

# Spectrophotometric Determination Of Montelukast Sodium And Desloratadine In Combined Dosage Form

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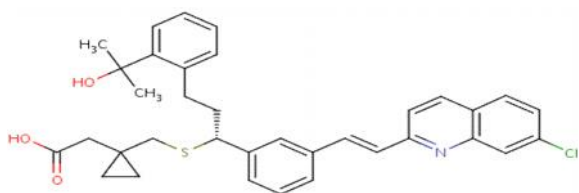
**Abstract:** Two Simple, fast, accurate, precise and economical UV- Spectrophotometric methods have been developed for simultaneous estimation of Montelukast Sodium (MTKT) and Desloratadine (DLOR) in combined tablet dosage form. Methanol was used as solvent. In method-I (Q-Absorbance Ratio Method) two wavelengths was selected, one which is an isoabsorptive point and other being the  $\lambda_{max}$  of one of the two components. MTKT and DESLO show an isoabsorptive point at 263.6 nm in methanol. The second wavelength used is 283 nm, which is the  $\lambda_{max}$  of MTKT in methanol. The linearity was obtained in the concentration range of 5-40  $\mu\text{g/ml}$  for MTKT and DESLO. In Method-II (Dual Wavelength Method) determination of MTKT at 345.0 nm and DESLO at 265.6 nm and 294 nm. For DESLO absorbance difference between two  $\lambda_{max}$  were selected. The linearity was obtained in the concentration range of 2.5-40  $\mu\text{g/mL}$  for MTKT and 2.5-25  $\mu\text{g/mL}$  for DESLO. LOD values are found to be 0.07  $\mu\text{g/mL}$  and 0.13  $\mu\text{g/mL}$  for MTKT and DESLO in method-I and 0.15  $\mu\text{g/mL}$  and 0.23  $\mu\text{g/mL}$  for MTKT and DESLO in method-II, respectively. LOQ values are found to be 0.20  $\mu\text{g/mL}$  and 0.39  $\mu\text{g/mL}$  for MTKT and DESLO in method-I and 0.46  $\mu\text{g/mL}$  and 0.69  $\mu\text{g/mL}$  for MTKT and DESLO in method-II, respectively. Percent label claim of the compounds were 98.9% and 100.25% in method-I and 99.62% and 99.85% in method-II for MTKT and DLOR respectively. The optimized methods showed good reproducibility with percent relative standard deviation less than 2.0%.

**Keywords:** Montelukast sodium, Desloratadine, Dual wavelength, Q-Absorbance Ratio Method.

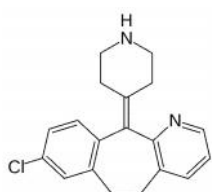
## 1.INTRODUCTION

Montelukast sodium (MTKT), 1-[[[(R)-m-[(E)-2-(7-chloro-2-quinolyl) vinyl]-[o-(1-hydroxyl-1-methylethyl)phenethyl]benzyl]thio)methyl] cyclo propaneacetate sodium is a leukotriene receptor antagonist, used in the treatment of asthma.<sup>(1)(2)(3)</sup>. It is not official in IP, BP and USP. Various analytical methods, such as liquid chromatography with fluorescence detection<sup>[4],[5],[6]</sup>, stereoselective HPLC for MTKT and its enantiomer<sup>(7)</sup>, simultaneous HPLC and derivative spectroscopic method with loratadine<sup>(8)</sup>, stability indicating HPLC method<sup>(9)</sup> 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<sup>3,8</sup>]pentadeca-1(11),3,5,7,12,14

hexaene.<sup>(2)(3)</sup> Desloratadine is a drug used to treat allergies. Various analytical methods, such as liquid chromatography<sup>(10)</sup>, Spectrophotometric, spectro fluorometric and HPLC determination of desloratadine in dosage forms and human plasma<sup>(11)</sup>, Stability-Indicating RP-UPLC with Sodium Benzoate<sup>(12)</sup>. 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<sup>(13)</sup>.



**Fig. 2: Chemical structure of Montelukast**



**Fig. 2: Chemical structure of Desloratadine**

## EXPERIMENTAL

### 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.

## Methods and Results:

### Standard stock solutions

Standard stock solutions of MTKT and DESLO, each of 1 mg/ml concentration in solvent methanol were prepared. For Method- I, from these stock solutions appropriate dilutions in the range of 5-40 µg/ml for MTKT and DESLO, respectively were prepared and analyzed. For Method-II, from these stock solutions appropriate dilutions in the range of 2.5-40 µg/ml for MTKT and 2.5-25 µg/ml for DESLO. Mixed standards were prepared in the ratio of 2:1, as the formulation contains MTKT and DESLO 10 mg and 5 mg, respectively.

### Method- I : Q-Absorbance Ratio Method

This method is applicable to the drugs that obey Beer's law at all wavelengths and the ratio of absorbances at any two wavelengths are a constant value, independent of concentration or pathlength<sup>(14)(15)</sup>. The solutions of 10µg/mL each of MTKT and DESLO were scanned in the wavelength range of 400 to 200 nm to obtain overlain spectra (Figure-3). Two wavelengths, 263.6 nm (Isoabsorptive point) and 283 nm ( max of MTKT) were selected for the formation of Q-absorbance equation. The calibration curves were determined in the concentration range of 5-40 µg/mL, for each of the drugs. The absorptivity co-efficient of each drug at both the wavelengths were determined. The concentration of individual components,  $C_{MTKT}$  and  $C_{DESLO}$  may be calculated using the following equations,

$$C_x = (QM - QY) A_1 / (QX - QY) a_{x1} \text{ ----- (1)}$$

$$C_y = (A_1 - A_{x1} C_x) / A_{y1} \text{ ----- (2)}$$

Where,

$$QX = a_{x2} / a_{x1},$$

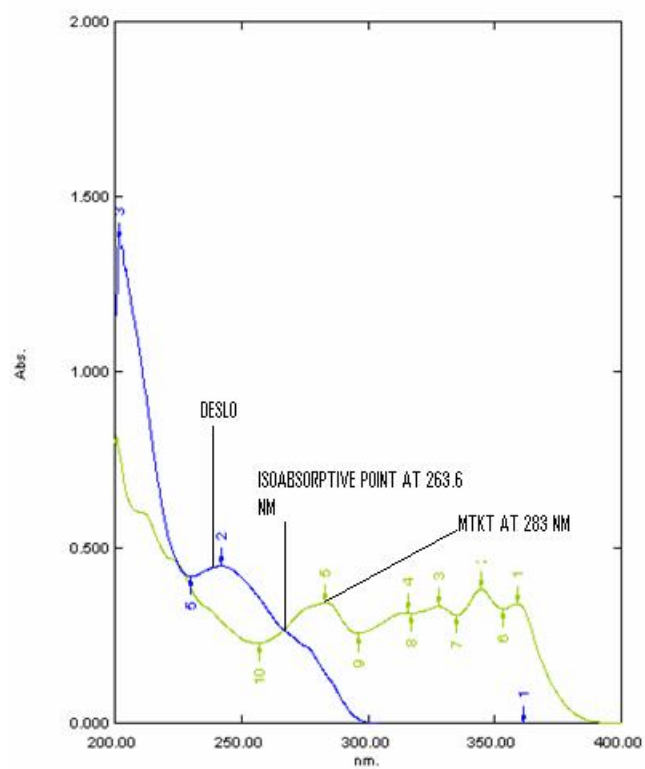
$$QY = a_{y2} / a_{y1},$$

$$QM = A_2 / A_1$$

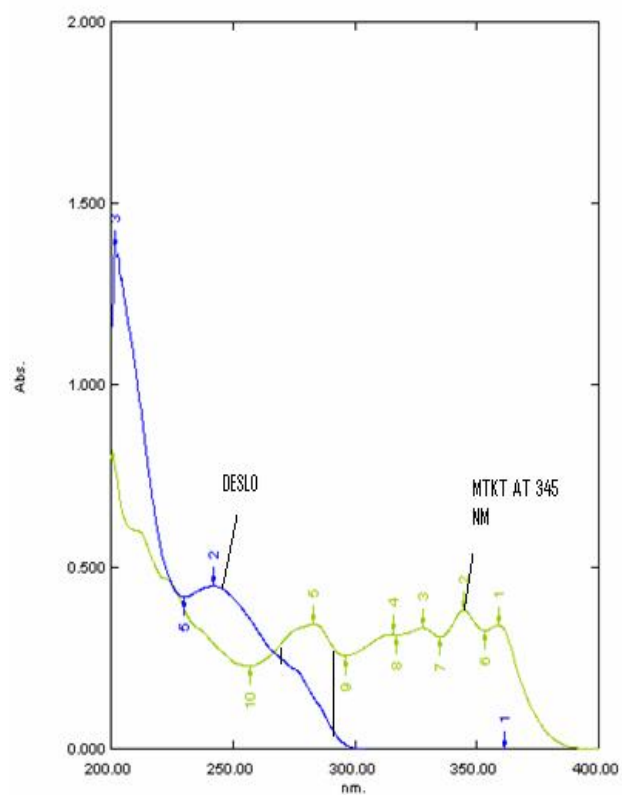
Where,  $A_1$  and  $A_2$  are absorbances of mixture at 263.6 nm and 283 nm;  $a_{x1}$  and  $a_{y1}$  are absorptivities of MTKT and DESLO at 263.6 nm;  $a_{x2}$  and  $a_{y2}$  are absorptivities of MTKT and DESLO respectively at 283 nm;  $QM = A_2 / A_1$ ,  $QX = a_{x2} / a_{x1}$  and  $QY = a_{y2} / a_{y1}$ .

### Method-II : Dual wavelength method

The utility of dual wavelength data processing programme is to calculate the unknown concentration of a component of interest present in a mixture containing both the components of interest and an unwanted interfering component by the mechanism of the absorbance difference between two points on the mixture spectra. This is directly proportional to the concentration of the components of interest, independent of the interfering components. The principle for dual wavelength method is "the absorbance difference between two points on the mixture spectra is directly proportional to the concentration of the component of interest". The method based on determination of MTKT at 345.0 nm and DESLO at 265.6 nm and 294 nm. For DESLO absorbance difference between two max were selected. The two drugs follow Beer-Lambert's law over the concentration range of 2.5-40 µg/mL for MTKT and 2.5-25 µg/mL for DESLO.



**Fig. 3 : Overlain spectra of 10 µg/ML of MTKT and DESLO**



**Fig 4: Overlain absorption spectra of the MTKT and DESLO**

**Method validation**

All the methods were validated as per ICH guidelines for parameters like Linearity, Accuracy and Precision<sup>(16)</sup>. 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.

**Stability**

Stability was observed by scanning the drug solutions in selected solvent system in time scan mode of UV spectrophotometer for 12 hours.

**Limit of detection and Limit of quantification**

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug were derived by calculating the signal-to-noise ratio (S/N, i.e., 3.3 for LOD and 10 for LOQ) using the following equations designated by International Conference on Harmonization (ICH) guidelines<sup>18</sup>.

$$LOD = 3.3 \times \sigma / S$$

$$LOQ = 10 \times \sigma / S$$

Where,  $\sigma$  = the standard deviation of the response and S = slope of the calibration curve

**Analysis of Marketed formulation**

To determine the content of MTKT and DESLO in commercial tablets (each tablet containing 10 mg MTKT and 5 mg DESLO), 20 tablets were weighed and finely powdered. A quantity of powder equivalent to 10 mg of MTKT and 5 mg of DESLO was weighed accurately and transferred to a 50 ml volumetric flask and the volume was made up with the solvent. It was sonicated for 30 minutes and then filtered through 0.5  $\mu$ m whatman paper. From the above prepared solution, further dilutions were prepared in the linearity range using solvent. The absorbance was taken at selected wavelengths and concentrations were found out. The analysis was done in six times.

**Table 1: Data showing linearity of the developed methods**

Methods	QAbsorbance ratio method		Dual wavelength method	
Parameters	MTKT	DESLO	MTKT	DESLO
Linearity range	5-40 $\mu$ g/mL	5-40 $\mu$ g/mL	2.5-40 $\mu$ g/mL	2.5-25 $\mu$ g/mL
Slope	0.040	0.029	0.039	0.026
Intercept	0.001	0.002	0.001	0.003
Correlation co-efficient	0.999	0.999	0.9998	0.9997

**Table 2: Data showing precision of the developed methods**

Methods	QAbsorbance ratio method		Dual wavelength method	
Parameters	MTKT	DESLO	MTKT	DESLO
Repeatability (RSD, n=6)%	0.12	0.25	0.19	0.15
Intraday(n=6) Precision (% R.S.D.)	0.12-0.17%	0.11-0.33%	0.13-0.86%	0.25-0.33%
Interday(n=6) Precision (% R.S.D.)	0.14-0.36%	0.10-0.17%	0.11-0.78%	0.12-0.33%
LOD ( $\mu$ g /ml)	0.07	0.13	0.15	0.23
LOQ ( $\mu$ g /ml)	0.20	0.39	0.11-0.78%	0.12-0.33%

**Table 3: Data showing recovery of the developed methods**

Drug	Level	Amount taken (µg/ml)	Amount added (µg/ml)	% Mean recovery $\pm$ S.D. (n = 3)	
				QAbsorbance ratio method	Dual wavelength method
MTKT	I	10	8	98.95 $\pm$ 0.35	99.67 $\pm$ 0.85
	II	10	10	99.33 $\pm$ 0.38	98.97 $\pm$ 0.26
	III	10	12	100.27 $\pm$ 0.32	99.64 $\pm$ 0.12
DESLO	I	5	4	103.4 $\pm$ 1.36	99.67 $\pm$ 0.56
	II	5	5	98.85 $\pm$ 1.05	99.23 $\pm$ 2.7
	III	5	6	99.42 $\pm$ 0.57	100.42 $\pm$ 0.37

**Table 4: Results of analysis of tablet dosage forms containing MTKT and DESLO**

Methods	QAbsorbance ratio method		Dual wavelength method	
Parameters	MTKT	DESLO	MTKT	DESLO
% Assay*	98.9	100.25	99.62	99.85
SD	0.81	0.40	0.99	0.95
%RSD	0.80	0.41	0.98	0.95

## RESULTS AND DISCUSSION

In the present work, two methods, namely, Q-absorbance ratio method and dual wavelength method were developed for the simultaneous spectroscopic 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.

### Q-Absorbance ratio Method

As shown in Figure-3, the overlain spectra of both drugs in 2:1 ratio (10 µg/mL of MTKT and 5 µg/mL of deslo) show a reproducible Iso-absorptive point at 263.6 nm. Thus estimation of drugs by Q-absorbance ratio equation method was carried out at 263.6 nm (Isoabsorptive point) and 283 nm (max of MTKT). The standard solutions of MTKT and DESLO were prepared to determine the absorptivity values of the subject analyte at the two selected wavelengths. The method showed good linearity in the range of 5-40 µg/mL. The absorptivity values of MTKT were found to be 290 and 400 at the wavelengths of 263.6 nm and 283 nm respectively and similarly the absorptivity values of DESLO were found to be 290 and 130 at the wavelengths of 263.6 nm and 283 nm respectively.

### Dual Wavelength Method

The overlain spectrum of the drugs suggested that a dual wavelength spectrophotometric method was the most suitable method for simultaneous

determination of MTKT and DESLO. In Dual wavelength method The diluted solutions were scanned over the wavelength range of 200 - 400 nm. From the overlain spectra, wavelengths 345.0 nm max of MTKT and 265.6 nm and 294 nm the max of DESLO were selected for quantitation by proposed method. For DESLO absorbance difference between two max were selected. For studying Beer's law, two series of different concentrations in range of 2.5-40 µg/mL for MTKT and 2.5-25 µg/mL for DESLO were prepared from stock solutions. The calibration curves were constructed at 345.0nm and absorbance difference between 265.6 nm and 294 nm respectively. The absorptivities (A1%, 1 cm) of both the drugs at both the selected wavelengths were determined.

## CONCLUSION

The proposed dual wavelength method gives accurate and precise results for determination of MTKT and DESLO in marketed formulation (tablet) without prior separation and is easily applied for routine analysis. The most striking feature of the dual wavelength method is its simplicity and rapidity. Method validation has been demonstrated by variety of tests for linearity, accuracy, precision and stability. The developed method has several advantages, as it is simple, accurate, precise and economical. The proposed method was successfully applied to determination of these drugs in commercial tablets.

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