Quality-By-Design Assisted UV Spectrophotometric Method for Estimation of Brimonidine Tartrate in Bulk and Pharmaceutical Dosage Forms

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Abstract:

A robust and economical UV spectrophotometric method was established and systematically validated for the quantitative determination of brimonidine tartrate in bulk drug and pharmaceutical dosage forms. The analysis was performed using a suitable solvent system, where brimonidine tartrate exhibited optimal absorbance at its characteristic wavelength. The method demonstrated linearity over a defined concentration range, conforming to Beer–Lambert's law with a high correlation coefficient. Validation of the proposed method was carried out in compliance with ICH guidelines. Method accuracy was verified through recovery studies, while precision was assessed by repeatability and intermediate precision experiments. The validated method exhibited satisfactory sensitivity, reproducibility, and robustness. Application of the method to a marketed pharmaceutical formulation confirmed its suitability for routine quality control, as no interference from formulation excipients was observed. Owing to its simplicity, rapidity, and cost-effectiveness, the proposed UV spectrophotometric method is well suited for regular analytical evaluation of brimonidine tartrate in quality assurance laboratories.

Keywords ; Brimonidine tartrate assay, UV–visible spectroscopy, Analytical method optimization, Regulatory validation, pharmaceutical formulation analysis, Quality assurance testing.

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Introduction

Brimonidine tartrate is a selective α_2 adrenergic receptor agonist widely used in ophthalmology for the management of glaucoma and ocular hypertension. It effectively reduces elevated intraocular pressure by decreasing aqueous humour production &enhancing uveoscleral outflow. It is commonly administered as ophthalmic solutions in concentrations such as 0.1- 0.2%.

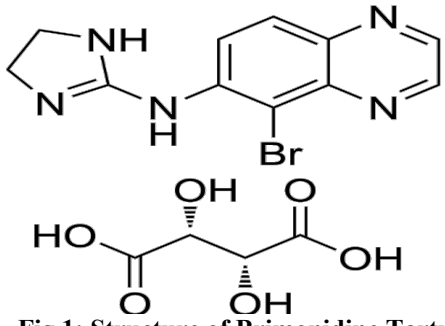


Fig.1: Structure of Brimonidine Tartrate

2. Materials and Methods

2.1 Chemicals and Reagents

- Brimonidine Tartrate (API)
- Distilled water (solvent)
- 0.01M HCL.
- Alphagan- formulation

2.2 Instrumentation

- UV-Visible spectrophotometer (Shimadzu UV-1800)
- Quartz cuvettes (1 cm path length)
- Electric digital balance (Shimadzu)

2.3 Selection of solvent

Brimonidine tartrate freely soluble in 0.01M HCL and water. On the basis of investigation 0.01MHCL was selected as a solvent.

Preparation of 0.01m HCL

In 25 ml of graduated flask take 0.02075 ml of concentrated HCL make up with distil water.

2.4 Preparation of Standard Stock Solution

Accurately weigh 5mg of Brimonidine tartarate and transfer into 10 ml volumetric flask. Add 5ml of solvent 0.01MHCL into volumetric flask to dissolve completely and finally make up the volume up to the mark with solvent.

Preparation of sample:

Accurately weigh 10mg of brimonidine tartrate. Transfer it into 10ml volumetric flask. Dissolve and dilute to volume with 0.1M HCL to obtain concentrations 0f 10 - 60µg/ml, using a micropipette.

2.5 Determination of λmax

Prepare a 10µg/ml solution of brimonidine tartrate scanned the solution in the wavelength range of 200-400nm&max absorbance((λmax) was observed at 240nm.

3. Validation Parameters

3.1 Linearity

Standard solutions of brimonidine tartrate in the conc range of 10–60 µg/mL were prepared& analysed under the optimized conditions. A calibration curve was constructed by plotting absorbance vs concentration & linearity was evaluated by linear regression analysis.

Table No.1: Linearity values of Brimonidine Tartrate

S.NO	CON(µg/ml)	ABS
1	10	0.156
2	20	0.249
3	30	0.343
4	40	0.436
5	50	0.510
6	60	0.606

fig 2. Calibration curve of Brimonidine tartrate

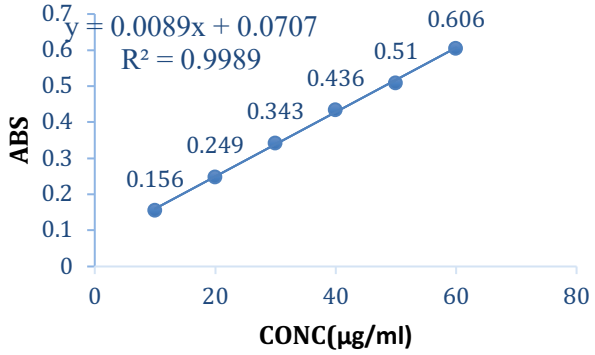
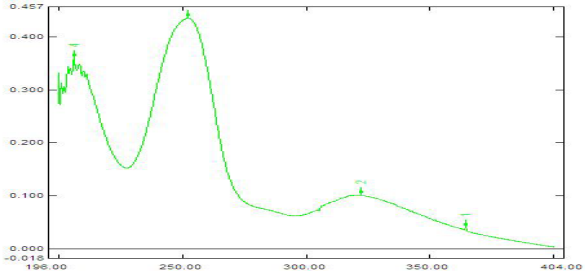


fig 3. Selected wavelength



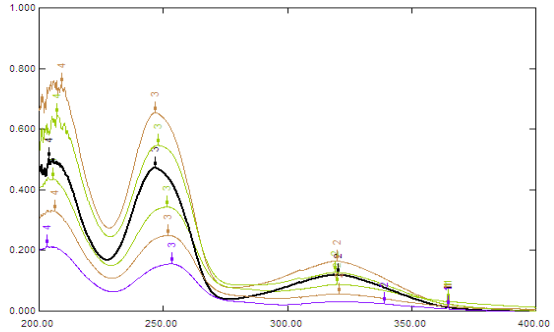


fig 4:Overlay of Brimonidine Tartrate

3.2 Accuracy (Recovery)

Pre-analysed samples were spiked with known quantities of the standard drug at 80%, 100%, and 120% of the nominal concentration. The spiked samples were analysed using the proposed method, and the percentage recovery was calculated to assess the accuracy of the method.

S. no	Spike level (%)	Absorbance	Amount added (µg/mL)	Amount found (µg/mL)	%Recovery	% Mean Recovery

1	80 %	0.43	40.025	39.59	98.92	100.61
2		0.44		40.51	101.22	
3		0.442		40.69	101.68	
4	100 %	0.535	50.031	49.26	98.46	100.30
5		0.538		50.28	100.49	
6		0.554		51.01	101.96	
7	120 %	0.64	60.038	58.93	98.15	99.79
8		0.66		60.77	101.22	
9		0.652		60.03	99.99	

Table No.2: Showing Accuracy results

3.3 Precision

The precision of the proposed UV spectrophotometric method was evaluated in terms of intra-day (repeatability) and inter-day (intermediate precision). Intra-day precision was assessed by analysing six replicate measurements of a standard brimonidine tartrate solution at the same concentration under identical experimental conditions within a single day. Inter-day precision was determined by analysing the same concentration on three consecutive days using the same analytical procedure**.**

Intra-day precision: six replicates %RSD = 1.51

Inter-day precision: same concentration analysed over 3 days → %RSD = 1.8

TableNo.3 Inter-Day Precision Performance of the Proposed Method

S.NO	**INTERDAY PRECISION (ABSORBANCE)**		
	Day 1	Day 2	Day 3
1	0.505	0.546	0.548
2	0.513	0.540	0.558
3	0.523	0.546	0.545
4	0.521	0.547	0.543
5	0.519	0.544	0.541
6	0.503	0.554	0.546
Mean	0.514	0.546167	0.546833
STD	0.007724	0.00418	0.005459
%RSD	**1.50**	**0.76**	**0.99**

Table No.4 : Intra-Day Precision Performance of the Proposed Metho

S.NO	**INTRADAY PRECISION(ABSORBANCE)**
1	0.505
2	0.512
3	0.523
4	0.511
5	0.525
6	0.525
Mean	0.516833
STD	0.00784
%RSD	**1.51**

3.4 Limit of Detection (LOD) and Limit of Quantification (LOQ)

The LOD and LOQ of the proposed UV spectrophotometric method were determined in accordance with the ICH Q2 (R1/R2) guidelines based on the calibration curve approach Linear regression analysis was performed to obtain the slope (S) and y-intercept of the calibration plot.

The standard deviation of the intercept **(σ)** was calculated from the regression data of the calibration curve.

- σ = standard deviation of intercept (0.0027)
- S = slope (0.018)

Table No.5: LOD&LOQ Values Obtained from Calibration Curve

S.NO	**Parameter**	**Standard Deviation**	**Slope**	**LOD&LOQ(µg/ml)**
1	Limit of detection (LOD)	0.00784	0.0089	2.90
2	Limit of quantitation (LOQ)			8.80

3.5 Robustness

The robustness of the developed UV spectrophotometric method was evaluated by introducing small, deliberate variations in the analytical conditions.

The wavelength of maximum absorbance was varied by ± 2 nm from the selected λmax analyses were performed at each altered wavelength.

For each modified condition, absorbance measurements were recorded and the results were evaluated by calculating the percentage relative standard deviation (%RSD) to assess the effect of the deliberate variations on the method performance**.**

Table No.6&7: Results showing Robustness data

S.no	Robustness parameter	Wave length(nm)	Absorbance ± Std. Deviation (n=3)	% RSD
1.	Wavelength (±3nm)	247nm	0.509 ± 0.00125	0.24
2.		250nm	0.521 ± 0.00163	0.31
3.		253nm	0.513 ± 0.00432	0.85

Table No.7: solvent proportion

S.no		Concentration	Absorbance ± Std. Deviation (n=3)	%RSD
1.	Solvent proportion	0.005M	0.542 ± 0.00544	0.99
2.		0.01M	0.547 ± 0.00809	0.56
3.		0.015M	0.522± 0.0045	0.85

STABILITY STUDIES:

Forced degradation studies of brimonidine tartrate were carried out to evaluate the stability of the drug substance under various stress conditions, in accordance with ICH guidelines. A standard solution of brimonidine tartrate was prepared in the selected solvent system and subjected to different stress environments, including acidic, alkaline, oxidative, photolytic, and thermal conditions.

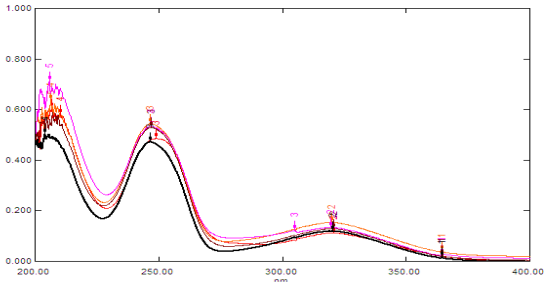
For acidic and alkaline degradation, aliquots of the standard drug solution were treated separately with appropriate concentrations of hydrochloric acid and sodium hydroxide, respectively, and maintained for a specified period at room temperature.

Following stress treatment, all samples were appropriately diluted and scanned over the wavelength range of 200–400 nm using UV spectrophotometry. The obtained spectra were compared with that of an unstressed sample, and overlay spectra were generated to evaluate any changes in spectral characteristics under the respective stress conditions.

Table No.8: Stress Degradation studies of Brimonidine Tartrate

S.No	Stress conditions	Absorbance	% Assay	% Degradation
1.	0.1M HCL	0.570	99.8	0.2
2.	0.1M NaOH	0.485	98.34	1.66
3.	Hydrogen peroxide (H2O2) 3% v/v	0.529	97.42	2.58
4.	Thermal (70oC)	0.544	98.52	1.48
5.	Photolytic (UV)	0.534	98.89	1.11

FIG 5: Overlay spectrum of Stability studies



overlay spectrum of Brimonidine Tartrate in various stress degradation studies

Results and Discussion

The proposed UV spectrophotometric method for the quantitative estimation of brimonidine tartrate was systematically evaluated through comprehensive validation studies in accordance with ICH guidelines. The method demonstrated a strong linear relationship between absorbance and concentration over the studied range, as evidenced by a high correlation coefficient (r^2 = 0.9989), confirming adherence to Beer–Lambert's law and suitability for quantitative analysis.

Accuracy studies conducted by the standard addition method revealed recovery values in the range of 99–100%, indicating that the method is free from interference by formulation excipients and is capable of producing reliable and unbiased results. Precision was assessed through intra-day and inter-day studies, with percentage relative standard deviation values consistently below 2%, demonstrating excellent repeatability and intermediate precision of the analytical procedure.

5. Conclusion

The developed UV spectrophotometric method for estimation of Brimonidine Tartrate is simple, precise, accurate, and validated as per ICH Q2(R1). It is recommended for routine analysis in bulk drugs and pharmaceutical formulations. In addition to its proven antiglaucoma efficacy, brimonidine tartrate has demonstrated neuroprotective potential and is also employed at low concentrations for the relief of ocular redness. The drug shows good ocular tolerability, rapid onset of action, and suitability for long-term therapy. Advances in pharmaceutical formulations, such as sustained-release systems and combination therapies, have further improved its therapeutic outcomes and patient compliance.

References

1. Mukthinuthalapati Mathrusri Annapurna,,"Novel Analytical Spectrophotometric Methods for the Quantification of Brimonidine Tartrate", Journal of chemical and pharmaceutical sciences,2015, 0974-2115.

2.Gunasekar Manoharan and Mohammed Al Bratty ,"Development and Validation of UV Spectrophotometric and RP-HPLC Techniques for Simultaneous Estimation of Brinzolamide and Brimonidine Tartrate", Oriental journal of chemistry, 2016, 32(2).

3.Bilal J. Shaikh and Indrayani D. Raut, "Validated Spectrophotometric Method for Estimation of Brimonidine Tartrate in Bulk and Pharmaceutical Formulation", Indian j pharm Sci. 2014, 76(3); 225-229

4.Prakash Bhagav, Pandurang Deshpande, Development and Validation of Stability Indicating UV Spectrophotometric Method for the Estimation of Brimonidine Tartrate in Pure Form, Der Pharmacia Lettre, 2010; 2(3);106 - 122.

5.S.S. Mandan, Development and Validation of HPLC Method for Estimation of Brimonidine Tartrate as Bulk Drug and in Ophthalmic Formulation; Journal of Drug Delivery & Therapeutics, 2017; 7 (7); 146-149.

6.Mandan SS, Nerpagar AV & Laddha UD (2017) – HPLC method development for estimating brimonidine tartrate. J Drug Delivery Ther;7(7):146-59. DOI:10.22270/jddt.v7i7.1616.

7.Aktham Mestareehi (2026) – Stability-indicating RP-HPLC quantification of brimonidine tartrate (with timolol maleate). Scientific Reports. DOI:10.1038/s41598-025-33716-x.

8.Hiral S. Popaniya et al. (2023) – Stability-indicating RP-HPLC method for brimonidine tartrate and timolol maleate in glaucoma treatment. IJBPAS 12(2):561-571.

9.Choradiya & Patil (2022) – Nanoemulsion formulation of brinzolamide and brimonidine tartrate. Thai J Pharm Sci. DOI:10.56808/3027-7922.2623.

10.Prabhu P et al. (2010) – Preparation/evaluation of brimonidine tartrate niosomes as ocular delivery system. Journal of Pharmaceutical Research and Health Care.