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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF EBASTINE AND MONTELUKAST SODIUM IN BULK AND MARKETED DOSAGE FORM

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ABSTRACT

A simple, rapid, accurate and precise Spectrophotometric method for simultaneous estimation of ebastine and montelukast sodium in bulk and marketed tablet dosage form has been developed. Method is based on solving simultaneous equation. Ebastine and montelukast sodium shows absorbance maximum at 255 and 345 nm respectively, so absorbance was measured at the same wave lengths for the estimation of ebastine and montelukast sodium. Both drugs obey the beer lamberts' law in the concentration range of 5-35µg/ml and 5-35µg/ml for ebastine and montelukast sodium respectively. Method is validated according to ICH guideline and carried out for analysis of ebastine and montelukast sodium in pure and marketed tablet dosage form.

KEYWORDS : *Ebastine, montelukast sodium, UV-Spectrophotometer, Simultaneous equation, Validation.*

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INTRODUCTION

Ebastine (EBS) chemically is 4-(4-benzhydryloxy-1-piperidyl)-1-(4-tert-butylphenyl) butan-1-one. It is a second generation H1 receptor antagonist that is indicated mainly for allergic rhinitis and chronic idiopathic urticaria. This agent also has no effects on cardiovascular and psychomotor functions, which occurred during treatment with classical antihistamine agents such as chlorpheniramine and diphenhydramine.

The structure of ebastine (Figure No.-1)

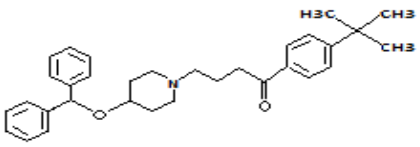

Figure No.-1 Structure of ebastine

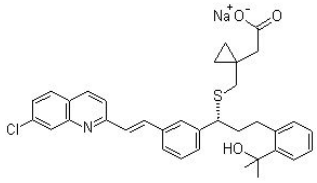

Figure No.-2 Structure of montelukast sodium

Montelukast sodium (MONT) is [R-(E)]-1-[[[1-[3-[2-(7-chloro-2quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropane acetic acid, monosodium salt (Figure no.2). It is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies. It is usually administered orally.The cysteinyl leukotrienes (LTC4, LTD4, LTE4) are potent inflammatory eicosanoids which is found in human airway (including airway smooth muscle cells and airway macrophages) and on other Pro-inflammatory cells (including eosinophils and certain myeloid stem cells) and it is released from various cells including mast cells and eosinophils. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both Early- and late-phase reactions and are associated with symptoms of allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction. Montelukast is an orally active compound that binds with high affinity and Selectivity to the CysLT1 receptor. Montelukast inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity.[2]

MATERIALS AND METHODS

Instruments

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu) with a pair of matched quartz cell of 1cm width was used for measuring absorbance. Elder digital balance was used for weighing and ultra sonicator of prama instruments used for sonicating the drug and sample solution.

Materials

Ebastine was gifted from Tonira pharma, Vadodara and Montelukast sodium was kindly gifted from Melody pharma, Mumbai. Tablets of Ebast-M were purchased from local market; each tablet was labelled to contain 10 mg of EBS and 10 mg of MNLT. All chemicals used for development were analytical grade.

Selection of solvent wavelengths

Drugs should have adequate absorbance in the same solvent for the simultaneous determination. In distilled water, montelukast sodium was not totally dissolved, possibility of water as solvent was ruled-out. In ethanol, ebastine absorbs at 255 nm and montelukast sodium absorbs at 345 nm, hence ethanol was selected as a possible solvent for analysis. These two wavelengths were selected for development of simultaneous equation.

Preparation of standard stock solution

About 10mg of ebastine and montelukast sodium pure drug was weighed accurately and transferred into 10ml volumetric flask. The volume was made up to 10ml using ethanol to obtain a solution that has a concentration 1000 µg/ml. 1ml of this stock solution was taken and then diluted up to 10 ml using ethanol to obtain a solution that has a concentration 100 µg/ml which is standard stock solution.

Preparation of sample stock solution

Twenty tablets were weighed accurately and their average weight was determined and crushed to powder. Powder quantity equivalent to 10 mg each of ebastine and 10 mg montelukast sodium was weighed. The powder was dissolved in a sufficient volume of ethanol and filtered through a Whatman filter paper of 125mm. Filtrate was made up to 10 mL with ethanol, 1 mL of filtrate was transferred to 10 mL volumetric flasks, and then the volume was made up with ethanol. Absorbance of this solution at 255 nm and 345 nm was recorded.

Procedure for calibration curve

To a series of 10ml volumetric flasks, carefully transferred aliquots of standard drug solution of ebastine and montelukast sodium (5 to 35 ml and 5 to 35 ml) respectively and the volume was made with the diluents. Calibration curve was recorded by taking absorbances on ordinates and concentration of the standard ebastine and montelukast sodium.

VALIDATION OF THE DEVELOPED METHOD[6, 7]

Linearity

For each drug, appropriate dilutions of standard stock solutions were assayed as per the developed methods. For method the Beer- Lambert's concentration range was found to be 5-35µg/mL for ebastine and 5-35µg/mL for montelukast sodium.

Accuracy

The recovery study was carried out as 80%, 100% and 120% of the test concentration as per ICH Guidelines. The recovery study was performed three times at each level.

Precision: Interday and Intraday precision

The interday and intraday precision was determined by assay of the sample solution on the intraday precision was determined by assay of the sample solution on the same day and on different days at different time interval respectively.(six replicate)

Ruggedness study

This study is carried out within laboratories and variation like different analyst. Ruggedness of the methods was assessed by carrying out assay 3 times with different analyst by using same equipment.

Limit of Detection

The detection limit is determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably detected.

$$\mathbf{LOD = 3.3 (SD / S)}$$

Where SD = the standard deviation of the response
S = the slope of the calibration curve

Limit of Quantitation

The quantitation limit is generally determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be quantified with acceptable accuracy and precise.

$$\mathbf{LOQ = 10 (SD / S)}$$

Where σ = the standard deviation of the response
S = the slope of the calibration curve

RESULT AND DISCUSSION

The ebastine and montelukast sodium shows solubility in ethanol. Linearity range for ebastine and montelukast sodium is 5-35µg/mL and 5-35µg/mL at respective selected wavelengths. We require to study two or more variables at a time; we study the relationship between these two or more variables. Value of coefficient of correlation always lies between -1 and +1.The coefficient of correlation for ebastine at 255nm and for montelukast sodium at 345 nm is 0.999 and 0.999 respectively, it shows good result. Ebastine and montelukast sodium shows limit of detection 0.1232 µg /mL and 0.1187µg /mL and limit of quantitation 0.3732 µg /mL and 0.3597 µg /mL respectively (See Table No.1).Both drugs shows good regression values at their respective wavelengths and the results of recovery study reveals that any small change in the drug concentration in the solution could be accurately determined by the proposed methods. (See Table No.3). Percentage estimation of ebastine and montelukast sodium from tablet dosage form by method is 99.93% and 100.18% with standard deviation<2 (See Table No.4). Precision is determined by studying the repeatability and intermediate precision. Repeatability result indicates the precision under the same operating condition over a short interval of time and interassay precision. Intermediate precision study expresses within laboratory variation in different days. In both intra and inter day precision study for both shows %RSD are not more than 2.0% which indicates good repeatability and intermediate precision. (See Table No.2)

CONCLUSION

The proposed method was found to be simple, accurate and rapid for the routine determination of Ebastine and Montelukast Sodium in tablet formulation. To study the validity and reproducibility of proposed methods, recovery studies were carried out. The methods were validated in terms of linearity, accuracy, precision & ruggedness. So, method can be successfully used for simultaneous estimation of Ebastine and Montelukast Sodium in combined dosage form.

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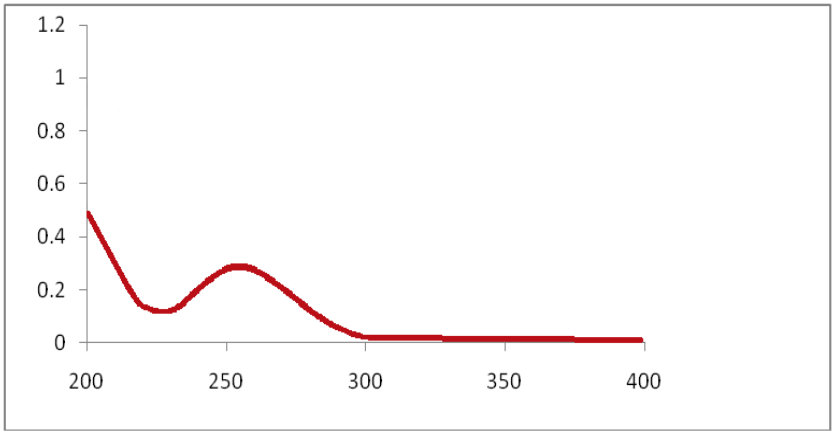

Figure No.-3: Spectra of ebastine.

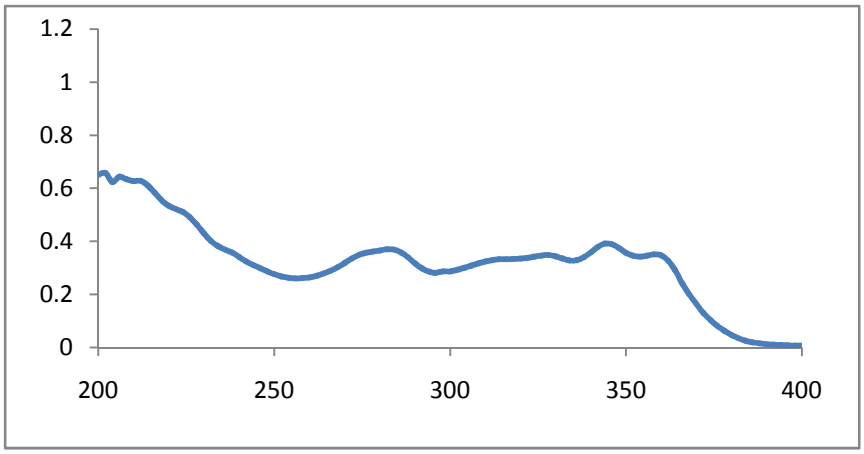

Figure No.-4: Spectra of montelukast sodium.

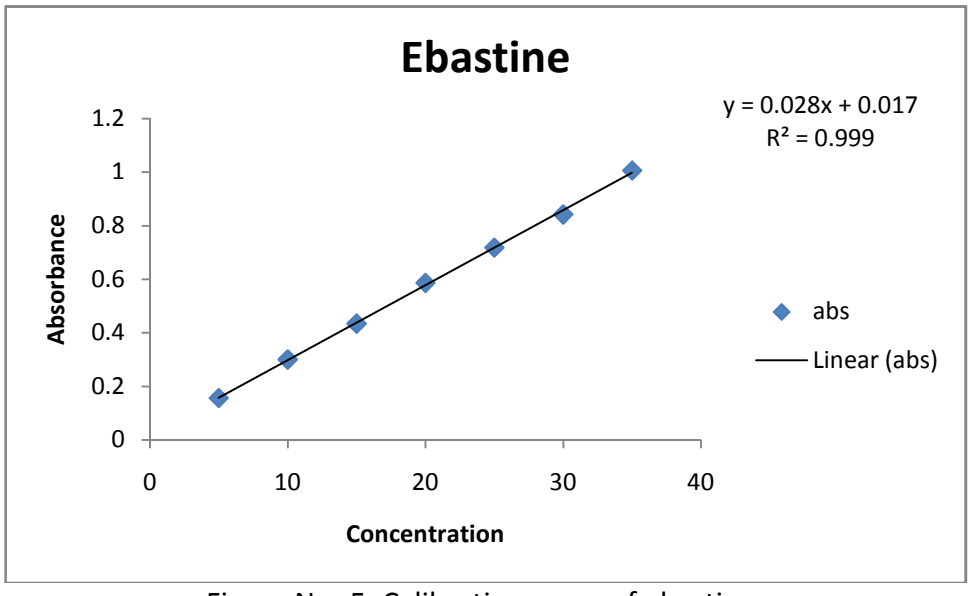

Figure No.-5: Calibration curve of ebastine.

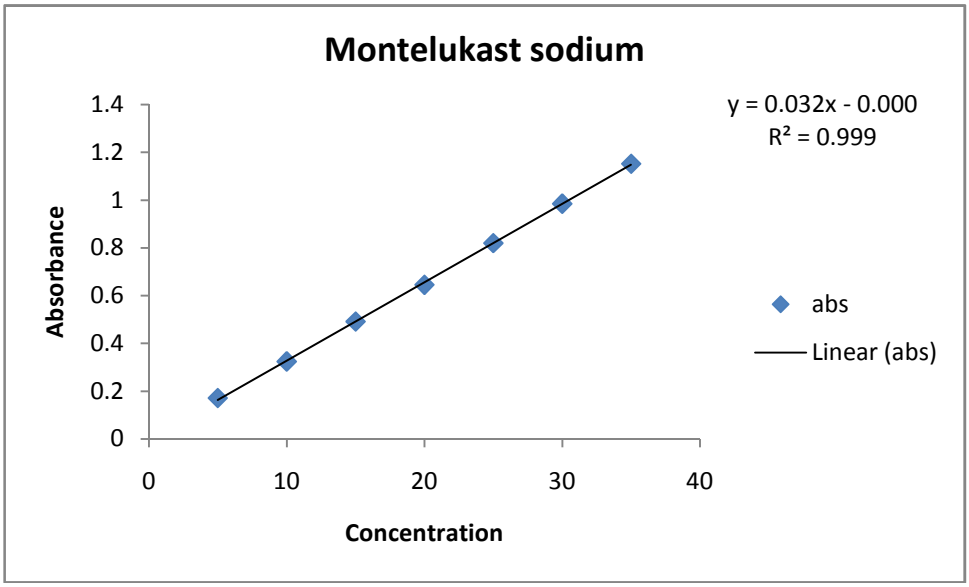

Figure No.-6: Calibration curve of montelukast sodium.

Parameter	Ebastine	Montelukast sodium
Wavelenth detection	255	345
Slop	0.028	0.032
Intercept	0.013	0.000
Correlation coefficient	0.999	0.999
Range	5-35µg /mL	5-35µg /mL
Regression equation	Y=0.028x+0.013	Y=0.032x-0.000
Limit of detection	0.1232 µg /mL	0.1187µg /mL
Limit of quantitation	0.3732 µg /mL	0.3597 µg /mL

Table 1: Result of linearity range, LOD and LOQ.

	Interday precision		Intraday precision	
	%Amount Found ± SD*	% RSD	%Amount Found ± SD*	% RSD
Ebastine	100.28 ± 0.2879	0.2871	100.49 ± 0.3717	0.3698
Montelukast sodium	100.23 ± 0.2944	0.2937	99.93 ± 0.1686	0.1687

Table No.2:-Result of precision. *Average of six determinations

Percentage level	Ebastine		Montelukast sodium	
	%Recovery ± SD*	% RSD	%Recovery ± SD*	% RSD
80%	100.48 ± 0.3361	0.3345	100.23 ± 0.0529	0.0528
100%	100.27 ± 0.3012	0.3003	101.9 ± 0.3163	0.3150
120%	100.21 ± 0.3436	0.3429	100.19 ± 0.4309	0.4309

Table No.3:-Result of Accuracy. *Average of six determinations

Marketed	Drug	Lable claim	Amount Found ± SD*	% Lable claim± SD*
Ebast-M	Ebastine	10mg	9.99 ± 0.4511	99.93 ± 0.4511
	Montelukast sodium	10mg	10.01 ± 0.4733	100.18 ± 0.4733

Table No.4:- Result of analysis of tablet formulation. *Average of three determinations

Marketed	Drug	Lable claim	Amount Found ± SD*	% Lable claim± SD*
Analyst 1	Ebastine	10mg	10.03 ± 0.1414	100.3±0.1414
	Montelukast sodium	10mg	10.05±0.5657	100.5±0.5657
Analyst 2	Ebastine	10mg	9.99±0.4511	99.93±0.4511
	Montelukast sodium	10mg	10.01±0.4733	100.18±0.4733

Table No.5:- Result of Ruggedness. *Average of three determination

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