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Research Article

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Simultaneous estimation of montelukast sodium and desloratadine by ratio spectra derivative spectrophotometry method in combined dosage forms

Rima M. Bankar*and Dipti B. Patel

Department of Pharmaceutical Analysis, S. K. Patel College of Pharmaceutical and Research, Ganpat University, Kherva, Mehsana , Gujarat, India

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ABSTRACT

Montelukast sodium is a leukotriene receptor antagonist, used in the treatment of asthma and Desloratadine is a drug used to treat allergies The combination formulation is used for the treatment of allergic rhinitis. The Ratio spectra derivative spectrophotometric method was developed for the simultaneous determination of Montelukast sodium (MTKT) and Desloratadine (DESLO) in combined dosage forms. The method depends on the use of the first derivative of the ratio-spectra obtained by dividing the absorption spectrum of binary mixtures by a standard spectrum of one of the compounds. The first derivative amplitudes at 218.6 and 262 nm were selected for the determination of MTKT and DESLO respectively. The wavelength interval (Dl) was selected as 8 nm. Methanol was used as the solvent. Both the drugs showed linearity in the range of 5-40µg/ml. The method was validated statistically and recovery studies were carried out. It was found to be accurate, precise and reproducible. The method was applied to the assay of the drugs in marketed formulation, which were found in the range of 99.47% to 101.25% of the labeled value for both Montelukast sodium and Desloratadine. Hence, the method here in described can be successfully applied in quality control of combined pharmaceutical dosage forms.

Keywords: Montelukast , Desloratadine, Ratio Spectra Derivative Spectrophotometry.

INTRODUCTION

Montelukast sodium (MTKT), 1-[({(R)-m-[(E)-2-(7- chloro-2-quinolyl) vinyl]-α-[o-(1-hydroxyl-1-methylethyl)phenethyl]benzyl}thio)methyl] cyclopropaneacetate sodium is a leukotriene receptor antagonist, used in the treatment of asthma.[1][2][3]. It is not official in IP, BP and USP. Various analytical methods, such as liquid chromatography with fluorescence detection[4],[5],[6], stereoselective HPLC for MTKT and its enantiomer[7],simultaneous HPLC and derivative spectroscopic method with loratadine[8],stability indicating HPLC method[9] for Montelukast sodium in tablets and human plasma have been reported. Desloratadine(DESLO),13-chloro-2-(piperidin-4-ylidene)-4-azatricyclo[9.4.0.0^{3,8}]pentadeca-1(11),3,5,7,12,14 hexaene.[2][3] Desloratadine is a drug used to treat allergies. Various analytical methods, such as liquid chromatography[10], Spectrophotometric, spectrofluorometric and HPLC determination of desloratadine in dosage forms and human plasma[11], Stability-Indicating RP-UPLC with Sodium Benzoate[12].The combined dosage forms of MTKT and DESLO are available in the market for the rhinitis and treatment of allergies and chronic urticaria. Present study involves development and validation of Q-Absorbance Ratio Method and Dual Wavelength Spectrophotometry method for the estimation of MTKT and DESLO in combination dosage form. The proposed methods were optimized and validated as per International Conference on Harmonization (ICH) guidelines[13].

A spectrophotometric method based on the use of the first derivative of the ratio spectra was first developed by Salinas et al[14][15]. for resolving binary mixtures. The objective of this work was to develop simple, precise and rapid ratio spectra derivative spectrophotometric method for combination drug products containing MTKT and DESLO.

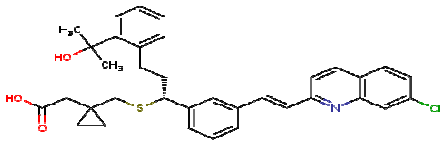

Fig. 1: Chemical structure of Montelukast

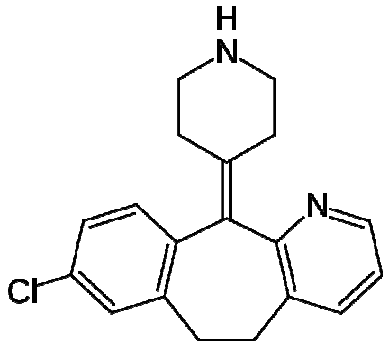

Fig. 2: Chemical structure of Desloratadine

EXPERIMENTAL SECTION

Instrument:
A shimadzu model 1700 (Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software.

Reagents and materials
MTKT and DESLO bulk powder was kindly gifted by Acme Pharmaceuticals Ltd., Mehsana, Gujarat, India, respectively. Methanol (AR Grade, S. D. Fine Chemicals Ltd., Mumbai, India) were used in the study.

Standard and Test Solutions
Preparation of Standard Solution
The standard stock solutions containing 1mg/ml, each of MTKT and DESLO were prepared separately by dissolving reference standards in Methanol and diluting with the same diluent. Standard solutions of both the drugs were prepared individually by dilution of the standard stock solutions with Methanol to obtain the concentration range of 5-40 µg/mL for each of the drugs.

Preparation of Test Solution
Twenty tablets were weighed and finely powdered in a mortar. A tablet powder equivalent to 10 mg for MTKT and 5mg for DESLO was accurately weighed and transferred to a 50 mL calibrated volumetric flask.The solution was sonicated for 30 min. Volume was made up to the mark with the same solvent. The solution was filtered through 0.45 µm nylon syringe filter. The resultant solution contained 200µg/ml for MTKT and 100 µg/ml for DESLO. The solution was further diluted with Methanol to get concentration of 10µg/ml for MTKT and 5 µg/ml for DESLO.

Ratio Spectra Derivative Method

This method works on two mechanisms viz. (1) Ratio and (2) Derivatization. In this method, the mixture spectra are divided with the divisor and first derivative spectra of these ratio spectra are generated. The main advantage of the ratio-spectra derivative spectrophotometry is the chance of doing easy measurements in correspondence of peaks so it permits the use of the wavelength of highest value of analytical signals (a maximum or a minimum). Moreover, the presence of a lot of maxima and minima is another advantage by the fact that these wavelengths give an opportunity for the determination of active compounds in the presence of other compounds and excipients which possibly interferes the assay [(16)]. For the determination of MTKT, the spectra of MTKT at increasing concentrations in methanol were divided by previously stored absorption spectrum standard solution of DESLO (20 µg/ml)to obtain the corresponding ratio spectra. Then the first derivative of the obtained ratio spectra were traced with interval of = 8 nm. In the binary mixtures ,content of MTKT was determined by measuring the first derivative amplitude at 218.6 nm, where there is no contribution or interference from DESLO.

On the other hand, for the determination of DESLO, an analogous procedure was followed. The spectra of DESLO at increasing concentrations were divided by previously stored spectrum of 15 µg/ml solution of MTKT and the first derivative of the developed ratio spectra were traced with= 8nm .In the binary mixtures, content DESLO was determined by measuring the first derivative amplitude at 262 nm, where there is no contribution or interference from MTKT.

First-derivative technique (D1) traced with $\Delta\lambda$=8 nm was used to resolve the spectral overlapping. The calibration curves were checked for linearity and linear behavior was observed in the concentration range of 5-40 µg/ml, for each of the drugs.

Method Validation

The method was validated as per ICH guidelines[(19)] for parameters like Linearity, Accuracy and Precision. The accuracy studies were carried out at different concentrations by spiking a known concentration of standard drug to the pre-analyzed sample and contents were reanalyzed by the developed method. Precision was studied by analyzing six replicates of sample solutions. Intermediate precision was determined in a similar manner on the next day using a different instrument.

RESULTS AND DISCUSSION

Zero-order absorption spectra of 10 µg/ml of each of MTKT and DESLO showed overlapping peaks that interfere with the simultaneous determination of this formulation as shown in Figure-3. So it was thought of interest to develop the ratio spectra derivative spectrophotometry method for the simultaneous estimation of MTKT and DESLO in commercially available tablet dosage forms. Methanol was used as the solvent. since both the drugs exhibit good solubility in it and no interference due to excipients of the tablet formulation were observed.

Ratio spectra Derivative Spectrophotometry Method

Th e absorption spectra of MTKT prepared at increasing concentrations in Methanol were recorded in the spectral region of 200.0-400.0 nm and divided by the previously stored spectrum of 20.0µg/ml DESLO in the same solvent and their ratio spectra were obtained as seen in the Fig-4a. Then, the first derivatives of ratio-spectra were recorded as shown in Fig. 4b which were plotted with the interval of nm and the values of the derivatives were measured at suitably selected wavelength for the determination of MTKT. The influence of the for obtaining the first derivative was tested and =8 nm was considered as suitable. The concentration of divisor can be modified, and different calibration graphs are then obtained. A concentration of 20.0 µg/ml of DESLO was considered as suitable .The calibration graph was established by measuring at the amplitude at 218.6 nm corresponding to a maximum wavelength.

For determining DESLO, an analogous procedure was followed. The ratio spectra were obtained by dividing the spectra of DESLO with previously stored spectrum of a 15µg/ml DESLO solution as shown in figure-5a and their first derivatives were calculated with the interval of =8 nm as shown in figure-5b. The values of the derivatives were measured at suitably selected wavelength for the determination of MTKT. A concentration of 15µg/ml of MTKT was considered as suitable. The calibration graph was established by measuring at the amplitude at 262 nm corresponding to a maximum wavelength.

Method validation

The developed method was validated for parameters like linearity, precision and accuracy. Themethod was found to be linear in the range of 5-40 µg/ml for both the drugs with correlation coefficient of 0.9996 and 0.9997 for MTKT and DESLO respectively. The data for linearity and precision are presented in the Table-1. The data for recovery study are shown in the Table-2. The low value of %R.S.D. indicates that the method is precise and accurate.

Application of method to Tablet dosage form

The proposed method after validation was applied to the simultaneous estimation of MTKT and DESLO in tablet dosage forms available commercially. The results obtained show the high reliability and reproducibility of the method. The results of the study are presented in Table-3.

Table-1: Data showing linearity and precision of the developed method

PARAMETERS	RATIO SPECTRA DERIVATIVE METHOD	
	MTKT	DESLO
Linearity Range	5-40 µg/ml	5-40 µg/ml
Slope	0.0019	0.0032
Intercept	0.0002	0.0008
Correlation Co-efficient	0.9996	0.9997
Repeatability (RSD, n=6)%	0.24	0.22
Intraday (n=6) Precision (% R.S.D.)	0.41-0.59	0.12-0.81
Interday (n=6) Precision (% R.S.D.)	0.26-0.5	0.12-0.47
LOD (µg /ml)	0.17	0.72
LOQ (µg /ml)	0.52	1.2

Table 2 : Recovery Data for the ratio spectra derivative method (n=3)

Drug	Level	Amount taken (µg/ml)	Amount added (µg/ml)	Amount Found (µg/ml)	% Mean recovery ± S.D. (n = 3)
MTKT	I (50%)	**10**	**5**	4.94	99.66 ± 0.75
	II (100%)	**10**	**10**	9.95	100.5 ±0.50
	III (150%)	**10**	**15**	15.1	100.9± 0.74
DESLO	I (50%)	**5**	**2.5**	2.53	101.65 ± 0.73
	II (100%)	**5**	**5**	5.03	99.58 ± 1.30
	III (150%)	**5**	**7.5**	7.53	100.55 ± 1.04

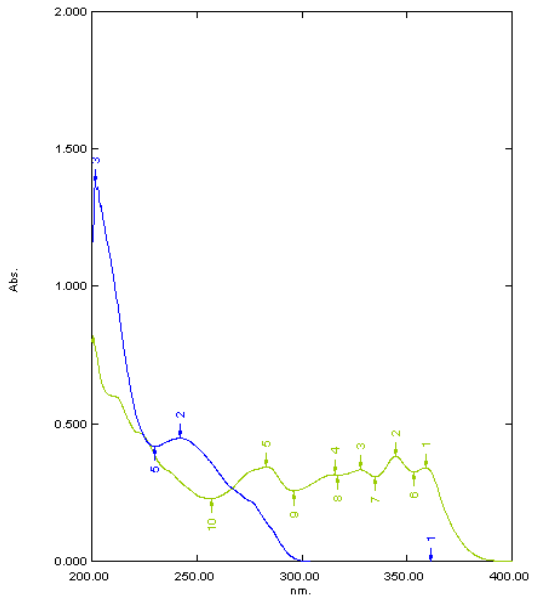

Figure-3: Overlain spectrum of 10 µg/ml of MTKT and DESLO

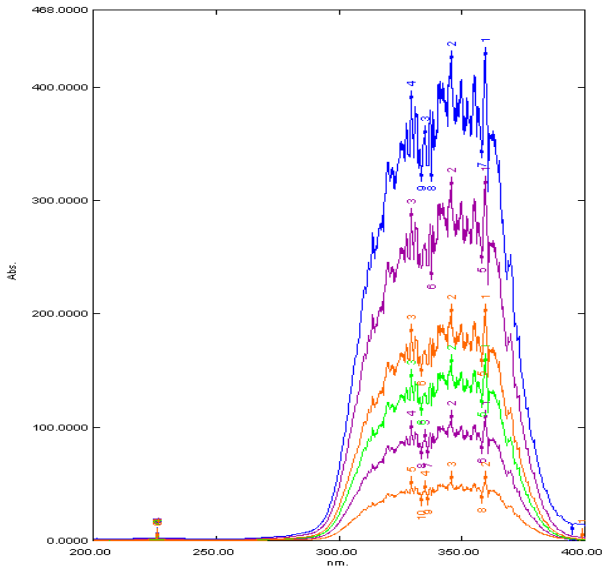

Figure-4a: Ratio spectra of MTKT when 20 µg/ml solution of DESLO is used as a divisor

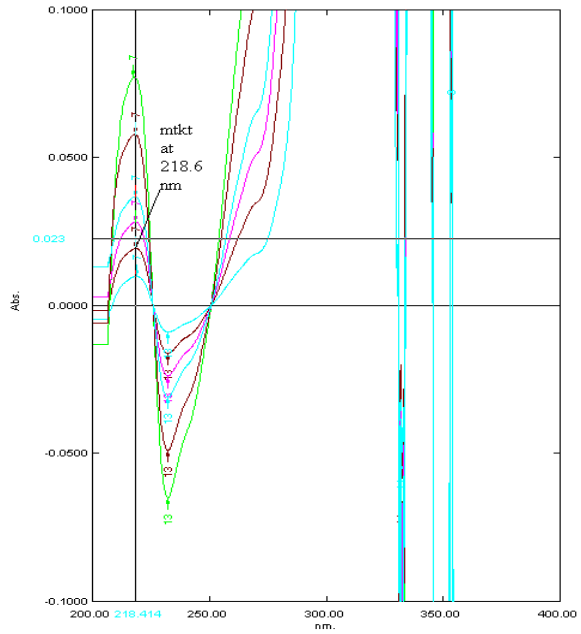

Figure-4b: First Derivative Ratio spectra for MTKT at 218.6nm

Table-3: Results of analysis of tablet dosage forms containing MTKT and DESLO

METHOD PARAMETERS	Ratiospectra Derivative Method	
	MTKT	DESLO
%Assay	99.47	101.25
SD	0.00010	0.00023
RSD	0.560	1.496

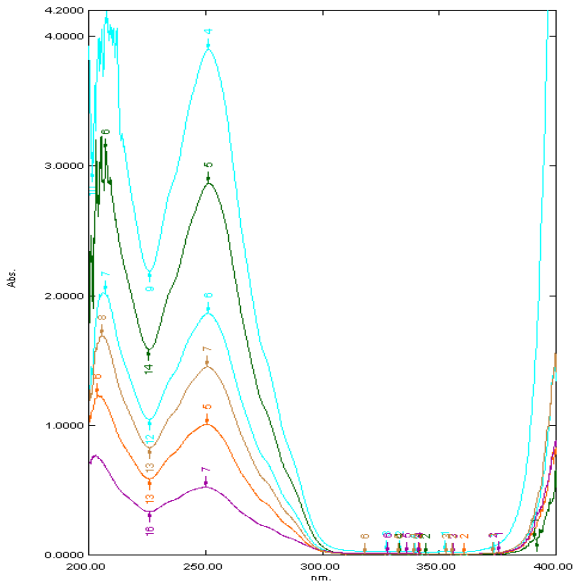

Figure-5a: Ratio spectra of DESLO when 15 µg/ml solution of MTKT is used as a divisor

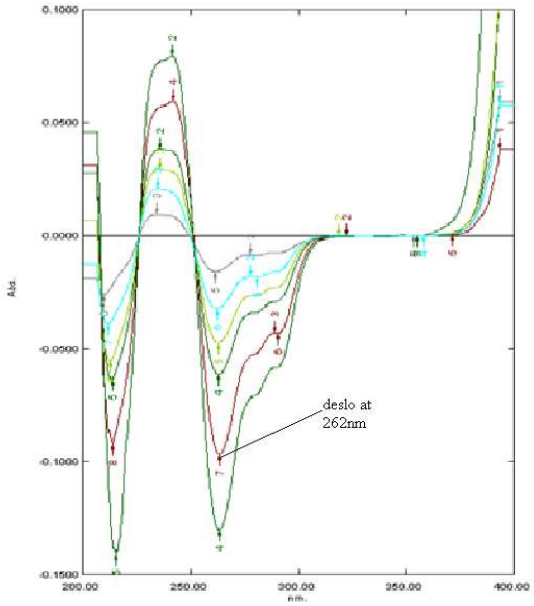

Figure-5b: First Derivative Ratio spectra for DESLO at 262nm

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