) for the Simultaneous Equation Method and using the multicomponent mode of the instrument for the Multicomponent method of analysis. The results of the analysis and statistical validation data of the tablet formulation are given in Table II.

Validation:-

The proposed methods were validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for the analyte[15].

Linearity:-

The linearity of pure drugs was evaluated by analyzing different concentration of the standard solution of FEX and MTKT at their respective wavelength maxima. For simultaneous equation method and multicomponent mode method, the linearity was found to be in concentration range of 24-144 µg/mL for FEX and 2-12 µg/mL for MTKT.

Precision:-

Precision of the methods was studied as intra-day and interday. Intra-day study was performed by analyzing, the three different concentration of drug for three times in the same day. Inter-day precision was performed by analyzing three different concentration of the drug for three days in a week

Accuracy:-

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%).

Table I: Optical Characteristics and Validation Data of FEX and MTKT for method A and B

Parameters	FEX	MTKT
Absorbance Maxima	259.0 nm	282.0 nm
Linearity range (µg/ml)	24-144	2-12
*Slope ± S.D.	0.001 ± 0.0002	0.047 ± 0.001
*Intercept ± S.D.	0.001 ± 0.0002	0.003 ± 0.0001
*Regression coefficient (r^2) ± S.D.	0.997 ± 0.001	0.999 ± 0.0002
*LOD (µg/ml)	0.66	0.007
*LOQ (µg/ml)	2	0.021

*Denotes average of six estimations.

Method A – Simultaneous Equation Method

Method B – Multicomponent mode analysis method

Table II: Statistical Validation Data of Tablet Formulation (MONTAIR FX).

Method	Drug	Label claim (mg)	Amount found* (mg)	% Amount Found*	± S.D.*	% R.S.D.
A	FEX	120 mg	119.91	99.92	0.5377	0.5381
	MTKT	10 mg	10.017	100.17	0.4500	0.4492
B	FEX	120 mg	120.02	100.01	0.0444	0.0444
	MTKT	10 mg	9.997	99.97	0.2659	0.2660

*Denotes average of six estimations.

Table-III: Results for Intra-Day & Inter-Day Precision studies.

Method	Drug	Intra -Day*			Inter- Day*		
		% Mean	S.D.*	% R.S.D.*	% Mean	S.D.*	%R.S.D.*
A	FEX	99.97	0.19	0.19	100.03	0.28	0.28
	MTKT	100.04	0.36	0.36	99.83	0.46	0.46
B	FEX	99.92	0.09	0.09	100.02	0.18	0.18
	MTKT	99.98	0.40	0.40	100.02	0.51	0.51

*Denotes average of six determination

Table IV: Statistical Validation of Recovery studies.

Level of % Recovery	Method	% Recovery*		% R.S.D.*	
		FEX	MTKT	FEX	MTKT
80	A	99.31	100.61	0.13	0.27
	B	100.01	99.89	0.03	0.10
100	A	99.91	100.16	0.65	0.25
	B	99.97	99.96	0.01	0.21
120	A	99.93	100.11	0.76	0.10
	B	99.95	100.11	0.11	0.28

*Denotes average of three estimations at each level of recovery.

RESULTS AND DISCUSSION

Under the experimental conditions described, linearity range was studied, methods were applied to analyse laboratory mixture and assay of tablet formulation were performed. The developed methods were validated as per ICH guidelines for linearity, repeatability, intermediate precision (inter-day and intra-day precision studies), accuracy, LOD and LOQ. The mean % content of tablet by method A were found to be 99.92 % and 100.17 % & for method B, 100.01 % & 99.97 % for FEX and MTKT respectively (Table II). The precision and accuracy studies carried out were within range and % RSD was less than 2 for FEX and MTKT respectively by both methods (Table III& IV).

CONCLUSION

FEX and MTKT are available in combined pharmaceutical dosage form for the treatment of allergic rhinitis. Here, two simple UV spectrophotometric methods Simultaneous Equation Method and Multicomponent Mode Method were developed for their simultaneous analysis. The standard deviation, relative standard deviation (RSD) calculated for the methods are low, indicating high degree of precision of the methods.. Method B has advantages over the Method A, as it does not involve any manual calculations. It directly gives the concentration of the components in the sample mixture. The method using multicomponent mode in a spectrophotometer is excellent for rapid analysis and it is simple and convenient way.

List of Symbols and Abbreviations

1. % : Percent
2. nm : Nanometer
3. µg/mL : Microgram Per Millilitre
4. UV : Ultraviolet
5. HPLC : High Performance Liquid Chromatography
6. HPTLC : High Performance Thin Layer Chromatography
7. FEX : Fexofenadine hydrochloride
8. MTKT : Montelukast sodium
9. ICH : International Conference on Harmonization
10. SD : Standard Deviation
11. RSD : Relative Standard Deviation
12. LOD : Limit of Detection
13. LOQ : Limit of Quantitation

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