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Original Article

DEVELOPMENT AND VALIDATION OF UV-SPECTROSCOPIC METHOD FOR ESTIMATION OF TIOTROPIUM BROMIDE IN API AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Objective: The current work intended towards the developed and validated UV spectrophotometric method for the estimation of Tiotropium Bromide in API and pharmaceutical formulation.

Methods: The UV spectrum of tiotropium bromide in methanol shows maximum absorbance at 230 nm. Calibration curve method was used for the estimation of tiotropium bromide in API and pharmaceutical formulation.

Results: Maximum absorbance obtained in 230 nm. Calibration curve plotted in concentration range 20-120 µm/ml exhibit the linearity relationship with line equation y=0.0057x+0.3319. The Accuracy was found to be 80-100.5%. The precision %RSD=0.1110, and the limit of detection(LOD)=4.12and limit of quantification (LOQ= 12.50. The method was found to comply all the validation parameters as per the ICH guideline in indicating the sensitivity of the method analyte.

Conclusion: This method is used as satisfactory for the routine analysis of tiotropium bromide in API and pharmaceutical dosage forms.

Keywords: Tiotropium bromide, UV Spectrophotometer, Methanol, Validation

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INTRODUCTION

The Tiotropium Bromide chemically is (1α, 2β, 4β, 5α, 7β,)-7-[(Hydroxydi-2-thieyl-acetyl) oxy]-9, 9-dimethyl-3-oxa-9-azoniatricyclo [3.3.1.0] [1]. Tiotropium is used as a maintenance treatment of chronic obstructive pulmonary disease (COPD). It may also be used as an add-on-therapy in people with moderate-to-severe asthma on medium to high dose inhaled corticosteroid (ICS) [2, 3] Tiotropium bromide smooth muscles relaxation and bronchodilation [4, 5]. A tiotropium metered inhalation spray is indicated for the maintenance of bronchospasms in COPD to prevent exacerbation of COPD and to treat asthma in patient six or more year old [6, 7]. It is used by inhalation through the mouth [8, 9]. Onset typically begins within half an hour and lasts for 24 h. It is not, however, approved for acute exacerbation of COPD or acute worsening asthma [10, 11].

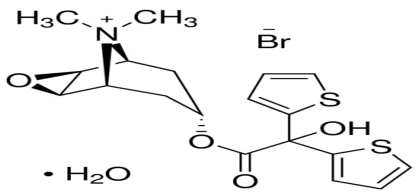

Fig. 1: Chemical structure of tiotropium bromide [1]

MATERIALS AND METHODS

Selection of solvent and instrument

Tiotropium bromide is dissolving in various solvents for trails of selecting the ideal solvent [12, 13]. Various solvents i.e. methanol, water, ethanol, acetonitrile. Tiotropium bromide is soluble in methanol, and better absorption was found to be at230 nm. UV-Visible Spectrophotometer (shimadzu AY220) [14-16]. Reagents and Materials is API-Tiotropium Bromide was obtained as a gift sample from the Vamsi Pharmaceutical Ltd. Solapur, Maharashtra. Capsule is purchased from the local pharmacy in Solapur. Brand name is Tiova (Cipla); methanol was used for this study.

Experimental work

Method development

Selection of detection wavelength

Dilution of Tiotropium bromide was prepared from the stock solution (50µg). Tiotropium bromide was scanned over a range of 200-400 nm. Drug showed maximum absorbance at 230 nm was selected as the wavelength for detection.

Preparation of standard drug solution

10 mg of Tiotropium bromide was weighed and transferred into a 10 ml volumetric flask containing methanol. Concentration of stock solution is (1000µg/ml). Then pipette out 2 ml form the stock solution and adjust to volume.

RESULTS AND DISCUSSION

Method validation

The method was validated for several parameters like a preliminary analysis of drug Linearity, Accuracy, Precision, Robustness, Ruggedness, Limit of Detection, Limit of Quantification and specificity of tiotropium bromide.

Preliminary analysis of drug

Observation and result of preliminary analysis of Tiotropium bromide.

Preliminary analysis of drug

Test	Observation	Result
Description	White powder	Complies
Solubility	Soluble in methanol and acetonitrile	Complies

The UV-Spectrum of Tiotropium bromide in methanol showed at max absorbance at 230 nm.

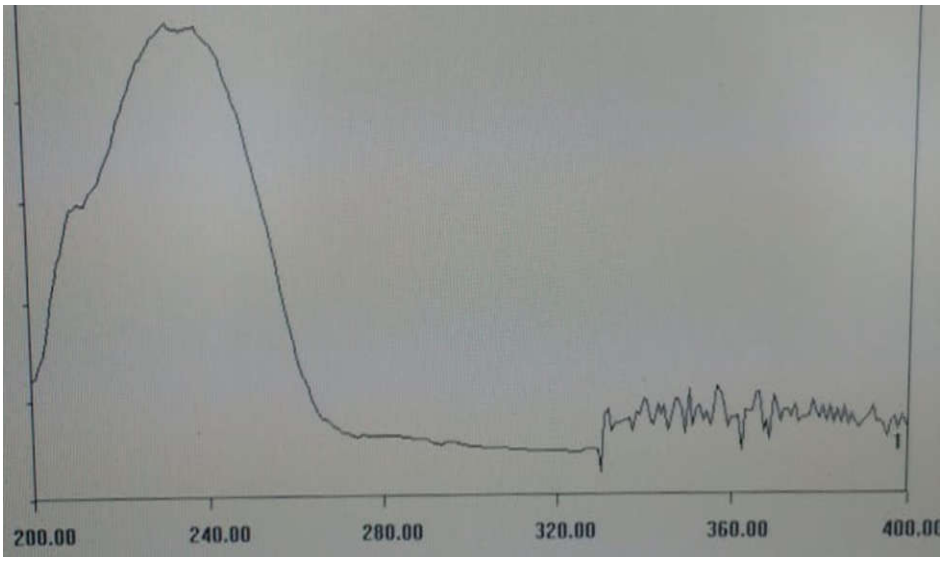

Fig. 2: UV visible spectrophotometer graph of tiotropium bromide

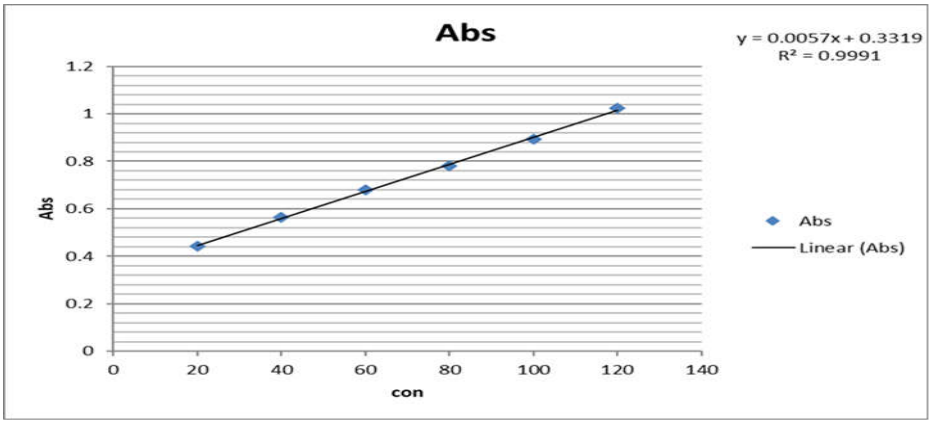

Fig. 3: Calibration curve for tiotropium bromide

Linearity and range

It is a linear relation between absorbance and concentration of drug was evaluated using three replicates over concentration range in 20-120(µg/ml) by making the replicates (fig. 3)

The wavelength for linearity was scanned at 230 nm. By taking five different concentrations for linearity the regression coefficient was found to 0.999 i.e. in the limit of standard. Hence linearity was found to be validated.

Accuracy

This study was carried out at three different levels that are 80%, 100%, 120%, by standard addition method. Analyzed sample by triplicate by according to the method. Known amount of standard tiotropium bromide was spike on the capsule sample. Check the absorbance and calculated (table 1)

Precision

Precision is defined as an analytical procedure is define the closeness of agreement between samples of measurements obtained from multiple sampling of the same homogenous sampling in specific conditions. It is determined by inter-day. Reading is taking 3 times on the same day. The percent relative standard deviation. (%RSD) was calculated (table 2)

Robustness

Robustness is a measure of its capacity of analytical procedure to remain unaffected by small changes or this method small deliberate variation in the method parameters. Main aim of this test is to create a method that allow for some variations in the parameters. In this study wavelength was change at±5 nm. Then robustness is calculated.

Table 1: Result of accuracy

S. No.	% level	Spike amount (µg/ml)	Spiked amount (wrt sample)	Abs.	Amount recovered	%RSD % recovery
1	80	79.440	79.4	0.829	80.651	0.9
2	100	99.300	99.3	1.051	100.550	0.3
3	120	119.160	119.2	1.227	100.5	1.5

Table 2: Result of intra-day morning precision

S. No.	Concentration (µg/ml)	Absorbance	SD	%RSD
1	60	0.678		
2	60	0.679		
3	60	0.679		
4	60	0.678	0.000753	0.111028
5	60	0.677		
6	60	0.678		

Table 3: Result of robustness

S. No.	Wavelength	Absorbance	SD	%RSD
1	230	0.444		
		0.434	0.006083	1.3919
		0.433		
		Avg= 0.43		
2	232	0.432		
		0.434	0.005859	1.3428
		0.443		
		Avg= 0.436		

By change in wavelength i.e. 232 nm. % RSD is less than 2% i.e. within the range. So parameter was validated (table 3)

Ruggedness

Ruggedness is defined as, reproducibility of the results when the defined method was performed under different analysts, laboratories, columns, chemicals, solvents, instruments, sources of reagents and etc.

Limit of detection

Detection limit is defined as, the lowest amount of analyte in a sample can be detected (table 6)

LOD= 3.3(SD/S) SD= Standard deviation, S= slope of the curve

Table 4: Result of ruggedness

Concentration (µg/ml)	Absorbance	Statistical analysis
60	0.678	Avg =0.678
60	0.679	SD =0.001
60	0.677	% RSD =0.147

Table 5: Result of ruggedness

Concentration (µg/ml)	Absorbance	Statistical analysis
60	0.679	Avg =0.678
60	0.678	SD =0.001
60	0.677	% RSD =0.147

By change in analyst and laboratory, there is no effect on absorbance with same conditions; hence, parameter was validated (table 4 and 5).

Table 6: Result of limit of detection

LOD(µg/ml)	4.12

Table 7: Result of limit of quantification

LOQ (µg/ml)	12.50

Limit of quantitation [17]

Limit of quantification is defined as; it is an individual analytical procedure is the lowest amount of an analyte in the sample, which can be an exact value (table 7)

LOQ=10(SD/S) SD= Standard deviation, S= slope of the curve

CONCLUSION

The proposed method is found to be accurate, precise, stable, linear, specific, and simple for quantitative estimation of tiotropium bromide in the bulk and pharmaceutical dosage form. Hence the present method is suitable for the routine assay of tiotropium bromide in bulk and pharmaceutical formulation.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. S Priyanka, M Anuradha, Kavita Waghray. A novel analytical method development and validation of Tiotropium bromide and formaterol fumarate pharmaceutical dosage form by using RP-HPLC method. Int J Curr Trend's Pharm Res 2019;7:25-30.
2. Anuja S Nevse, Savita Yadav, Ravindra Purohit, Janhavi R Rao. Development and validation of HPTLC method for estimation of Tiotropium bromide monohydrate in dry powder inhalation dosage form. World J Pharm Pharm Sci 2016;5:795-802.
3. Suthakaram R, Bikshapathi D, Sudha Parimala. Rp–HPLC method development and validation for quantitative estimation of Tiotropium bromide and oldaterol. Int J Biomed Investigation 2018;1:2581-4745.
4. Raman N Kanchave, Sanjay R Chaudhari, Mayura Kale, Rajendra D Wagh. Simultaneous estimation of formaterol fumarate and tiotropium bromide by RP-HPLC in dry powder inhaler. Inventi J 2013;4:976-3813.
5. Ravi P Pulla, BS Sastry, Y Rajendra Prasad, N Appala Raju. RP-HPLC method for simultaneous estimation of formaterol fumarate, tiotropium bromide and ciclesonide in pharmaceutical metered dose inhalers. Asian J Res Chem 2011;4:585-90.
6. K Srinivasu, J Venkateswara Rao, N Appala, K Mukkanti. Simultaneous RP-HPLC method for the estimation of formaterol fumarate and Tiotropium bromide in the pharmaceutical dosage form. Asian J Chem 2010;22:3943-8.
7. Ehab Farouk Elkady, Marwa Hosnytammam, Ayman Abo Elmaaty. Development and validation of RP-HPLC method for simultaneous estimation of tiotropium bromide, formaterol fumarate and olodaterate HCL in bulk and method dose aerosols, application to olodaterol HLC forced degradation study and degradation kinetics. Springer; 2017.
8. ICH, Q2 (R1) Validation of analytical procedures: text and methodology, International conference on harmonization; 1996.
9. Dave Sign, Arjun Ravi, Katie Kane, Tess Schmalbach, Dvid L Hava. The pharmacokinetics, pharmacodynamics and tolerability of PUR0200, A novel tiotropium formulation in chronic obstructive pulmonary disease. Br Clin Pharmacol 2018;84:2097-105.
10. Bhairam Bhoomalah, Anireddy Jayashree. Simultaneous quantification of olodaterol and tiotropium bromide by high-performance liquid chromatography. Asian J Chem 2017;29:145.
11. Sunita Sule, Sushma Ambadekar, Abhay Singh, Phalguni Naik. A rapid and stability-indicating RP-HPLC method for simultaneous determination of tiotropium bromide, formaterol and ciclesonide in a dry powder inhaler. World J Pharm Res 2014;3:819-30.
12. Jngduan Chi, Fumin Li, Rand Jenkins. Ultrasensitive sub-pg/ml. Determination of tiotropium bromide in human plasma by 2D HPLC-MS/MS. Challenges Solution 2016;8:385-95.
13. Jaime Algorta, Laura Andrade, Marte Medna, Valentin Kirkov, Sacha Arsova, Fumine Li. Pharmacokinetic bioequivalence of two inhaled tiotropium bromide formulation in healthy volunteers. Springer 2016;36:753-62.
14. Jung Sunwoo, Su-Jin Rhee, Seung Hwan Lee, In-Jn Jang. Pharmacokinetic characteristics of fluticasone, salmeterol, and tiotropium after concurrent inhalation. Transl Clin Pharmacol(TCP) 2017;25:85-92.
15. BD Shah, Susu Kumar, Yogesh C Yada. Analytical method development and validation of tiotropium bromide and formaterol fumarate metered-dose inhaler by using RP-HPLC method. Asian J Biochem Pharm Res 2011;1:145-58.
16. Anjali P Kokane, Varsha Tegeli, Bhagyashri S Shinde. UV spectroscopy method development and Validation for estimation of Ipratropium bromide in API and pharmaceutical dosage form. Int J Chem Pharm Res 2020;12:69-73.
17. Mohammed bouhajb, Zia Tazd. An evaluation of the pharmacokinetics of tiotropium following a single-dose inhalation in healthy subjects using an ultra-sensitive bioanalytical method. Taylor Francis Online 2019;45:1915-20.