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SIMULTANEOUS ESTIMATION OF MONTELUKAST SODIUM AND ACEBROPHYLLINE IN BULK AND COMBINED DOSAGE FORM BY UV SPECTROPHOTOMETRIC METHOD

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ABSTRACT

In the present work a simple, sensitive, accurate and reproducible ultraviolet spectrophotometric absorption correction method was developed and validated for the simultaneous estimation of Montelukast sodium and Acebrophylline in bulk and marketed tablet dosage form**.** Methanol was used as a solvent to prepare stock solutions. Montelukast sodium was estimated directly at 345 nm as Acebrophylline showed no interference with zero absorbance at this wavelength. Both the drugs showed absorbance at 334 nm. Thus the amount of Acebrophylline was estimated by correcting the absorbance of Montelukast sodium for interference at 334 nm. Absorptive values were used for this purpose. The method obeyed Beer's law in the concentration range of 5-10 mcg/ ml for Acebrophylline and 100-200 mcg/ mL for Montelukast sodium. The developed analytical method was found to be accurate and precise after its validation as per ICH guidelines. Thus, by using proposed method, simultaneous estimation of Montelukast sodium and Acebrophylline can be successfully carried out in bulk and in combination dosage form of tablet as well.

Keywords: Absorption correction method, Acebrophylline, Montelukast Sodium, Simultaneous estimation

INTRODUCTION

Pulmonary disease and particularly asthma has become a major health issue in the developing countries. Montelukast, Lornoxicam, and Acebrophylline are some of the efficient agents used for the treatment of asthma. Montelukast sodium (MNT), the chemical name of which is [R-(E)]-1-[[[1-[3-[2-(7-chloro-2-quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropane acetic acid, monosodium salt, is a leukotriene receptor antagonist. It is used for the treatment of asthma and to relieve symptoms of seasonal allergies. By binding to the cysteinyl leukotriene receptor (CysLT1), it blocks the action of leukotriene D4 and secondary ligands LTC4 and LTE4 on the CysLT1 in the lungs and bronchial tubes. This reduces the bronchoconstriction caused by the leukotriene which results in less inflammation **[1, 2]**. Acebrophylline(ACB), 1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-7H-Purine-7-aceticacidwithtrans4-[[(2-amino-3,5dibromophenyl)methyl]amino]cyclohexanol is a xanthine derivative. It is used as a bronchodilator for the treatment of bronchial asthma and COPD in adults. By lowering viscosity and increasing the serous gel phase, Acebrophylline alters mucus gel secretion phase. Acebrophylline increases the mucociliary clearance by enhancing ciliary motility **[3, 4]**.

As per literature review, spectrophotometric, spectrofluorometric, RP-HPLC and HPTLC methods are available for the estimation of Montelukast sodium **[5-12]** and acebrophylline **[13-18]** individually, bulk and in pharmaceutical formulations. But very few analytical methods have been reported till date for combination of these two drugs. The present research work aims to develop a simple, sensitive, accurate and reproducible UV method for simultaneous estimation of Montelukast sodium and Acebrophylline in combined dosage form. The present work describes absorbance correction spectroscopic method for the determination of Montelukast and Acebrophylline in tablet dosage form. The proposed method was validated as per the ICH (International Conference on Harmonization) guidelines.

EXPERIMENTAL

MATERIALS

Acebrophylline (ACB) and Montelukast (MNT) were obtained from Lupin Pharmceutical Pvt ltd (Pune) and Macleods Pharmaceutical Pvt ltd. (Mumbai) as gift samples respectively. Methanol AR grade was used in the study. An UV-Visible double beam spectrophotometer, Varian Cary 100, with 10 mm matched quartz cells was used for the estimation of drugs. Electronic balance, Model Shimadzu AUW-220D, was used for weighing.

METHODS

Preparation of ACB Stock (Working Standard) Solution:

To prepare stock solution of ACB (1000 µg/ml), accurately weighed 25 mg of ACB was transferred to 25 ml volumetric flask, dissolved and diluted up to mark with methanol. To obtain working standard solution of 100 µg/ml of ACB, the solution was further diluted with methanol.

Preparation of MNT Stock (Working Standard) Solution:

To prepare stock solution of MNT (1000 µg/ml), accurately weighed 25 mg of MNT was transferred to 25 ml volumetric flask, dissolved and diluted up to mark with methanol. To obtain working standard solution of 100 µg/ml of MNT, the solution was further diluted with methanol.

Selection of wavelength of maximum absorption-

Overlay spectra of Acebrophylline and Montelukast sodium was obtained by scanning the solutions containing appropriate concentration of ACB and MNT in methanol by using UV spectrophotometer in the range of 400-200 nm. From this overlay spectra **(Figure 1)**, analytical wavelengths for detection of both the drugs were selected.

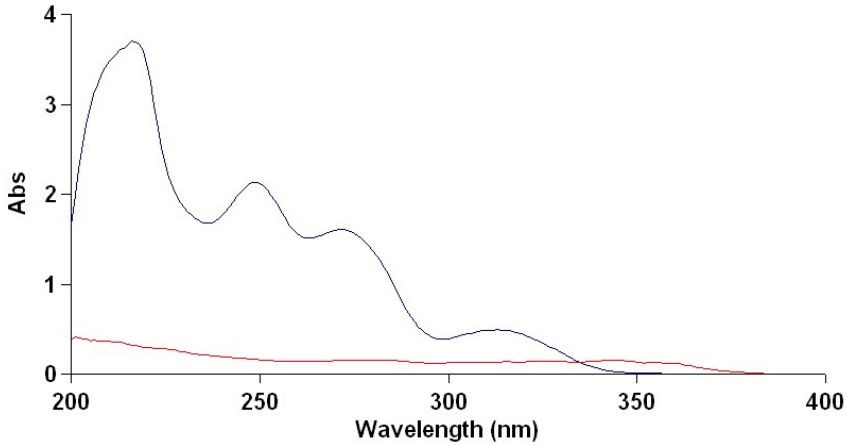

Figure 1: Overlay spectra of Acebrophylline and Montelukast sodium

Stability study – The absorbance of solution was taken for two hours at the interval of 15 minutes.

Calibration curve

Preparation of standard solutions for calibration curve:

Working standard solutions of ACB and MNT were diluted with methanol to get six replicate series of standard solutions having concentration range of 100-200 µg/ml for ACB and 5-10 µg/ml for MNT.

Preparation of Calibration Curves:

Absorbance of prepared standard solutions having concentration 100,120,140,160,180 and 200µg/ml for ACB and 5, 6, 7, 8, 9 and10 µg/ml for MNT were measured at 313.70 nm and 345.00 nm respectively. Calibration curves of absorbance against concentration were plotted for both drugs **(Figure 2)**. Using these calibration curves absorptivity coefficients were determined at both the wavelengths.

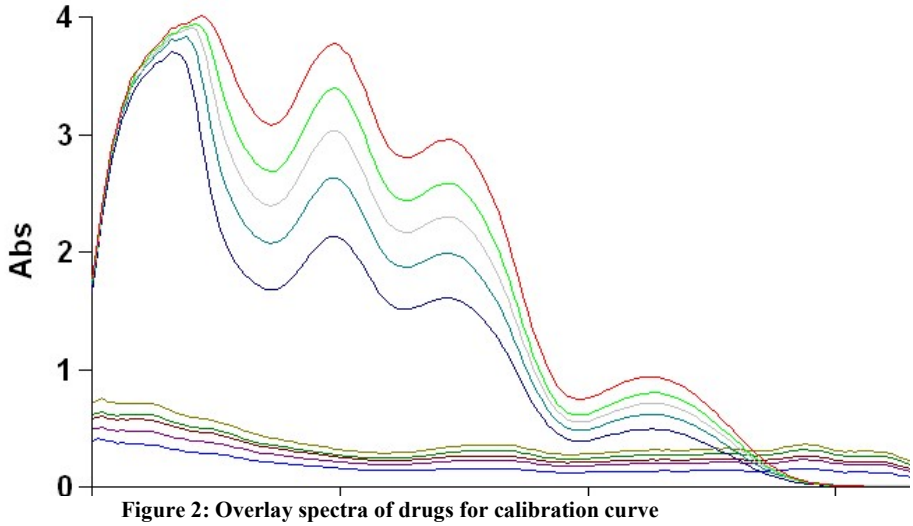

Figure 2: Overlay spectra of drugs for calibration curve

Analysis of formulation

Twenty tablets (TELEKAST-A) were weighed to determine the average weight and then triturated to get a fine powder. An accurately weighed quantity of powder equivalent to 20 mg of ACB was transferred to 20 mL volumetric flask and a minimum quantity of methanol was added to dissolve the substance. The volume was made up to 20 ml with the methanol. The solution was sonicated for 15 minutes, centrifuged for another 15 minutes at 100 rpm and filtered through Whatmann filter paper No. 41 to get a clear solution. Further dilutions were made by diluting 1.0 mL into 10 mL with methanol to obtain 100 mcg/ mL solution of ACB which also contained 5 mcg/ mL of MNT theoretically. The absorbance of sample solution was measured at all selected wavelengths. The content of ACB and MNT in sample solution of tablet was calculated. This procedure was repeated for six times.

VALIDATION OF THE ANALYTICAL METHOD [19]

The method was validated with respect to linearity, precision, LOD (Limit of detection), LOQ (Limit of quantitation), accuracy and ruggedness.

Linearity

Linearity was checked by diluting standard stock solution at six different concentrations i.e., 100,120,140,160,180 and 200µg/ml for ACB and 5, 6, 7, 8, 9 and

10 µg/ml for MNT. Acebrophylline was linear with the concentration range of 100-200 µg/ ml at 313.70 nm. Montelukast sodium was linear in the concentration range of 5-10 µg/ ml at 345 nm. Calibration curves (n=6) of absorbance against concentration were plotted for both drugs **(Figure 3 and 4)**. Optical parameters were calculated.

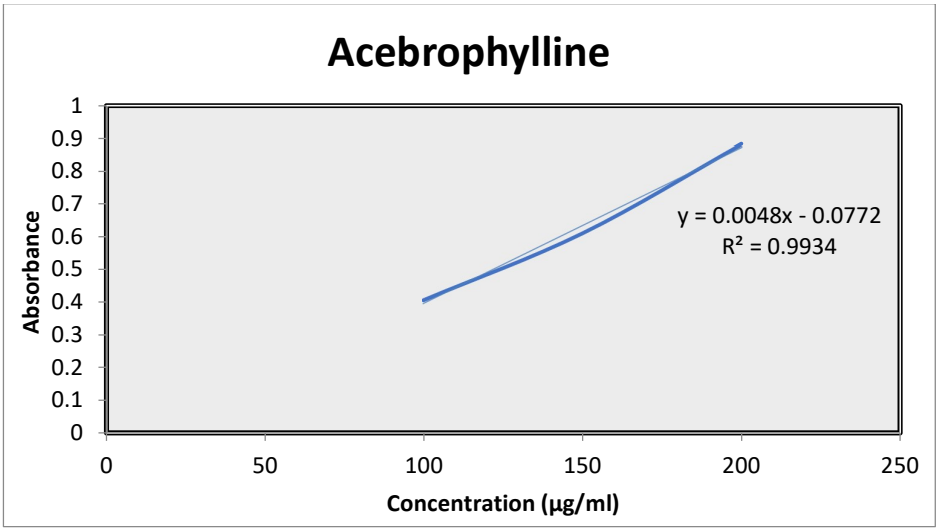

Figure 3: Linearity graph of Acebrophylline

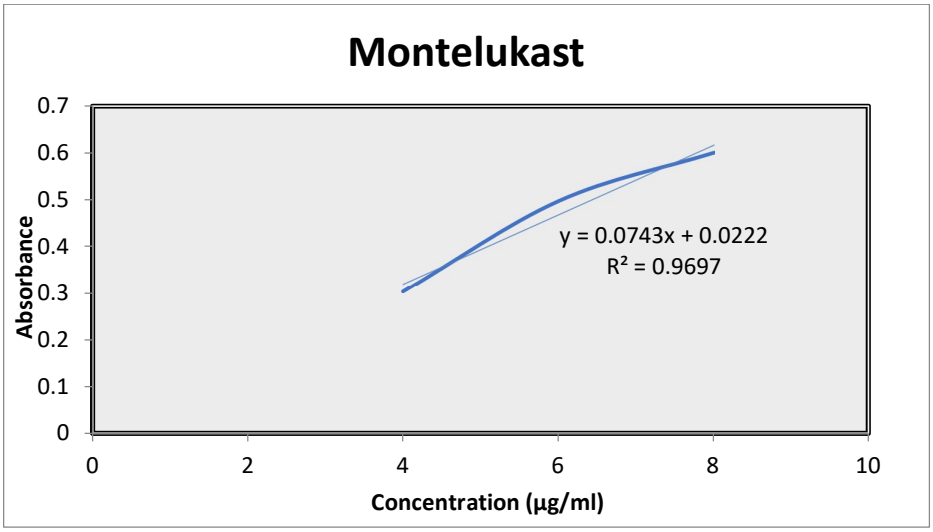

Figure 4: Linearity graph of Montelukast sodium

Precision

Formulations were analysed for six times with the same concentration to confirm the repeatability of the method (precision). To check the intermediate precision of the method, intraday and inter day analysis was carried out. For that the analysis of formulation was repeated three times on the same day and on three successive days. The

amount of each drug present in the tablet formulation was determined **(Table 1)**.

LOD & LOQ

LOD (k = 3.3) and LOQ (k = 10) of the proposed method were established according to ICH definitions and reported in **Table 2**. In this study, LOD and LOQ were calculated using the standard deviation of the response and the slope of the corresponding curve as per the the following equations

LOD = 3.3 SD/S

LOQ = 10 SD/S

Where SD is the standard deviation of the absorbance of the sample and S is the slope of the calibrations curve.

Accuracy

Recovery study was carried out to check accuracy of the developed method. Each level was repeated three times (n = 3). A known quantity of pure drug was added to the preanalyzed formulation and the proposed method was followed. Percentage recovery was calculated from the amount of drug found **(Table 2)**.

Table 1: Precision

Parameters	Drug	Label claim	Amount taken	Amount found	S.D	C.O.V
Precision (interday)	Acebrophylline	200mg	20mg	19.88	0.02	1.1
	Montelukast sodium	10mg	1mg	1.01	0.38	0.9
Precision (Intraday)	Acebrophylline	200mg	20mg	19.75	0.05	1.2
	Montelukast sodium	10mg	1mg	0.92	0.24	0.9

Table 2: Accuracy (recovery study)

Drug	Label claim (mg)	Amount taken (mg/tab)	Amount found (mg/tab)	% Recovery	S. D	L.O.D (µg/ml)	L.O.Q (µg/ml)
Acebrophylline	200	100	99.97	99.97	0.8	4.916	14.89
Montelukast sodium	10	5	4.81	96.24	0.115	0.835	2.533

RESULTS AND DISCUSSION

The developed method was based upon the direct estimation of Montelukast sodium at 345 nm as at this wavelength Acebrophylline showed zero absorbance and no interference. At 334 nm, these two drugs showed absorbance. To estimate the amount of Acebrophylline, the absorbance of Montelukast sodium were corrected for interference at 334 nm by using absorptivity values. The method obeyed Beer's law in the concentration range of 5-10 mcg/ ml for Acebrophylline and 100-200 mcg/mL for Montelukast sodium. The developed analytical method was found to be accurate, precise, sensitive and reproducible after its validation as per ICH guidelines. Thus, by using proposed method, simultaneous estimation of Montelukast sodium and Acebrophylline

can be successfully carried out in bulk and in combination dosage form of tablet as well.

Stability of solution- The solution was found to be stable for two hours.

CONCLUSION

A simple, sensitive, accurate and specific UV spectrophotometric absorption correction method was developed for the determination of Montelukast and Acebrophylline, in pure form and in pharmaceutical formulation. The developed method was validated as per the ICH guidelines and it was found to be accurate and precise. Thus, the proposed method can be successfully applied for simultaneous determination of Montelukast sodium and Acebrophylline in bulk and in combined tablet dosage form.

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