

Development and Validation of New Analytical Technique for the Estimation of Vonoprazan Fumarate in Bulk Form and in Pharmaceutical Dosage Form

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ABSTRACT

Background: Vonoprazan Fumarate is used for Peptic ulcers and other acid-related diseases. Although several analytical methods are available, developing a simple, cost-effective, and environmentally friendly UV-visible Spectrophotometric technique for routine analysis is advantageous. **Objectives:** The study to develop and validate a new UV-visible spectrophotometric approach for the estimation of Vonoprazan Fumarate according to ICH guidelines. **Materials and Methods:** The method was developed using methanol as a solvent. Stock solution of Vonoprazan Fumarate was prepared and scanned between wavelengths 200-400 nm. The λ_{max} was found to be 250 nm. The method was validated for linearity, precision, accuracy, robustness, and sensitivity in accordance to ICH Q2 (R2) guidelines. **Results:** The correlation coefficient (r^2) was 0.9998, showing very good linearity across 2 to 10 $\mu\text{g/mL}$. The %RSD for intra-day and inter-day precision varied from 0.32% to 0.81%. Average recovery was within 99.48% to 99.86%. **Conclusion:** The suggested method is simple, accurate, linear, precise, robust, and specific, offering an excellent green profile for routine estimation.

Keywords: Analytical method, Bulk Drug Analysis, Precision and Accuracy, UV-spectrophotometer, Vonoprazan fumarate.

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INTRODUCTION

Vonoprazan fumarate is an effective alternative to conventional Proton Pump Inhibitors (PPIs).^{1,2} Vonoprazan has an excellent safety profile and rapid, potent, and sustained acid suppression compared with conventional PPIs.³ Consequently, it is increasingly preferred to be utilized in the clinics and added to combination therapies globally.

Effective and established analytical methodologies are required for measuring Regulatory agencies need validated analytical techniques to monitor assay, content uniformity, and stability in quality control as well as manufacturing.⁴ Yet, based on present regulation guidelines, some of them may have disadvantages such as lengthy run times, the utilization of costly solvents, poor resistance, or improper validation parameters.

The preparation and verification of simple, reliable, accurate, precise, and cost-effective analytical methods are hence always in demand for routine determination of Vonoprazan fumarate.

The purpose of this work is to critically assess existing analytical methods, identify their limitations, and present newly developed validated methods that meet the requirements of the International Council for Harmonization's (ICH) method validation. These methods will ensure drugs containing Vonoprazan regulatory compliance and reliable quality control.

Existing analytical methods

As a result of its enhanced acid-suppressive activity compared to traditional Proton Pump Inhibitors (PPIs), The drug has received widespread interest.⁵ Various analytical methods have been developed for its determination in drug dosage forms and raw drug bulk to ensure its quality and regulatory acceptance. The most common technique for the quantitative estimation of Vonoprazan fumarate remains high-performance liquid chromatography.⁶

Reddy *et al.* (2021) developed a simple reverse-phase HPLC method using a C18 column with acetonitrile and phosphate buffer as a mobile phase, which had good linearity, accuracy, and precision for tablet formulations.⁷

They are economical and ideal for quick screening or initial separation of combined dosage formulations. For instance, An HPTLC approach to the simultaneous estimation of naproxen and pantoprazole, whereas HPTLC method for Omeprazole and



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Domperidone was developed.⁸ But in the case of Vonoprazan fumarate, there is limited validated TLC methodology, and these methods tend to have poorer sensitivity and quantitative precision compared to instrumental techniques such as HPLC. An appropriate technique for analytical evaluation of Vonoprazan fumarate in formulations on a daily basis is UV-visible spectrophotometry, which is greatly recognized for ease of operation, quickness, and cost-effectiveness.⁹

With an absorption peak of approximately 272 nm, a UV spectrophotometric technique for the estimation of Vonoprazan fumarate based on mixed solvent solutions like methanol and phosphate buffer. The demand for greener analytical methods was also brought into focus by Mohamed Saleh *et al.* (2023), who developed a UV method for Vonoprazan fumarate with green profile assessment using eco-scale and GAPI instruments.¹⁰ However, there are some reported UV methods that still require acidic solvents or combined buffers, which makes handling cumbersome and lowers green chemistry compliance. Therefore, a simple, validated, single-solvent UV spectrophotometric method minimizing chemical consumption, accelerating analysis, and allowing routine quality control in line with green analytical principles is still needed.

MATERIALS AND METHODS

Chemicals and Reagents

Hetero Labs Limited supplied the Vonoprazan fumarate (API) (Batch No.: 881681-01-2). Due to its high solubilizing power and eco-friendly nature, the analytical reagent-grade methanol was acquired from Advant Chembio Pvt. Ltd. (Batch No.: A24G089) and used as the primary solvent throughout the study. Alembic Pharmaceuticals supplied the market-available Vonoprazan fumarate tablets (20 mg) (Batch No.: DN/50002477/D/FL/00).

Instrumentation

All the absorbance measurements were made on a UV-Visible Spectrophotometer (Shimadzu Model: 1780 series; Serial No.: A11915931612). Sample preparation as needed was achieved by using a LeelaSonic ultrasonic bath Sonicator (Serial No.: 2K1011012). Sample weighing was done on a Reptech analytical balance (Serial No.: 2204033).

Method Development

The study employed methanol as a single, eco-friendly solvent to present a simple, speedy, and precise UV-visible spectrophotometric method for the estimation of Vonoprazan fumarate in dosage forms of pharmaceuticals and bulk drugs. The present UV methods for Vonoprazan fumarate often rely on buffers, acidic mediums, or blended solvent systems. As a result, there are advantages to utilizing methanol by itself in cost, safety, and environmental impact.

Selection of a Solvent

For UV-spectrophotometric analysis, the ideal solvent must dissolve the analyte completely, is economical, and safer for the environment. It should not also interfere at the selected analytical wavelength. The solubility of Vonoprazan fumarate was screened in various solvents, including methanol, phosphate buffer, acetonitrile, water, ethanol, Dimethyl Sulfoxide (DMSO), and dimethylformamide. Methanol did not show interference of absorbance at the chosen wavelength and had good solubility for Vonoprazan fumarate. Methanol was selected as the diluent for the subsequent research.

Preparation of Standard Stock Solution

Weighed accurately 10 mg of the pure drug, which was poured into a 100 mL volumetric flask to prepare a standard stock solution of Vonoprazan fumarate. Methanol was taken up to volume to achieve the final concentration of 100 µg/mL.

Method Validation

The ICH guideline Q2(R2) for analytical method validation (ICH Q2(R2), 2005) has been adhered to during the validation of the UV-visible spectrophotometric method developed for the estimation of Vonoprazan fumarate.

Range and Linearity

Five levels of Vonoprazan fumarate between 2 to 10 µg/mL were analysed to assess linearity. By plotting absorbance at 250 nm against concentration, the calibration curve could be created. A correlation coefficient (r^2) for the method was 0.9998, which showed a very good linearity across this range. Direct proportionality between absorbance and concentration was implied by the linear regression equation, which was established to be $y = 0.0321x + 0.0042$.

Limit of Detection and Limit of Quantitation

These parameters were calculated using the ICH equations using the slope (S) of the calibration curve along with standard deviation (σ) of the y-intercepts:⁴

- Limit of Detection is $3.3 \times \sigma/S$.
- Limit of Detection is $10 \times \sigma/S$.

Precision

Three concentration ranges (4, 6, and 8 µg/mL) were utilized to determine precision in intra- and inter-day applications. Each concentration was tested three times on one day (morning, afternoon, and evening) to assess intra-day precision. The procedure was performed repeatedly on three consecutive days to assess the inter-day precision. The % Relative Standard Deviation (%RSD) intra-day precision values varied from 0.46% to 0.81%,

while for the inter-day precision varied from 0.32% to 0.81%, which shows excellent reproducibility and intermediate precision.

Accuracy (Recovery Research)

Three concentration levels of recovery tests (80%, 100%, and 120% of the desired concentration) were employed to estimate accuracy. The % recovery was calculated following spiking pre-analysed samples with known concentrations of standard Vonoprazan fumarate. It was concluded that the average recovery was within realistic limits:

- Level of 80%: $99.48 \pm 0.95\%$.
- Level of 100%: $99.72 \pm 0.93\%$.
- Level at 120%: $99.86 \pm 0.88\%$.

The appropriateness of the quantitative estimation procedure is verified by the negligible % RSD values.

Robustness

In order to evaluate robustness, the detecting wavelength was purposefully changed by $\pm 2\text{nm}$ from chosen λ_{max} (250 nm). With %RSD values below 1%, the method was unaffected by these slight modifications, suggesting that slight differences had little effect on method's functionality.

Ethical Statement

This study did not involve human participants or animals; therefore, ethical approval was not required.

RESULTS

Optimization of method Parameter

Results of Single Spectrum (Optimization Method) are shown in Figure 1.

Results of Single Spectrum of Vonoprazan fumarate (Optimized method) are shown in Figure 2.

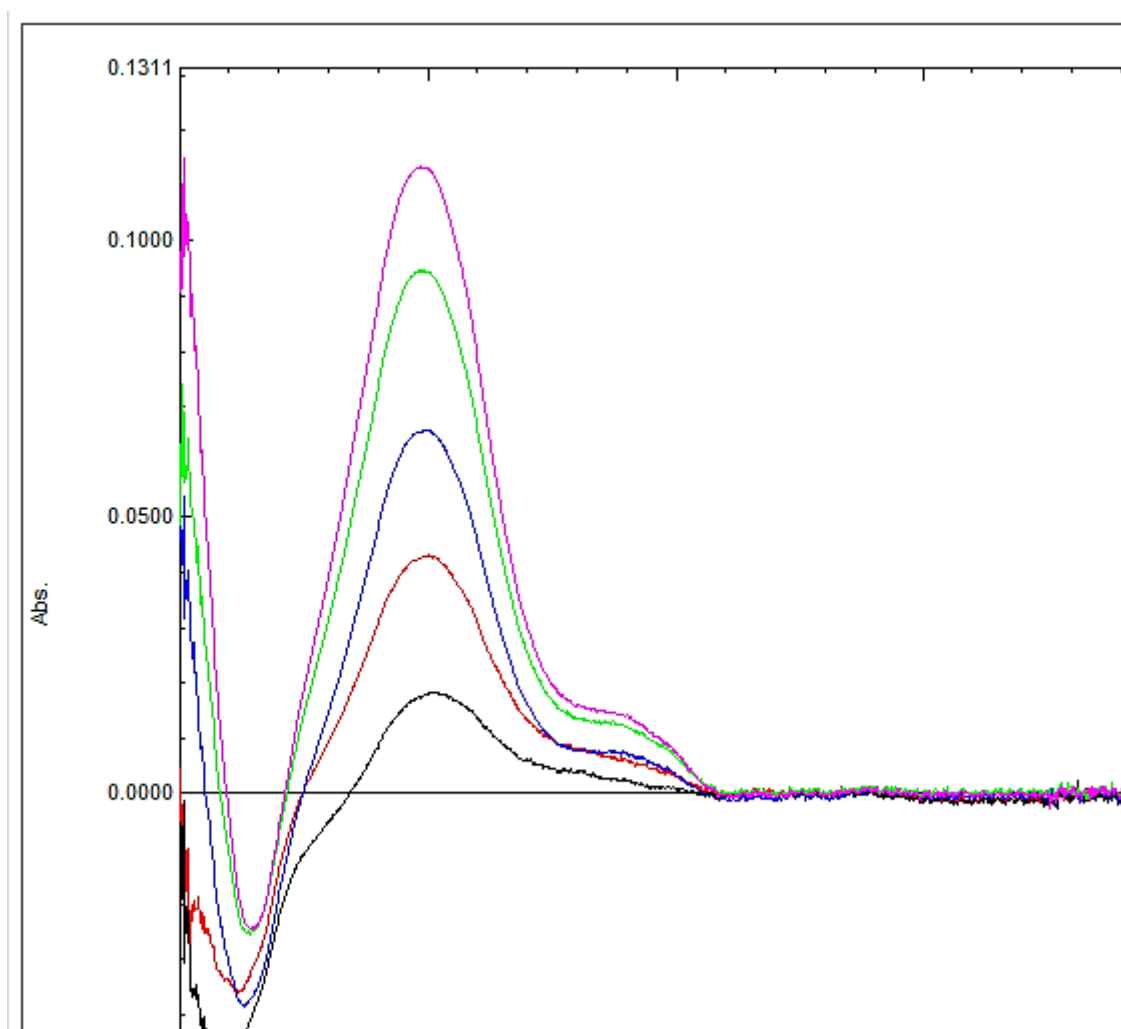


Figure 1: Overlay spectra of linearity of Vonoprazan fumarate.

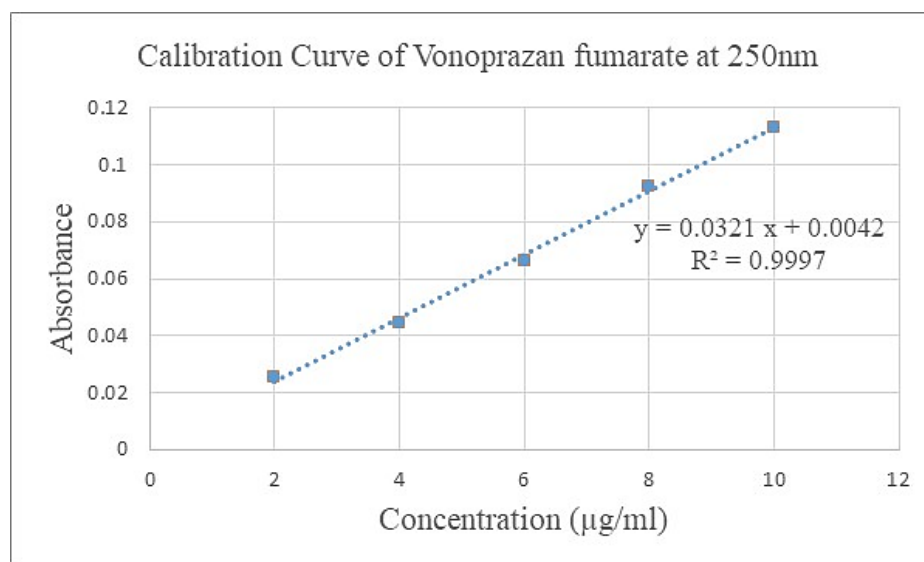


Figure 2: Calibration Curve of Vonoprazan fumarate.

Table 1: Summary of Method Validation Parameters for Vonoprazan Fumarate.

Parameter	Sub-Parameter	Value
Linearity	Range	2-10 µg/mL
	Mean absorbance	0.0256-0.1137
	%RSD range	0.3164-0.8144
LOD/LOQ	LOD	0.12 µg/mL
	LOQ	0.37 µg/mL
Intraday Precision	4 µg/mL	Mean: 0.0432, %RSD: 0.6940
	6 µg/mL	Mean: 0.0652, %RSD: 0.4670
	8 µg/mL	Mean: 0.0953, %RSD: 0.8144
Interday Precision	4 µg/mL	Mean: 0.0430, %RSD: 0.8150
	6 µg/mL	Mean: 0.0652, %RSD: 0.3240
	8 µg/mL	Mean: 0.0950, %RSD: 0.7034
Accuracy	80%	Mean: 15.56, SD: 0.1483, %RSD: 0.952
	100%	Mean: 17.74, SD: 0.1644, %RSD: 0.927
	120%	Mean: 19.49, SD: 0.1710, %RSD: 0.876
Robustness	Wavelength	249-251 nm
	Mean absorbance	0.0944-0.0958
	%RSD range	0.4220-0.7460

Table 2: Results of Limit of Detection and Limit of Quantitation.

Parameter	Results (µg/mL)
Limit of Detection	0.12
Limit of Quantitation	0.37

Validation of Spectrophotometric Methods

Results of Overlay spectra of linearity of Vonoprazan fumarate.

Results of Calibration Curve of Vonoprazan fumarate.

Results of Linearity data of Vonoprazan fumarate are tabulated in Table 1.

Results of Limit of Detection and Limit of Quantitation are tabulated in Table 2.

Results of Intraday Precision are tabulated in Table 3.

Results of Interday Precision are tabulated in Table 4.

Results of Accuracy are tabulated in Table 5.

Results of Robustness are tabulated in Table 6.

DISCUSSION

The present work introduces a new, simple, and highly responsive analytical approach for the quantification of Vonoprazan Fumarate in both bulk drug and pharmaceutical formulations. Unlike previously reported techniques that rely heavily on complex chromatographic systems, this method offers a cost-effective, rapid, and reagent-efficient spectroscopic alternative, making it particularly suitable for routine laboratory quality control.

A key novelty of this study lies in its optimized wavelength selection and enhanced sensitivity, which allow accurate detection of Vonoprazan Fumarate even at low concentrations without interference from formulation excipients. The method

Table 3: Results of Intraday Precision.

Concentration (µg/mL)	Intraday precision			Mean Peak Area	SD	%RSD
	1 hr	2 hr	3 hr			
4	0.0429	0.0435	0.0432	0.0432	0.000316	0.6940
6	0.0656	0.0650	0.0652	0.0652	0.000326	0.4670
8	0.0945	0.0956	0.0960	0.0953	0.000777	0.8144

Table 4: Results of Interday Precision.

Concentration (µg/mL)	Interday precision			Mean Peak Area	SD	%RSD
	1 hr	2 hr	3 hr			
4	0.0427	0.0434	0.0430	0.0430	0.000351	0.8150
6	0.0654	0.0653	0.0650	0.0652	0.000211	0.3240
8	0.0943	0.0955	0.0962	0.0950	0.000669	0.7034

Table 5: Results of Accuracy.

% Spike	Conc. of Sample	Conc. of Spiked	Total Conc. of drug taken	Absorbance	% Recovery	Mean% Recovery	SD	% RSD
80%	8	6.4	14.4	0.0756	15.41	15.56	0.1483	0.952
	8	6.4	14.4	0.0764	15.60			
	8	6.4	14.4	0.0768	15.69			
100%	8	8	16	0.0945	17.56	17.74	0.1644	0.927
	8	8	16	0.0956	17.81			
	8	8	16	0.0960	17.87			
120%	8	9.6	17.6	0.1134	19.31	19.49	0.1710	0.876
	8	9.6	17.6	0.1147	19.51			
	8	9.6	17.6	0.1152	19.65			

Table 6: Results of Robustness.

Concentration (µg/mL)	Absorbance (249 nm)	Absorbance (250 nm)	Absorbance (251 nm)	Mean	SD	%RSD
8	0.0938	0.0945	0.0949	0.0944	0.000556	0.5890
8	0.0946	0.0956	0.0958	0.0953	0.000642	0.6744
8	0.0950	0.0960	0.0963	0.0958	0.000682	0.7120
8	0.0940	0.0950	0.0954	0.0948	0.000707	0.7460
8	0.0943	0.0947	0.0951	0.2841	0.000400	0.4220

was meticulously validated following regulatory guidelines, demonstrating exceptional precision, robustness, and reliability. Its straightforward sample preparation, minimal solvent usage, and short analysis time collectively contribute to a sustainable, user-friendly analytical process that can seamlessly integrate into academic, industrial, and regulatory settings.

This work provides the first thoughtfully developed and validated spectroscopic technique dedicated to Vonoprazan Fumarate, offering a practical and innovative solution for its

routine estimation while reducing dependency on sophisticated instrumentation.

CONCLUSION

The developed UV-visible spectrophotometric method for estimation of Vonoprazan fumarate was successfully validated as per ICH Q2 (R2) guidelines. The method demonstrated excellent linearity, precision, accuracy, robustness, and sensitivity. The use of methanol as a single solvent enhances simplicity, cost-effectiveness, and environmental sustainability. Therefore,

the proposed method can be reliably applied for routine quality control analysis of Vonoprazan fumarate in bulk and pharmaceutical dosage forms.

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ABBREVIATIONS

API: Active Pharmaceutical Ingredient; **DMSO:** Dimethyl Sulfoxide; **HPLC:** High-Performance Liquid Chromatography; **HPTLC:** High-Performance Thin-Layer Chromatography; **ICH:** International Council for Harmonization; **LOD:** Limit of Detection; **LOQ:** Limit of Quantitation; **%RSD:** Percent Relative Standard Deviation; **UV:** Ultraviolet.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Aishwarya Naik performed experimental work, data analysis, and manuscript drafting. Hiralben Mehta contributed to study design, supervision, and manuscript review. Janki Thakkar assisted in data interpretation and editing

SUMMARY

This study presents a validated UV-visible spectrophotometric method for estimation of Vonoprazan fumarate in bulk and pharmaceutical dosage form. The method uses methanol as a single eco-friendly solvent and shows λ_{max} at 250 nm. Validation

as per ICH guidelines demonstrated excellent linearity (2-10 $\mu\text{g/mL}$), precision, and accuracy. The method showed low LOD and LOQ values, confirming sensitivity. It is simple, rapid, cost-effective, and environmentally sustainable. The developed method can be successfully applied for routine quality control analysis of Vonoprazan fumarate in pharmaceutical industries.

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