Spectrophotometric Method For Simultaneous Estimation of Montelukast Sodium and Ebastine in Bulk and Their Combined Tablet Dosage Form

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ABSTRACT

A simple spectrophotometric method has been developed for simultaneous estimation of Montelukast Sodium and Ebastine from tablet dosage form. Absorbance correction method in which absorbance is measured at two wavelengths, 345 nm at which Ebastine has no absorbance and 253 nm at which both the drugs have considerable absorbance. This method was found linear between the range of 5-25 μg/ml for Montelukast Sodium and Ebastine. The accuracy and precision were determined and found to comply with ICH guidelines. This method showed good reproducibility and recovery with % RSD in the desired range. The method was found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of Montelukast Sodium and Ebastine in their combined tablet dosage form.

Keywords: Montelukast Sodium, Ebastine, Absorbance correction method.

Montelukast Sodium(MNKT) chemically, (S,E)-2-(1-((1-(3-(2-(7-chloroquinolin-2-yl) vinyl)phenyl)3-(2-(2-hydroxypropan-2-yl) phenyl)propylthio)methyl)cyclopropyl) acetic acid[1,2] is a Cysteinyl leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies.[3–5] Literature survey reveals that assay of Montelukast Sodium in bulk and tablet dosage form is official in Indian Pharmacopoeia 2010.[6] Ebastine (EBA), chemically, 4-(4-benzhydryloxy-1-piperidyl)-1-(4-tert-butylphenyl) butan-1-one is a non-sedating H_1 antihistamine.[7] Assay of Ebastine in bulk form is official in British Pharmacopoeia.[8] Literature survey reveals that analytical methods, including U.V. spectrophotometer, and HPLC methods, are available for the determination of Montelukast in pharmaceutical dosage forms. The analytical methods

reported for estimation of MNKT and EBA alone and with other drug combination are U.V spectrophotometry,[9–17] HPLC,[18–24] HPLC/PDA,[25] LC-MS[26] and HPTLC[27–29] methods. The combination of Montelukast sodium and Ebastine has recently been introduced into the market. However, so far, no method was reported for the simultaneous estimation of Montelukast sodium and Ebastine, in combination. The proposed method is rapid, simple, accurate, and reproducible, and can be successfully employed in the routine analysis of both these drugs simultaneously, in tablet dosage form. The proposed method is optimized and validated as per the ICH guidelines.[30] In the present work, a successful attempt has been made to estimate both these drugs simultaneously using Simultaneous Equation and Absorbance Correction method by UV spectrophotometer. This study

attempts to useful for routine quality control of Montelukast sodium and Ebastine in pharmaceutical formulation. Structures of both the drugs (MNKT and EBA) are shown in (Figure 1).

MATERIALS AND METHOD

Instruments

Instrument used was an UV-Visible double beam spectrophotometer, make: SHIMADZU (model UV-1800) with a pair of 1 cm matched quartz cells. All weighing was done on analytical balance mettler toledo.

Reagents and chemicals

A pure drug MNKT was obtained as gift sample from Alembic Pharmaceuticals, Vadodara and EBA was procured as gift sample from Kivi labs Pvt, Baroda. Methanol AR was used as solvent. Calibrated glasswares were used throughout the work.

Marketed formulation

The marketed formulation studied was Ebast-M tablets manufactured by Micro labs Pvt ltd. Each tablet contains 10 mg Montelukast sodium and 10 mg Ebastine.

Preparation of standard stock solution

Accurately weighed quantity of MNKT (10 mg) and EBA (10 mg) were transferred to two separate 100 ml volumetric flasks, dissolved in little amount of methanol and diluted to the mark with methanol (stock solutions: 100 µg/ml of MNKT and EBA).

Preparation of working standard solution

15 µg/ml of MNKT and EBA solution was prepared by diluting 1.5 ml of stock solution to 10 ml with methanol.

Absorbance correction method

Absorbance correction method uses the absorbances at two selected wavelengths, one at λmax of one drug where other drug also shows considerable absorbance and other being the wavelength at which the first drug has practically nil absorbance. From the stock solutions, working standard solutions of MNKT and EBA (15µg/ml) were prepared by appropriate dilution and were scanned in the entire UV range to determine the suitable wavelengths. MNKT and EBA have λmax at 345 nm and 253 nm respectively. Both the drugs were found to have considerable absorbance at 253 nm while at 345 nm only MNKT has absorbance. The wavelengths selected for analysis were 253 nm and 345 nm for EBA and MNKT respectively as shown in (Figure 2). A series of standard solutions ranging from 5-25 µg/ml of MNKT and EBA were prepared separately and the absorbances of solutions were measured at 253 nm and 345 nm. A calibration curve was prepared by plotting absorbance versus corresponding concentration of drug. The concentration of two drugs in sample solution was calculated by using following equations:

$$C_{MNKT} = A1 \, / \, ax1 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(1)$$

$$C_{EBA} = \frac{A_2 - a_{X2} \, C_{MNKT}}{a_{Y2}} \quad \dots\dots\dots\dots\dots\dots\dots\dots.......(2)$$

Where, A_1 and A_2 are the absorbances of mixture at 345 nm and 253 nm respectively,

a_{x1} and a_{x2} are absorptivities of MNKT at 345 nm and 253 nm respectively,

a_{y2} is absorptivity of EBA at 253 nm,

C_{MNKT} is concentration of MNKT,

C_{EBA} is concentration of EBA.

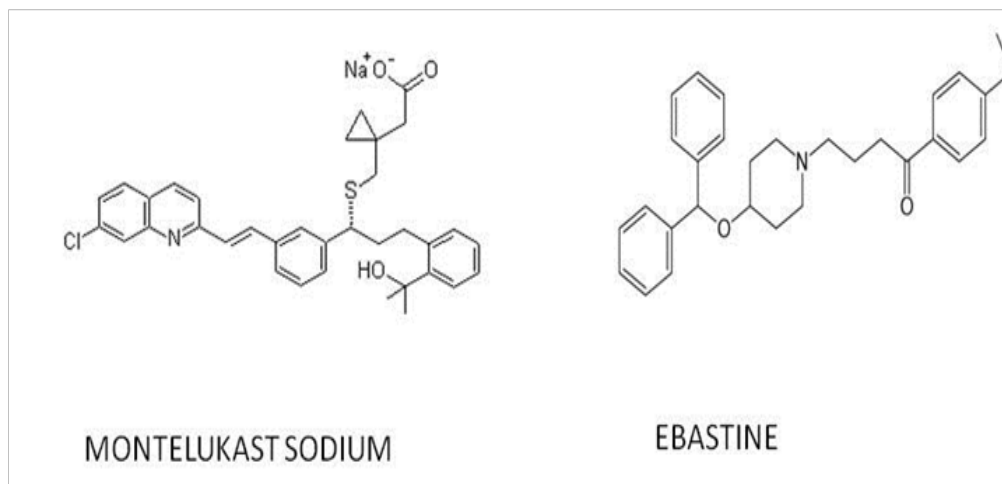Assay of tablet formulation by Absorbance Correction method:

Figure 1: Chemical structures of the analytes

Ten tablets were weighed and crushed to obtain a fine powder. An accurately weighed tablet powder equivalent to about 10 mg of MNKT and 10 mg of EBA was transferred to 100 ml volumetric flask and dissolved in 50 ml of methanol. The volume was made up to the mark using methanol as solvent. The resulting solution was filtered through Whatmann filter paper and 1.5 ml of this filtrate was appropriately diluted to get concentration of 15 µg/ml of MNKT and 15 µg/ml of AF. Absorbance of sample solutions was measured at 345 nm and 253 nm and the concentration of two drugs in the sample were determined using Equations (1) and (2).

RESULTS AND DISCUSSION

The proposed methods were validated as per ICH guideline. The plot of absorbances versus respective concentrations of MNKT and EBA were found to be linear in the concentration range of 5-25 µg/ml for both drugs with correlation coefficient 0.9993 at 345 nm and 0.9999 at 253 nm for Absorbance correction method. Precision was calculated as interday and intraday varia-

tions and % RSD was found to be less than 2 for both the drugs shown in Table 1 and Table 2. The accuracy of method was determined at 80, 100 and 120 % level. The % recovery ranges from 98.91 to 100.33 for this method as shown in Table 3. The % RSD of ruggedness for MNKT ranges from 0.32 to 1.02%, at 253 nm it was found to be 0.29 to 1.91% and 0.41 to 0.90% for MNKT and EBA respectively. Results for all validation parameters are presented in (Table 1, 2 and 3). The two methods can be successfully used for simultaneous estimation of MNKT and EBA in their combined tablet dosage form. Marketed tablets were analyzed and results obtained were in the range of 98-102 % (Table 3).

CONCLUSION

The proposed method give accurate and precise results for determination of MNKT and EBA in marketed formulation (tablet) without prior separation and are easily applied for routine analysis. The most striking feature of both the method is its simplicity and rapidity. Method validation has been demonstrated by variety of tests
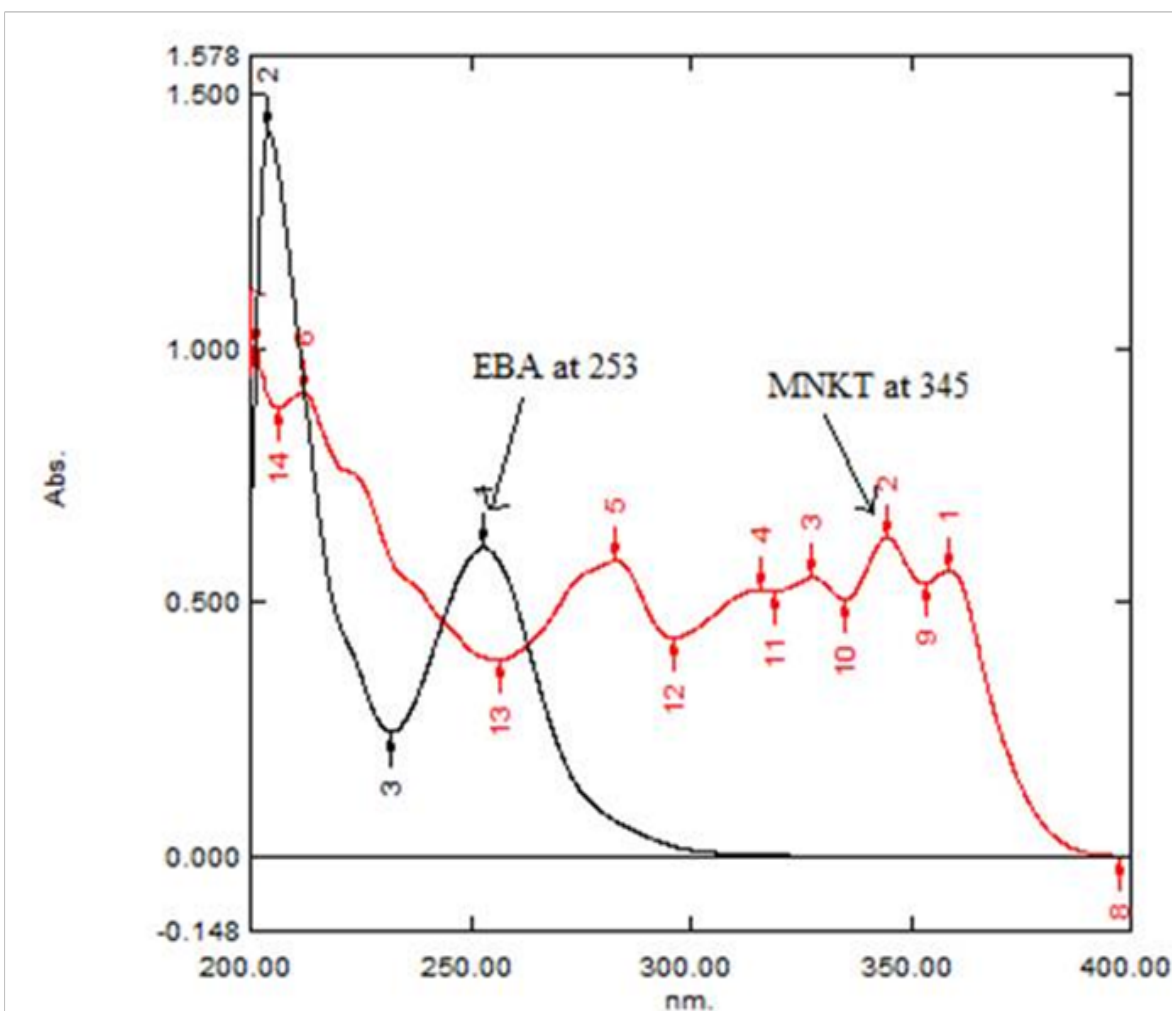

Figure 2: Overlain spectra of MNKT and EBA for Absorbance Correction Method in methanol

for linearity, accuracy, precision and ruggedness. The developed method has several advantages, as they are simple, accurate and precise. The proposed method was successfully applied to determination of these drugs in commercial tablets.

ACKNOWLEDGEMENT

Table 1. Validation Parameters for Absorbance Correction Method

PARAMETERS	MNKT		EBA
	345	253	253
Linearity range	5-25 µg/ml		
Correlation Coefficient	0.9993	0.9989	0.9999
Precision	% RSD		
Repeatability	2.00	0.510	1.00
Intraday	0.18-1.43%	0.48-1.16%	0.24-0.52%
Interday	0.23-0.82%	0.50-0.95%	0.45-0.93%
% Recovery	98.91-99.66%		99.38-100.33%
Ruggedness	0.29-1.91%	0.50-1.16%	0.14-0.90%

Table 2. Recovery studies

Name of Drug	Amount of Drug Added (µg/ml)	AC %Recovery*	SD
MNKT	5	99.45	0.05
EBA		99.38	0.005
MNKT	10	99.6	0.047
EBA		99.96	0.035
MNKT	15	98.91	0.072
EBA		100.3	0.049

Table 3. RESULTS OF SIMULTANEOUS ESTIMATION OF MNKT AND EBA IN MARKETED FORMULATION.

Method	mg/tablet		%of label claim* ± S.D.	
	MNKT	EBA	MNKT	EBA
Method II(AC)	10	10	99.75±0.04	99.89±0.02

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