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Difference Spectrophotometric Method for The Estimation of Ipratropium Bromide in Bulk Drug

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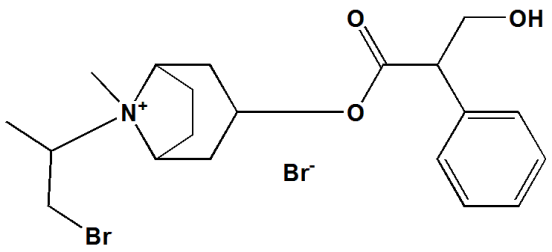
ABSTRACT

A simple, precise and sensitive UV method has been developed for the estimation of Ipratropium Bromide in bulk drug form by Difference Spectrophotometric method. Ipratropium Bromide has exhibited maximum absorbance at about 212 nm and 214.60 nm in acidic and basic solution respectively. Beer's law was obeyed in the concentration range of (2.5 – 12.5) µg/ml in both the cases. The percent recovery was found to be 98.79 – 99.62% and the LOD and LOQ were found to be 2.89 µg/ml and 8.76 µg/ml respectively. The proposed method was successfully applied for the determination of Ipratropium Bromide in bulk drug. As per ICH guidelines the results of the analysis were validated statistically and were found to be satisfactory.

INTRODUCTION

Ipratropium bromide chemically known as (1R, 3R, 5S, 8R)-3-(3-hydroxy-2-phenylpropanoyl) oxy)-8-methyl-8-(propan-2-yl)-8-azabicyclo (3.2.1) octan-8-ium bromide is a muscarinic antagonist structurally related to atropine but often considered safer and more effective for inhalation use. It is used for various bronchial disorders, in rhinitis, and as an anti arrhythmic. It blocks muscarinic cholinergic receptors, without specificity for subtypes, resulting in a decrease in the formation of cyclic guanosine monophosphate (cGMP). It is freely soluble in water and methanol, sparingly soluble in ethanol, and insoluble in lipophilic solvents such as ether, chloroform and fluorocarbons. The combination preparation ipratropium bromide/salbutamol is a formulation containing ipratropium bromide and salbutamol sulphate used in the management of chronic obstructive pulmonary disease (COPD) and asthma.



ipratropium bromide

Ipratropium bromide shows improved absorbing interference by the technique of difference spectrophotometry. Thus the objective of the present study was to develop new Analytical difference spectrophotometry method & its validation parameters for the proposed method according to ICH guidelines for the estimation of Ipratropium bromide bulk drug.

EXPERIMENTAL METHODS

Chemicals and Reagents:-

Ipratropium bromide [Bulk Drug] used were of Analytical Reagent grade gift sample from Vamsi Labs Ltd. Industries Solapur, Maharashtra, India, Sodium hydroxide and 1N Hydrochloric acid were used and Double distilled water was used throughout the analysis.

Instrumentation:-

A Shimadzu 1800 UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements.

Selection of Common Solvent:-

1N HCl and 1N NaOH were selected as a common solvent for developing spectral characteristics of drug.

Preparation of Solvent:-

For the preparation of 1N HCL, 85 ml of HCl mixed in 1000 ml distilled water and for the 1N NaoH 42mg of sodium hydroxide dissolved in 1000 ml distilled water mixed properly and filter to get clear solution.

Preparation of Solution:-

Standard stock solution containing Ipratropium Bromide was prepared by dissolving 10 mg in 100 ml of Distilled water and then diluted with 1N NaOH and 1N HCl separately to get series of dilution ranging from 2.5-12.5 µg/ml and then absorbance recorded at 214 nm and 212 nm respectively against reagent blank. Calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range of 2.5-12.5 µg/ml.

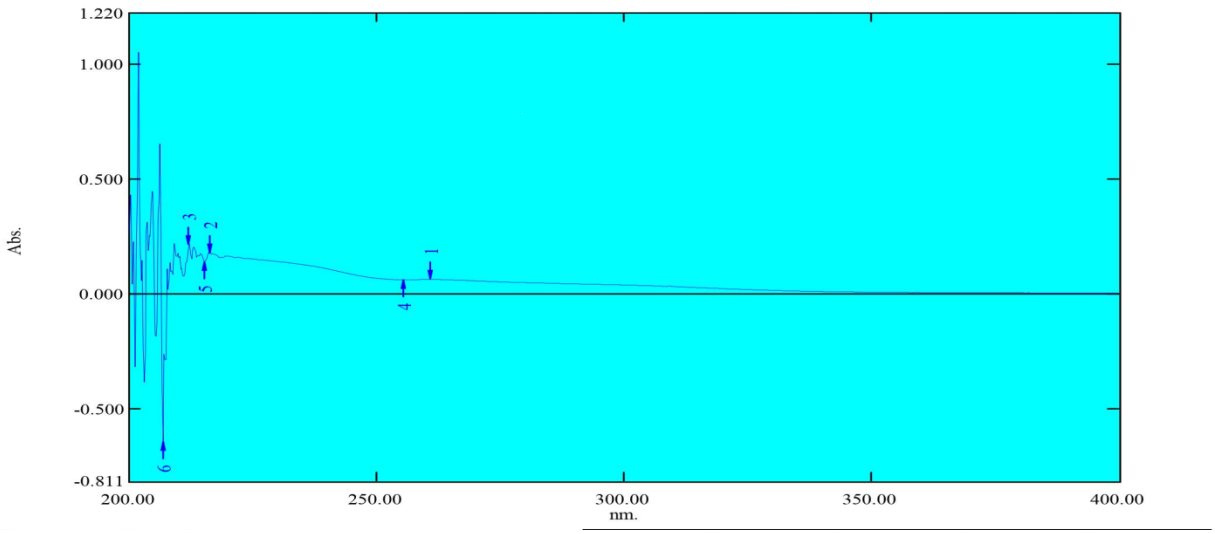


Figure No.1: 1N HCL with λmax 212 nm

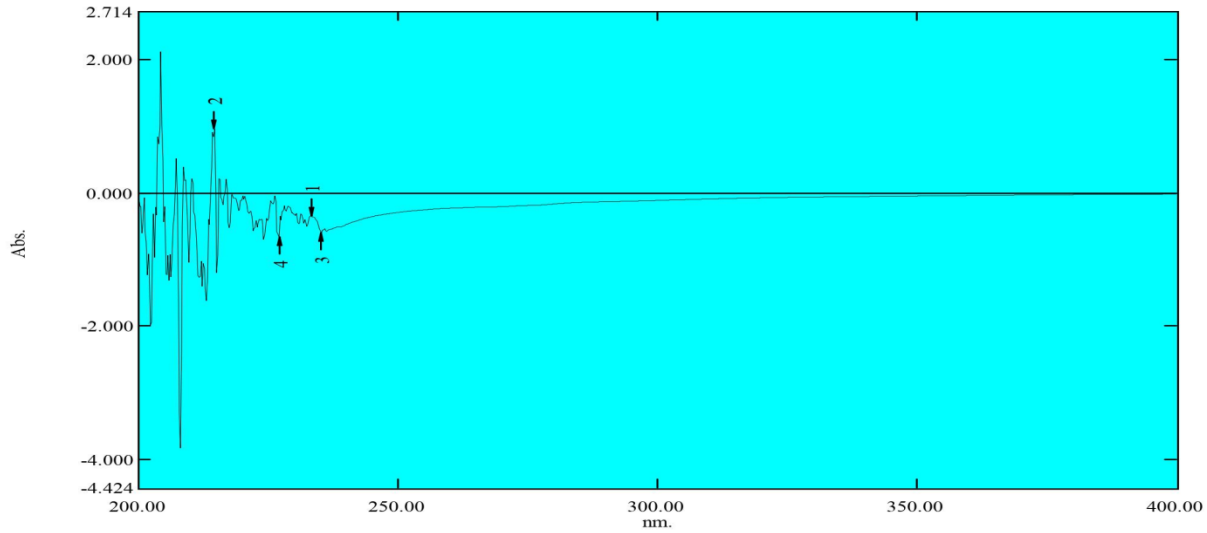


Figure No.2: 1N NaOH with λmax 214 nm

Table No.1: Linearity of Ipratropium Bromide by Difference Spectrophotometry

Sr. No.	Concentration of Ipratropium Bromide (µg/ml)	Absorbance at 212 nm (1N HCL)	Absorbance at 214 nm (1N NaOH)	Difference in Absorbance
1.	2.5	0.115	0.079	0.036
2.	5	0.198	0.142	0.056
3.	7.5	0.285	0.196	0.089
4.	10	0.380	0.271	0.109
5.	12.5	0.491	0.349	0.142

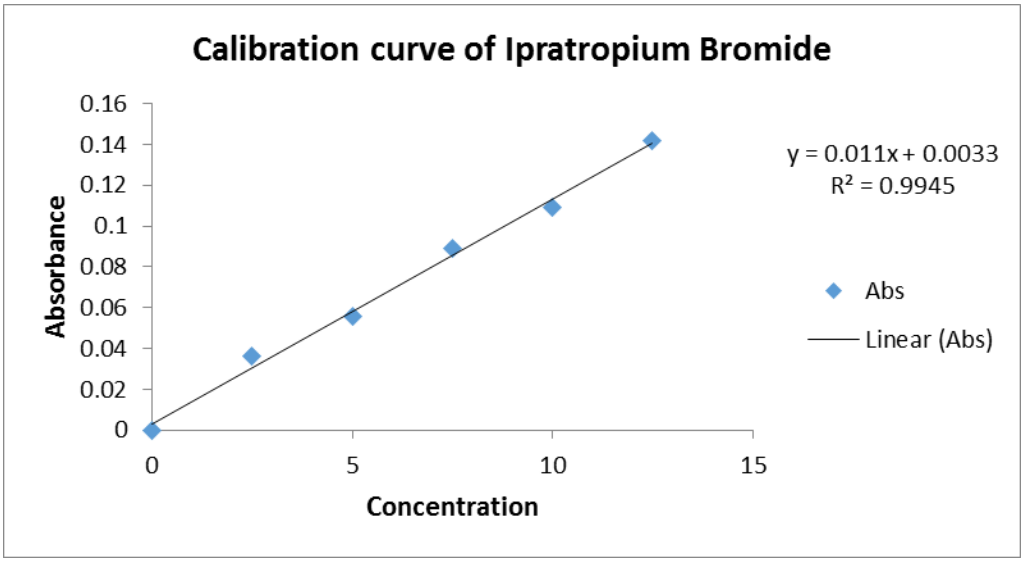


Figure No.3: Calibration curve of Ipratropium Bromide

METHOD VALIDATION:-

Linearity, precision and sensitivity were investigated as method validation parameters.

Linearity:-

Linearity is defined as an ability of the analytical procedure to obtain test results, which is directly proportional to the concentration of the analyte in the sample. The linearity range of ipratropium bromide is 2.5-12.5 µg/ml.

Accuracy:-

The Accuracy is defined as, analytical procedure it expresses the closeness of an agreement between the value that is accepted and either as a true conventional value. This study was carried out at three different levels that are 80%, 100%, 120%, by the standard addition method. Analyzed samples by triplicate by according to the method. Known amount of standard ipratropium bromide was a spike on the capsule sample. Check the absorbance and calculated % RSD and % recovery of ipratropium bromide.

LOD and LOQ:-

Detection limit is defined as the lowest amount of analyte in a sample can be detected. It is calculated based on the standard deviation of the absorbance of the same concentration that is a standard stock solution of ipratropium bromide. Limit of quantification is defined as; it is based on the standard deviation of the peak area of the same concentration that is standard

solution prepared. The limit of detection (LOD) and limit of quantification (LOQ) were calculated from the regression analysis data according to the following formula,

$$LOD = 3.3\ \sigma/S \text{ and } LOQ = 10\ \sigma/S$$

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

Precision:-

The reproducibility and repeatability of the derivative method were obtained by the follow-up of Intraday and Interday precision data for two concentrations within the linearity range. The mean, standard deviation (SD) and the relative standard deviation (RSD) were calculated.

Table No.2: Result of accuracy

Sr.No.	% Level	Spiked Concentration (µg/ml)	Amount recovered (µg/ml)	Absorbance	% Recovery	% RSD
1.	80 %	4.98	4.92	0.186	98.79	0.15
2.	100 %	7.93	7.90	0.279	99.62	0.20
3.	120 %	9.99	9.91	0.372	99.19	0.27

(Values are expressed as Mean ± SD of 3 readings)

Table No.3: Result of LOD and LOQ of ipratropium bromide

Drug	LOD (µg/ml)	LOQ (µg/ml)
Ipratropium bromide	2.89 (µg/ml)	8.76 (µg/ml)

Table No.4: Characteristics and validation parameters of Ipratropium Bromide

Parameters	**Values**	
	NaOH (214 nm)	**HCL (212 nm)**
Beer's law limit (µg/ml)	2.5 - 12.5	2.5 - 12.5
λmax (nm)	214 nm	212 nm
Regression equation (Y=a + bc)	y = 0.011x + 0.003	
Correlation coefficient (r^2)	0.996	
Slope (b)	0.011	
Intercept (a)	0.003	
Recovery (%)	103.61 ± 9.75	
SE of Intercept	0.004312	
SD of Intercept	0.009641	
LOD (µg/ml)	2.89 (µg/ml)	
LOQ (µg/ml)	8.76 (µg/ml)	

Table No.5: Precision results evaluated as % RSD values

Concentration (µg/ml)	**Intraday precision %RSD**		**Interday precision %RSD**	
	HCL	**NaOH**	**HCL**	**NaOH**
5	1.47	1.56	1.43	1.61
7.5	1.23	1.70	1.21	1.71

(Values are expressed as Mean of 3 reading)

RESULTS AND DISCUSSION:-

Linearity: - The linearity range of ipratropium bromide is 2.5-12.5 µg/ml.

Accuracy: - The result of accuracy data as shown in table 2. with % recovery and % RSD. The % recovery was found to be in the range of 98.79-99.62 % and % RSD is below 2.

LOD and LOQ:-

The limit of detection (LOD) and limit of quantification (LOQ) of ipratropium bromide was found to be 2.89 (µg/ml) and 8.76 (µg/ml) respectively.

Precision:-

The result of precision (Intraday and Interday precision) data is found to be 1.47, 1.43 & 1.56, 1.61 at concentration 5 µg/ml and 1.23, 1.21 & 1.70, 1.71 at concentration range 7.5 µg/ml of HCl and NaOH respectively.

The optical characteristics such as Beer's law limits, percent relative standard deviation, and accuracy were found to be within the limits and satisfactory. All of the analytical validation parameters for the proposed method were determined according to ICH guidelines. The method was found to provide high degree of precision and reproducibility. The recovery studies showed that the results were within the limit indicating no interference. The proposed method is simple, sensitive, accurate and precise and can be successfully employed for the routine analysis of the Ipratropium Bromide in bulk drug.

CONCLUSION:

The proposed method is simple, accurate, precise and selective for the estimation of Ipratropium Bromide in bulk drug. The method is economical, rapid and do not require any sophisticated instruments contrast to chromatographic method. Hence it can be effectively applied for the routine analysis of Ipratropium bromide in bulk drug.

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