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Research Article

DEVELOPMENT AND VALIDATION OF SIMULTANEOUS EQUATION METHOD FOR ESTIMATION OF MONTELUKAST SODIUM AND LEVOCETIRIZINE DIHYDROCHLORIDE BY UV SPECTROPHOTOMETRIC METHOD

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ABSTRACT

A Simple, accurate, precise and rapid UV spectrophotometric method has been developed for the simultaneous estimation of Montelukast sodium and Levocetirizine dihydrochloride, in pure form. The stock solution was prepared in phosphate buffer (pH 6.8) followed by the further required dilutions with pH 6.8. This method involves the formation and solving of simultaneous equation at 245 and 231nm, as absorbance maxima of Montelukast sodium and Levocetirizine dihydrochloride, respectively. Beer's law obeyed the concentration range of 5-30 mcg/ml and 4-24 mcg/ml, for Montelukast sodium and Levocetirizine dihydrochloride, respectively. The results of analysis were validated statistically and by recovery studies. The % RSD for the recovery study was less than two. The proposed method can be effectively applied for the simultaneous estimation of two drugs in bulk and in combined dosage form.

Keywords: Levocetirizine dihydrochloride , Montelukast sodium , Simultaneous Equation Method, UV Spectrophotometric method.

INTRODUCTION

Montelukast sodium 2- [1-[(R)-[3-[2(E)-(7-chloroquinolin-2-yl) vinyl] phenyl] - 3-[2- (1-hydroxy-1-methylethyl) phenyl] propyl -sulfanylmethyl] cyclopropyl] acetic acid sodium salt (Fig. 1) is a fast acting and potent cysteinyl leukotriene receptor antagonist which is being used in the treatment of asthma[1]. The only leukotriene modifier approved by the US Food and Drug Administration for use by children from 2 to 12 years of age.

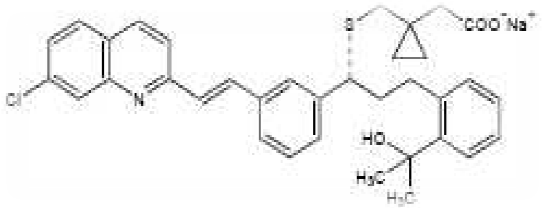

Fig 1: Structure of Montelukast sodium

A rapid onset of action is seen after the administration of Montelukast sodium, with improvement seen on the first day of treatment and these positive effects may be additive to those of inhaled corticosteroids[2]. While inhaled beta-agonists are still considered the first-line therapy for treatment of asthma, Montelukast sodium may be given due consideration for use as first line therapy in patients with mild persistent asthma, for additional control in those who remain symptomatic during treatment with inhaled corticosteroids, for patients that are steroidphobic, or for those who have difficulties with compliance. It is also reduce the bronchoconstriction caused by the leukotriene and result in less inflammation. Montelukast inhibits the actions of LTD4 at the CysLT1 receptor, preventing airway edema, smooth muscle contraction, and enhanced secretion of thick, viscous mucus[2,3].

Levocetirizine 2-[2-[4-[(*R*)-(4-chlorophenyl)-phenyl methyl] piperazinyl-1-yl]ethoxy] acetic acid, the *R*-enantiomer of racemic cetirizine, is aselective, potent, H1-antihistamine compound indicated for the treatment of allergic rhinitis and chronic idiopathic urticaria[4]. The recommended dosing of Levocetirizine is 5 mg per day. It has a rapid onset action and works by blocking histamine receptors. It does not prevent the actual release of histamine from mast cells, but prevents the binding to its receptors. This in turn prevents the release of other allergy chemicals and increased blood supply to the area, and provides relief from the typical symptoms of hay fever. Levocetirizine dihydrochloride, and Montelukast sodium combination tablet is a recently introduced for COPD preparation in Indian market. Montelukast only a few chromatographicmethods have been reported for the determination of Montelukast and Levocetirizine, in individual and in combination with other drugs in the open literature[5].

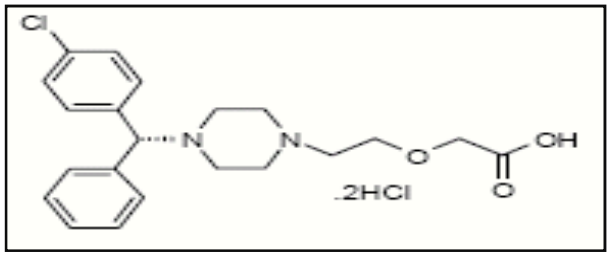

Fig 2: Structure of Levocetirizine dihydrochloride

MATERIALS AND METHODS

INSTRUMENTATION

UV double beam spectrophotometer (Shimadzu Model 1800) was employed with automatic wavelength correction with a pair of 1 cm matched quartz cells.

Chemicals and reagents

Montelukast sodium and Levocetirizine dihydrochloride pure drug were received as gift samples from Morpen lab(HP – Solon) and Micro lab (Banglore -India) respectively.

Preparation of standard stock solution and calibration curve

Standard stock solution of pure drug containing 50mg/ml of MTKT and 40mg/ ml of LCTZ were prepared in phosphate buffer (ph-6.8) system. The working standard solutions of these drugs were obtained by dilution of the stock solution in the Ph-6.8. Series of solutions with conc. 5-30 µg/ ml of MTKT and 4 – 24 µg/ ml of LCTZ respectively were used to prepare calibration curve. Solutions were scanned and proposed methods were applied. For determination of absorptivity values, calibration curves using standard serial dilutions of individual drugs were plotted.

Simultaneous determination

The Simultaneous Equation Method of analysis based on the absorption of the drug MTKT and LCTZ at their λmax. Two wavelength selected for the development of Simultaneous Equation are 245 nm (λ1) and 231nm (λ2). Absoptivities of both the drugs at both the wavelengths were determined Equations obtained for the estimation of concentration were,

$$Cx = \frac{(A_1 * y_2) - (A_2 * y_1)}{x_1 y_2 - x_2 y_1}$$

$$Cy = \frac{(A_2 * x_1) - (A_1 * x_2)}{x_1 y_2 - x_2 y_1}$$

Where A1 and A2 are absorbance of Sample solution at 245 and 231 nm respectively

x_1= Absorptivity of MTKT at 245 nm

x_2 = Absorptivity of MTKT at 245 nm

y_1 = Absorptivity of LCTZ at 231 nm

y_2= Absorptivity of LCTZ at 231nm

Cx and Cy are concentration of MTKT and LCTZ in sample solution[6,7,8].

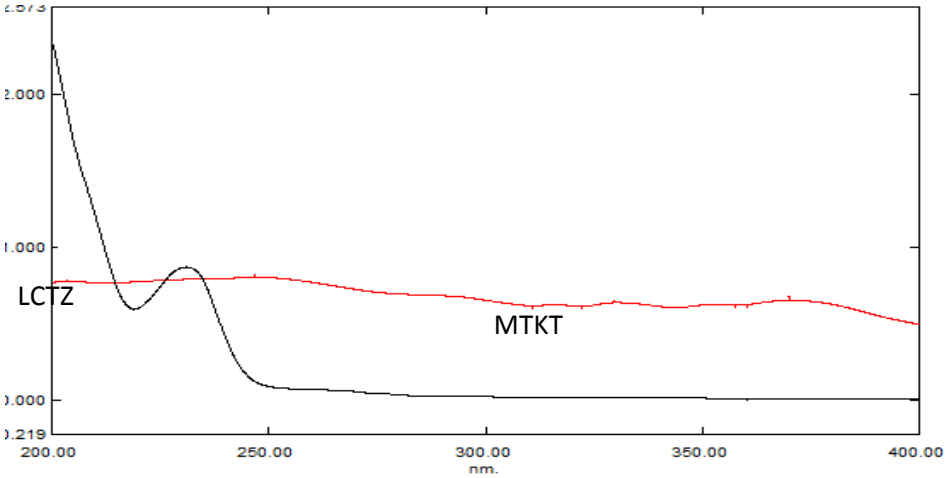

Figure 3: Overlain spectra of Montelukast sodium and Levocetirizine dihydrochloride

METHOD OF VALIDATION:

Linearity: For each drug, appropriate dilutions of standard stock solutions were assayed as per the developed methods.

The Beer-Lambert's concentration range is 5-25 µg/mL for Montelukast sodium and 4-24 µg/mL for Levocetirizine dihhdrochloride. The linearity data shown in Table 1.

Table 1: Spectral and Linearity Characteristic Data.

Parameters	Montelukast Sodium	Levocetirizine dihydrochloride
λ_{max} (nm)	245	231
Linearity range (µg/ml)	5-30	4-24
Correlation coefficient (r^2)	0.9998	0.999
Slope (m)	0.027	0.033
Regression equation	y=0.027x	y=0.333 x

Robustness of the method:
Small deliberate changes in the wavelength (±5nm) were introduced and the effects on the results were examined and values are reported in Table no 2.

Drugs	Averages	S.D	R.S.D
MTKT	0.147	0.0020	0.5214
LCTZ	0.125	0.0030	0.5521

Precision of the method:
Precision of the methods was determined by repeating assay 3 times. To study intraday precision, method was repeated 3 times in day and the average % RSD was calculated. Similarly the method was repeated on three different days and average % RSD was calculated and the values are reported in Table 3(a) and (b).

Table 3(a): Intraday Precision (n=3)

Drugs	Averages	S.D	R.S.D
MTKT	0.273	0.0045	1.65
LCTZ	0.256	0.0043	1.67

Table 3(b): Interday Precision (n=3)

Drugs	Averages	S.D	R.S.D
MTKT	0.282	0.0025	0.89
LCTZ	0.261	0.0027	1.03

Accuracy:
Accuracy was confirmed by recovery study as per ICH guidelines Q2R1[9]at three different concentration levels 80%, 100%, 120% by replicate analysis (n = 3). Here to a sample solution drug solutions were added and then percentage of drug content was calculated. From the recovery study it is clear that the method is accurate for quantitative estimation of Montelukast sodium and Levocetrizine dihydrochloride, as the statistical parameters are within the acceptance range. The results of are shown in Table 4.

Table 4: Result of Recovery Study

	% Recovery ± SD	
Drug	Montelukast sodium	Levocetirizine dihydrochloride
80%	88.5± 0.26	90.2 ± 0.20
100%	91.2 ± 0.45	92.3 ± 0.50
120%	95.6 ± 0.57	96.5 ± 0.32

RESULTS AND DISCUSSION

The Beer- Lambert's concentration range is 5-30 µg/mL, and 4-24 µg/mL for Montelukast and Levocetirizine dihydrochloride at 245 nm, and 231 nm wavelengths with coefficient of correlation 0.9998, and 0.999 respectively. Drugs show good regression values at their respective wavelengths. Further, the precision of the method was confirmed by Intraday and Interday analysis. The % RSD values for Intraday and Interday analysis was found to be 1.65 and 0.89 for Montelukast sodium, 1.68 and 1.03 for Levocetirizine dihydrochloride, respectively From validation, the developed method was found to be simple, accurate, precise, and rapid. Hence the proposed method could be effectively applied for the routine analysis of Montelukast sodium and Levocetrizine dihydrochloride. The % recovery was found to be in the range of 88.5 to 95.6 for Montelukast sodium, 90.2 to 95.5 for Levocetrizine dihydrochloride. This ensures the accuracy of the method.

CONCLUSION

The results of study indicate that the proposed UV spectroscopic methods are simple rapid, precise and accurate. The proposed methods are simple, rapid and validated in terms of linearity, precision, accuracy, reproducibility, and can be used successfully for routine simultaneous estimation of Montalukast sodium and Levocetrizine dihydrochloride in pure dosage form. The proposed method was successfully applied to determination of these drugs in commercial tablets.

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