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Research Article

SIMULTANEOUS DETERMINATION OF MONTELUKAST SODIUM AND BAMBUTEROL HYDROCHLORIDE IN TABLET DOSAGE FORM BY ULTRAVIOLET SPECTROPHOTOMETRY

Pushpa Latha E*, Abiram L
Shanthiram College of Pharmacy, Nandyal, Kurnool (Dist), A.P.

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*Corresponding author's email: **latha.pushpa999@gmail.com**

ABSTRACT
A simple, accurate, and precise dual wavelength spectrophotometric method was developed for simultaneous determination of Montelukast Sodium (MTKT) and Bambuterol Hydrochloride (BAM) in combined pharmaceutical dosage forms. The method based on determination of MTKT at 322.0 nm using its absorptivity value and BAM at 266.0 nm after deduction of absorbance due to MTKT. The two drugs follow Beer-Lambert's law over the concentration range of 1-10 µg/mL for MTKT and 5-40 µg/mL for BAM. The recovery of the MTKT and BAM were found to be 99.87 ± 1.13 & 99.87 ± 1.13100 %. Validation of the proposed methods was carried out for its accuracy, precision, specificity and ruggedness according to ICH guidelines. The proposed methods can be successfully applied in routine work for the determination of MTKT and BAM in combined dosage form.

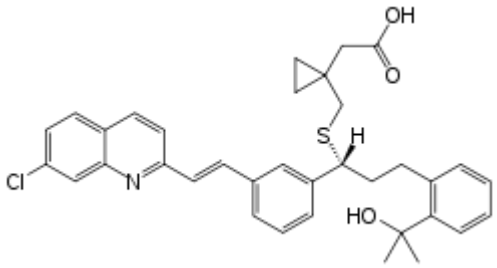
KEY WORDS: Montelukast sodium, Bambuterol hydrochloride, UV Spectrophotometric method.

INTRODUCTION

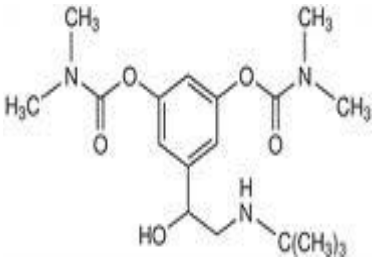
Montelukast sodium (MTKT), 1-[({(R)-m-[(E)-2-(7- chloro-2-quinolyl) vinyl]-α-[o-(1-hydroxyl 1-methylethyl)phenethyl]benzyl}thio)methyl] cyclopropaneacetate sodium is a leukotriene receptor antagonist,used in the treatment of asthma[1,2,3]. It is not official in IP, BP and USP. Various analytical methods,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

method [9] for Montelukast sodium in tablets and human plasma have been reported. Bambuterol hydrochloride (BAM), (RS)- 5 - (2-tert-butylamino-1-hydroxyethyl) – m - phenylene bis (dimethylcarbamate) hydrochloride is a direct acting sympathomimetic with predominantly – adrenergic activity (β_2 -agonist)[10]. It is an ester prodrug of β_2 adrenergic agonist terbutaline[2]. Bambuterol hydrochloride is official in BP [11]. Different HPLC methods have been reported for the estimation of BAM in pharmaceutical dosage form[12,13]. The drug has been also estimated by solid-state NMR [14]. The combined dosage forms of MTKT and BAM are available in the market for the prophylaxis and treatment of chronic asthma and chronic bronchitis in pediatrics.

At present one HPLC method [15] has been reported for simultaneous determination of MTKT and BAM in formulations. Present study involves development and validation of Spectrophotometric method for the estimation of MTKT and BAM in combination dosage form.



Montelukast sodium



Bambuterol hydrochloride

EXPERIMENTAL METHODS

Instrument

All absorption spectra were recorded with a UV-2202 UV/Vis double beam spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cells (Systronics).

Reagents and chemicals

API working standards of Montelukast sodium (MTKT), Bambuterol hydrochloride (BAM) and were obtained from Natco Pharma Ltd. and test samples (bi layered tablets with composition MTKT-10 mg and BAM equivalent to Bambuterol-10 mg) were obtained from local market. Water is used as solvent.

METHOD DEVELOPMENT

Standard stock solutions of MTKT and BAM, each of 1mg/ml concentration in water were prepared. From these stock solutions appropriate dilutions in the range of 1-10 µg/ml and 5- 40 µg/ml for MTKT and BAM, respectively were prepared and analyzed. Mixed standards were prepared in the ratio of 1:1, as the formulation contains MTKT and BAM 10 mg and 10 mg, respectively. and scanned over the range of 200-400 nm and the overlain spectra was observed for development of suitable method for analysis.

Validation of the Method

Linearity

Linearity of the proposed method was verified by analyzing five different concentrations in the range of 1-10 µg/ml for MTKT and 5-40 µg/ml for MTKT and BAM, respectively. Each concentration was made in triplicate.

Accuracy

The accuracy of the method was performed by conducting the recovery studies (80, 100 and 120%) of pure drugs from marketed formulation, by standard addition method. The actual and measured concentrations were then compared.

Precision

The intra day precision of the developed method was evaluated by analyzing samples of three different concentrations of MTKT (6, 8 and 10 µg/ml) and BAM (10, 20, and 40µg/ml) in triplicates on the same day. The inter day precision was evaluated from the same concentration on three consecutive days, precision was evaluated from the same concentration by three different analysts.

Stability

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

Analysis of Marketed formulation

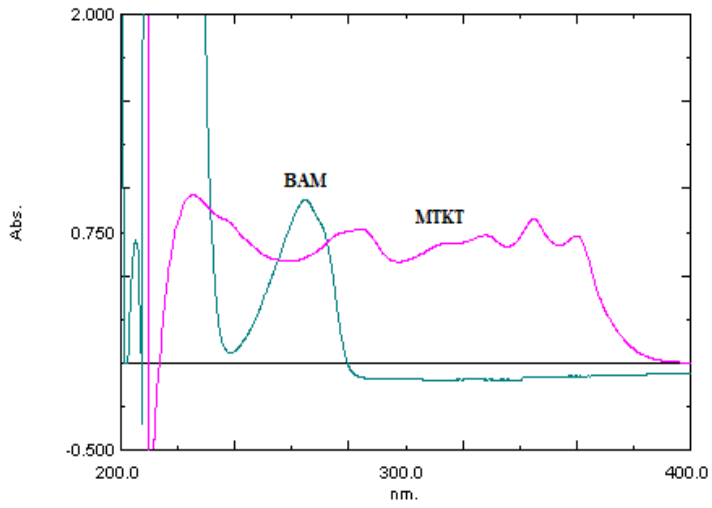
To determine the content of MTKT and BAM in commercial tablets (each tablet containing 10 mg MTKT and 10 mg BAM), 20 tablets were weighed and finely powdered. A quantity of powder equivalent to 10 mg of MTKT and 10 mg of BAM was weighed accurately and transferred to a 50 ml volumetric flask and the volume was made up with the solvent. It was sonicated for 30 minutes and then filtered through 0.5 µm 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 triplicates.

RESULTS AND DISCUSSION

Method development and Validation

The overlain spectrum of the drugs suggested that a dual wavelength

spectrophotometric method was the most suitable method for simultaneous determination of MTKT and BAM. In Dual wavelength method The diluted solutions were scanned over the wavelength range of 200 - 400 nm. From the overlain spectra (Figure.1), wavelengths 322.0 λ_{max} of MTKT and 266.0 nm the λ_{max} of BAM were selected for quantitation by proposed method. For studying Beer's law, two series of different concentrations in range of 1-10 µg/mL for MTKT and 5-40 µg/mL were prepared from stock solutions. The calibration curves were constructed at 322.0 and 266.0 nm respectively. The absorptivities (A 1%,1 cm) of both the drugs at both the selected wavelengths were determined. The quantitative determination of MTKT is carried out by using A (1%, 1cm) value at a 322.0 nm where BAM, interfering substance does not have any absorption and quantitation of BAM is carried out by subtracting absorption due to MTKT, interfering drug in the overlapping region of spectrum, on the basis of its absorption ratio at two wavelengths.



Overlain absorption spectra of the MTKT and BAM

Linearity

The calibration curves of MTKT and BAM were linear in the range of 1-10 µg/ml and 5-40 µg/ml respectively. The regression equations of calibration curves were Y_{MTKT} = 0.079x - 0.0224, r^2 =0.9998 and Y_{BAM} =0.021x + 0.0075, r^2 =0.9997 for MTKT and BAM, respectively. The data are shown in table 1.

TABLE 1: OPTICAL CHARACTERISTICS OF THE PROPOSED METHOD

Parameters	MTKT	BAM
Wavelength for measurement (nm)	322.0	266.0
Beer's Law limit (µg /ml)	1-10	5-40
Sandell's sensitivity (µg/cm2/0.001 absorbance unit)	1.37×10^{-2}	4.54×10^{-2}
Regression equation(*Y)	y = 0.079x - 0.0224	y = 0.021x + 0.0075
Correlation coefficient (r2)	0.9998	0.9997
Relative standard deviation (%) (n=5)	1.27	0.63

Accuracy

The percentage recovery was calculated of pure drugs from marketed formulation by standard addition of pure drugs at a known concentration and excellent recoveries were obtained. The respective % recovery for MTKT was found to be 99.87 ± 1.13 and that of BAM was found to be 99.95 ± 1.02 respectively. The results of accuracy studies are shown in table 2.

Precision

The intraday precision showed a relative standard deviation (R.S.D. %) of 0.97 - 1.28% for MTKT and 0.73- 1.45 % for BAM. The inter day precision showed a R.S.D. % were 1.69 - 1.72% and 1.46 - 1.57% for MTKT and BAM, respectively. Intra day, inter day precision of method is illustrated in table 2.

TABLE 2. SUMMARY OF VALIDATION PARAMETERS FOR THE PROPOSED METHOD

Parameters	MTKT at 322.0 nm	BAM at 266.0 nm
Concentration range (µg /ml)	1-10	5-40
LOD (µg /ml)	300ng/ml	2mcg/ml
LOQ (µg /ml)	900ng/ml	7mcg/ml
Accuracy (recovery, n=6), %	99.87 ± 1.13	99.95 ± 1.02
Repeatability (RSD, n=6)%	0.43	0.98

Precision (RSD)% Intraday (n=6) Interday (n=6)	 0.97 -1.28% 1.69 - 1.72%	 0.73- 1.45 % 1.46 - 1.57%

Application of the Method in Tablets

The proposed UV method was applied for the determination of MTKT and BAM in their combined pharmaceutical formulations and the results are shown in table 3. The high percentage recoveries (98.9-99.2) and low %CV (0.11-0.45) values confirm the suitability of the proposed method for the routine determination of these components in combined formulation.

TABLE 3: ASSAY RESULTS FOR TABLETS USING THE PROPOSED METHOD

Formulation	Amount of drug taken (mg)		Amount of drug found (mg) %		Amount found (n=6) ± SD	
	MTKT	BAM	MTKT	BAM	MTKT	BAM
Tablet	10	10	9.98	9.99	99.87 ± 1.13	99.95 ± 1.02

CONCLUSION

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. Method validation has been demonstrated by variety of tests for linearity, accuracy, precision and stability.

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