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Development and validation of RP-HPLC method for fast dispersible tablets of vonoprazan fumarate: Quantification and its application to forced degradation studies

Atta-Ur-Rehman[1], Farya Zafar[1]*, Kiran Qadeer[2] and Huma Ali[3]
[1]Department of Pharmaceutics, Faculty of Pharmacy, University of Karachi, Pakistan
[2]Department of Pharmaceutical Chemistry, Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Karachi, Pakistan
[3]Department of Pharmaceutics, Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Karachi, Pakistan

Abstract: **Background**: Vonoprazan fumarate (VF) is indicated to treat drug-induced peptic and gastroduodenal ulcers. Various chromatographic, fluorometric and spectrophotometric methods have been reported for the quantification and identification of known and unknown impurities of VF in pharmaceutical formulations and biological samples. **Objectives**: The study aimed to develop a robust and cost-effective HPLC validated method for the analysis of VF. The method is also capable of detecting all possible degradation products and is used to characterize the stability of the VF. **Methods**: An RP-HPLC method with UV detection (254 nm) using C8 column (4.6 X 150mm, 5µm) was developed and validated for the quantification of VF and used to detect all possible degradation products in fast-dispersible tablets. The method validation of fast dispersible VF tablets was performed by adopting various standard validation parameters (i.e. linearity, precision, accuracy, specificity, limit of detection, limit of quantitation and robustness). The forced degradation studies have been carried to investigate the stability of the VF as per ICH guidelines. **Results**: The tR of VF was 2.6 min. The method showed reproducibility within ±2%. The forced degradation studies show that VF is highly prone to degradation under alkaline conditions, while exhibiting greater stability in acidic media. The oxidative stress, photo and thermal degradation of VF show comparatively lesser degradation or relatively greater stability of VF. **Conclusion**: A simple, robust and cost-effective chromatographically validated method has been established to analyze fast-dispersible VF tablets and has been successfully applied to the stability characterization of VF.

Keywords: Forced degradation studies; Method validation; RP-HPLC; Vonoprazan fumarate

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INTRODUCTION

Vonoprazan fumarate (VF) (Fig. 1) is 1-(5-(2-fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1 H-pyrrol-3- 1H-pyrrol-3-yl)-N-methyl methanamine mono fumarate (Qiao *et al*., 2017; Yoneyama *et al*., 2016). It is a potassium competitive acid blocker (PCAB) and indicated to treat the drug-induced peptic and gastroduodenal ulcers, reflux esophagitis and eradication of Helicobacter pylori (Howden *et al*., 2025; Zhang *et al*., 2025; Mori and Suzuki, 2019) while eyes irritation is the major side effect that has also been reported (Cayman, 2022). Various high-performance liquid chromatographic (HPLC), spectrophotometric and chromatographic methods have been studied for the evaluation of VF. An ecofriendly chromatographic method for the analysis of VF with amoxicillin and clarithromycin has been developed (Ali *et al*., 2025). A similar method has also studied for H. Pylori abolition by triple therapy protocol with amoxicillin, metronidazole and vonoprazan (Mahghoub *et al*., 2024). The mixture of VF and aspirin was analyzed by using the ultraviolet spectrophotometric method (Abdelazim *et al*., 2023). A sustainable tri-hued method for the simultaneous estimation of binary and ternary mixtures of VF in combined pharmaceutical formulation and artificial gastric fluid has been reported by HPLC (Aboras *et al*., 2025). High-Performance Thin Layer Chromatography–a densitometric technique for the determination of vonoprazan fumarate as a stability-indicating method has also been reported (Parmar *et al*., 2025). The liquid chromatographic with mass spectrometric (LC-MS) analysis for the estimation of VF and the identification of known and unknown impurities of VF by using HPLC-UV technique has also reported (Liu *et al*., 2016). Liquid Chromatography with Mass Spectrometry (LC-MS) was used to quantify vonoprazan pyroglutamate and VF in rat plasma and tissues (Qiao *et al*., 2018). The LC–MS for the evaluation of VF and its metabolites in biological samples has also been reported (Yoneyama *et al*., 2016). An LC-ESI-MS/MS technique was established for the quantification of N-nitroso vonoprazan in pharmaceutical dosage forms and the active pharmaceutical ingredient (API) (Abuothman *et al*., 2024). Fluorometric analysis was employed for VF analysis in biological samples (Saraya *et al*., 2022). Ultrasensitive derivatization-free fluorimetric quantification of vonoprazan using a factorial design approach. were reported (El Hamd *et al*., 2024). ICH guidelines state that forced degradation studies have been very valuable for investigating the stability of drug samples in various pharmaceutical formulations under various stress conditions. Forced degradation analysis has also

**Corresponding author:* e-mail: farya.zafar@uok.edu.pk

been helpful in evaluating degradation products formed under stressed conditions in drug samples (Iram *et al*., 2016). Degradation studies of Clarithromycin, amoxicillin and vonoprazan in a pharmaceutical formulation were reported (Anusha & Sowjanya, 2024). Another study was conducted to observe the forced degradation effects on the film coated tablet of VF (Alzaghal *et al*., 2024).

The objective of this study is to design a simple, robust and cost effective HPLC method and its validation for the estimation of VF. This method is also able to detect all the possible degradation products which assure the quality of VF. The suggested methodology has also been successfully adopted to quantify VF in commercially available dosage forms and to characterize the stability of pharmaceutical products according to the ICH guidelines (ICH, 2023).

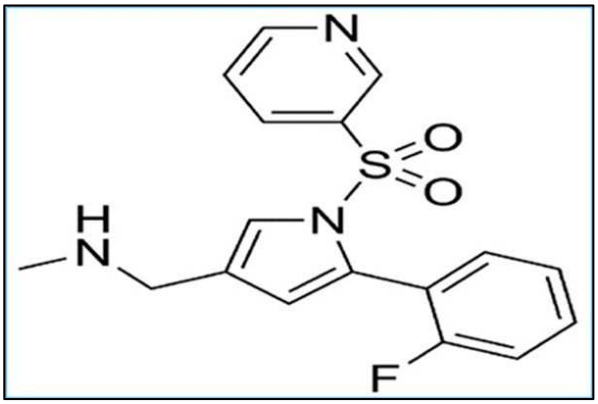

Fig. 1: Chemical structure of vonoprazan.

MATERIALS AND METHODS

Materials

Vonoprazan fumarate (VF) was obtained from Jiangxi Synergy Pharmaceutical Co., Ltd. Acetonitrile (HPLC grade) and analytical-grade solvents and reagents were obtained from Merck & Co., USA. All the reagents and samples were filtered and degassed using a Millipore filtration system, followed by sonication. Deionized water was consumed through the experiment using Millipore Milli-Q plus system.

Chromatographic conditions for HPLC analysis

The HPLC (LC-20AT, Shimadzu, Japan) with a diode-array detector (SPD-M20A, Shimadzu, Japan) was used to analyze VF. The analytical column was C8 (4.6 × 150mm, 5µm), Promosil Cat. No. PM851505-0. Serial No.039678. The injection volume was 20 µl with a flow rate of 1.5 ml/min. The chromatographic analysis was conducted at room temperature (25±1°C). The mobile phase and all solutions were sonicated prior to use. A wavelength of 254 nm was employed for the detection of VF. The method validation was also performed for the analysis of the drug in forced-degraded samples.

Preparation of buffer

Trifluoroacetic acid (1.2 ml) was taken in HPLC water (1000 ml), mixed, dissolved and adjusted to pH 3.0 with ammonia solution.

Preparation of mobile phase

500 ml of buffer (pH 3.0) and 500 ml of acetonitrile were taken, mixed well, filtered through a 0.45-micron filter and degassed.

Preparation of standard solution

Accurately weighed 13.6 mg of VF tablet powder (10mg of Vonoprazan) was placed in a 100 ml volumetric flask with 50 ml of mobile phase, then sonicated. The final volume had a concentration of 100 µg/ml or 0.1mg/ml.

Preparation of sample solution

Twenty tablets of VF, accurately weighed and crushed in a mortar and pestle to a fine powder, were taken. Approximately 100 mg of powder of crushed tablets having 10 mg of VF was taken into a volumetric flask (100 ml), stirred the solution by adding 50 ml of diluent manually for 5 min then sonicated (2 min). The final volume had a concentration of 100 µg/ml or 0.1mg/ml.

Forced degradation studies and stability studies

This method was developed to establish stability profile of the drug sample and its formulation as per the ICH guidelines (ICH, 2005). Fast dispersible (newly formulated) twenty tablets of VF were crushed to fine powder. Six replicate samples containing 100 mg of VF in 100 ml and their degraded samples were analyzed for the determination of VF under the following stress conditions:

Thermal degradation

The sample solution was exposed in thermal oven (DZ-1BCII) at a temperature of 50 ºC for 3 hr. To observe the effect of thermal degradation by chromatographic analysis, samples were withdrawn at 60 min intervals for up to 3 hrs.

Photodegradation

The photodegradation studies of drug sample were investigated by placing the sample solution under UV lamp at a wavelength of 300-800 nm for 3 hrs at room temperature. A 20 µl sample was collected at 60 min intervals for up to 3 hrs for further chromatographic analysis.

Chemical degradation

Oxidative degradation

1 ml of hydrogen peroxide (3.0%) is added to the sample solution and then kept for 3 hrs at 25±1°C. To observe oxidative degradation, the sample was withdrawn (20 µl) at 60-minute intervals up to 3 hrs for analysis.

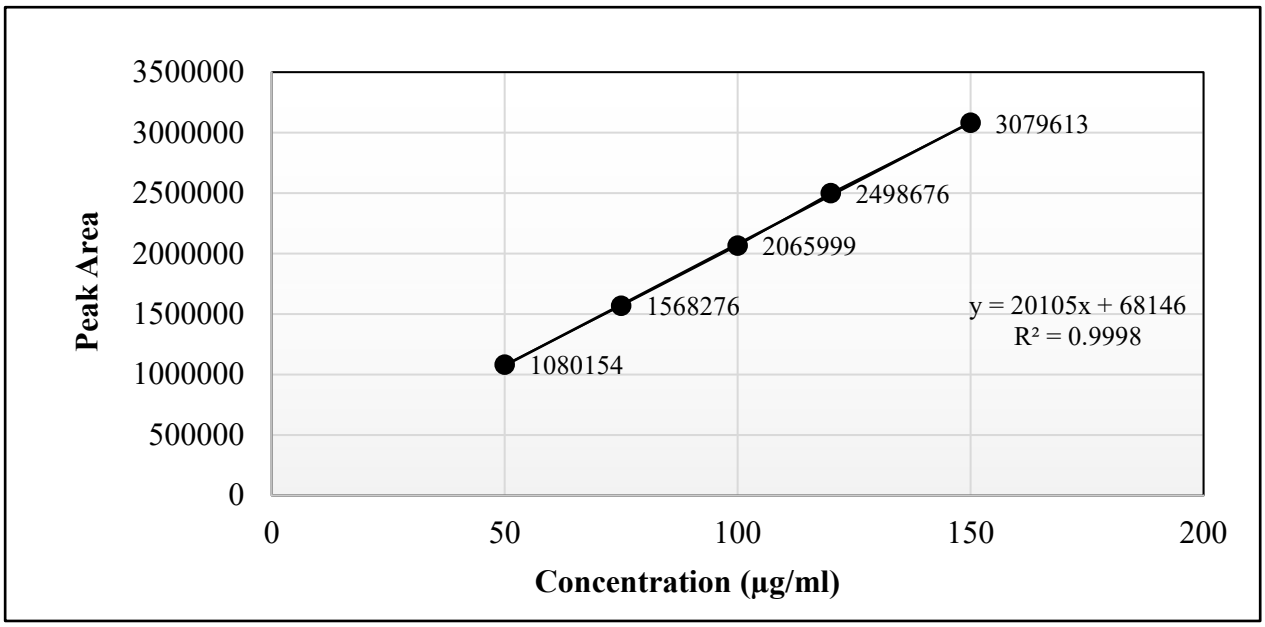

Fig. 2: Linearity plot of Vonoprazan fumarate 50–150 µg/ml).

Table 1: Validation data of VF.

Parameters	Results
Recovery range (%)	99.95-101.71
Accuracy ± SD[a]	100.57±1.105
(% RSD[b])	1.098
System suitability: (% RSD)	0.206
Retention time (min)	2.6
Theoretical plates	12,692
Tailing factor	1.595
Precision/Ruggedness (%RSD)	0.85
Intermediate precision (% RSD)	0.904%
95% CI (%)	100.81-101.89
Reproducibility (% RSD)	0.46
Specificity	No Interference observed at wavelength 254 nm
Linearity	0.9998
Detection limit (DL) (µg/ml)	2.33
Quantitation limit (QL) (µg/ml)	7.06
Robustness	No significant changes observed
Flow rate (ml/min) (%RSD)	1.0±0.2ml/min (0.097% RSD)
pH of mobile phase (%RSD)	3.0±0.2 (0.547 % RSD)
Detection wavelength (%RSD)	254±2.0nm (0.420% RSD)
Solution stability	Solution was stable at 7 days at room temperature.

[a]SD; Standard Deviation.

[b]RSD; Relative Standard Deviation.

Acidic hydrolysis/degradation
The sample solution containing hydrochloric acid (HCl) (1N, 1 mL) was kept at room temperature for 3 hrs. 20 µl sample was withdrawn for the HPLC analysis at zero time and after 3 hrs to observe the degradation of the sample after acidic hydrolysis.

Alkaline hydrolysis/degradation
The sample solution, added with 1 ml of sodium hydroxide (NaOH) (1N), was stored at room temperature for a period of 3 hours. A sample (20 µl) was taken for the chromatographic analysis at zero time and after 3 hours to observe the degradation of the sample.

Solution stability
The solution of dispersible tablets of VF (control and sample) was kept in a firmly sealed volumetric flask. The solutions were stored at room temperature for 7 days. The solutions were analyzed every 24 hrs.

Statistical analysis
All results are calculated from triplicate measurements through mean ± standard deviation method. Statistical investigation was executed using one-way analysis of variance (ANOVA) in Microsoft Excel. Results are statistically significant, as P-values are below 0.05. The statistical analysis showed that the P-values were below 0.05, indicating significant results.

RESULTS

Method validation
The following parameters have been evaluated for the method validation of VF:

System suitability
System suitability was assessed using six sample solutions of the VF standard (10 µg/ml) prior to sample analysis. The parameters used to evaluate system suitability are relative standard deviation (% RSD) < 2%, column theoretical plates (12,692) and a tailing factor of 1.595, all obtained from the chromatograms.

Linearity
Standard solutions of VF (five samples) having a concentration range of 50–150 µg/ml were prepared and analyzed. The linearity plot was obtained for peak area vs. concentration in micrograms per milliliter (Fig. 2). The method was found to be linear, with a correlation coefficient of 0.9998 (Table 1).

Accuracy
The method accuracy was established by analyzing the sample solution of VF at the concentration levels of 50, 100 and 150%. Accuracy was expressed as recovery (%) and RSD (%) of the sample. The validation data shows that the %recovery ranges in between 99.22-102.47% and the % RSD value is < 2% (Table 2).

Sensitivity [Limit of detection (DL) and limit of quantification (QL)]
It is estimated by employing the standard deviation (SD) and the slope and represented as:

$$DL = 3.3\ \sigma / S \quad \text{(Eq. 1)}$$

Limit of quantification was estimated by:

$$QL = 10\ \sigma / S \quad \text{(Eq. 2)}$$

where σ is the SD and S is the slope of the linearity curve. The DL and QL of the method were 2.33 and 7.06 µg/ml (Table 1).

Robustness
Method robustness was observed using minor intended variations in the procedure parameters like flow rate (±0.2 ml min^{-1}), wavelength (±2 nm) and pH (±0.2 unit). The % RSD value is < 2% (Table 1).

Specificity
A VF standard solution at 100 µg ml^{-1} was prepared. Placebo was made by using the excipients, i.e., mannitol, fumaric acid, hydroxypropyl cellulose, crospovidone, magnesium stearate and aspartame. Then, the standard, placebo and sample solution were injected and observed to be selective at the same wavelength for the vonoprazan sample solution (100 µg/ml) and the placebo solution (Fig. 3). Noise and Interference were monitored carefully in the chromatogram.

Precision
The analysis of six replicate tablet samples (100 mg per 100 ml) was carried out. Method precision was determined by assay and system precision, as indicated by % RSD values. The data show that the % RSD is < 2% (Table 1).

Ruggedness (Intermediate precision)
The results of intermediate precision show that the RSD is < 2%, with the 95% confidence interval (CI) ranging from 100.81% to 101.89% (Table 1).

Forced degradation studies
The major degradation of VF results due to alkaline hydrolysis, with 33.12 % degradation after 3 hours, having two major degradation peaks (Fig. 4-a). The oxidative stress VF shows about 5.22% degradation, with one significant degradation peak (Fig. 4-b). Photodegradation of VF observed with one degradation peak which results 5.57% degradation (Fig. 4-c). The thermal degradation of VF shows a single peak at 3.56% (Fig. 4-d). VF degradation is less than 2% under acidic conditions. The summary of VF degradation is given in table 3. The forced degradation results revealed that VF is highly susceptible to degradation in alkaline media and resistant to degradation under acidic hydrolysis (Fig. 5).

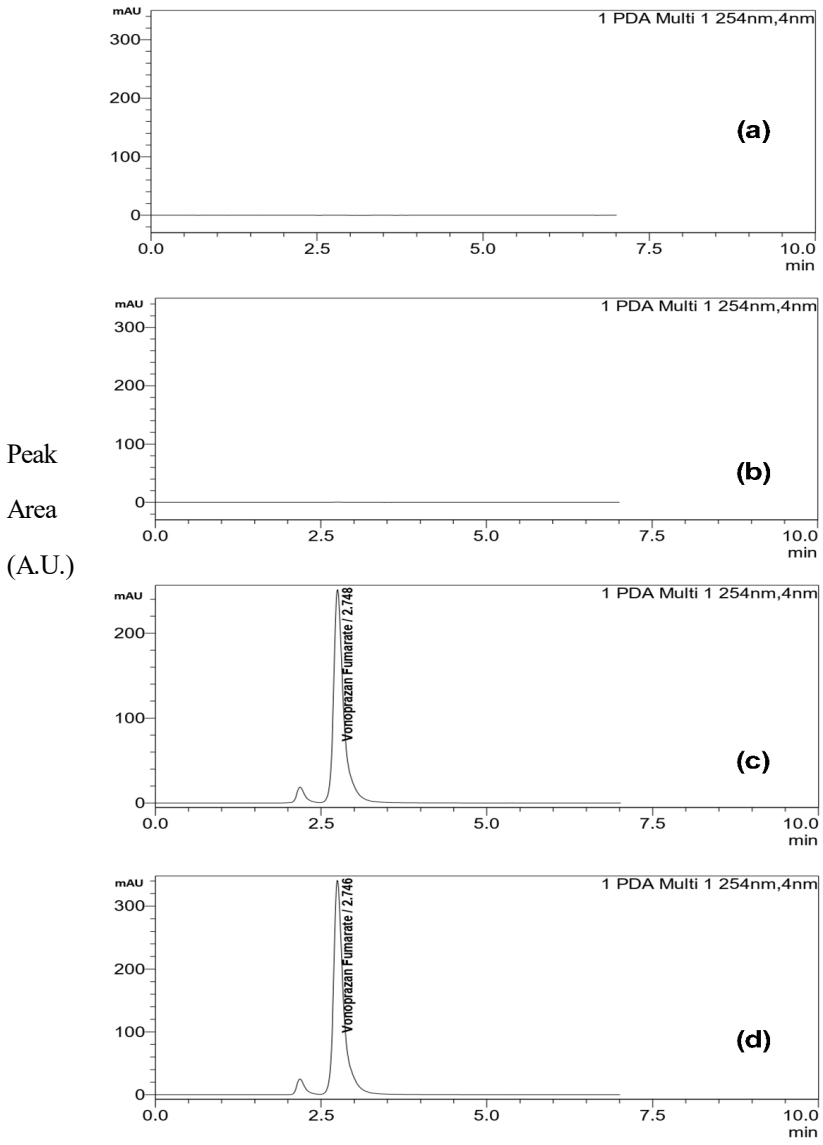

Fig. 3: Chromatogram of vonoprazan fumarate. (a) Blank solution; (b) Placebo; (c) Standard; (d) Sample solution.

Table 2: Analysis of VF for accuracy & recovery

Sample #	Solution (%)	Amount of drug added (mg)	Amount of drug recovered (mg)	Recovery (%)	Mean (%)
1	50	7.30	7.48	102.47	101.71
2		6.80	6.86	100.82	
3		7.50	7.63	101.85	
4	100	13.9	13.80	99.33	100.05
5		14.3	14.34	100.26	
6		13.5	13.58	100.57	
7	150	21.0	20.84	99.22	99.95
8		20.5	20.43	99.66	
9		20.9	21.11	100.98	

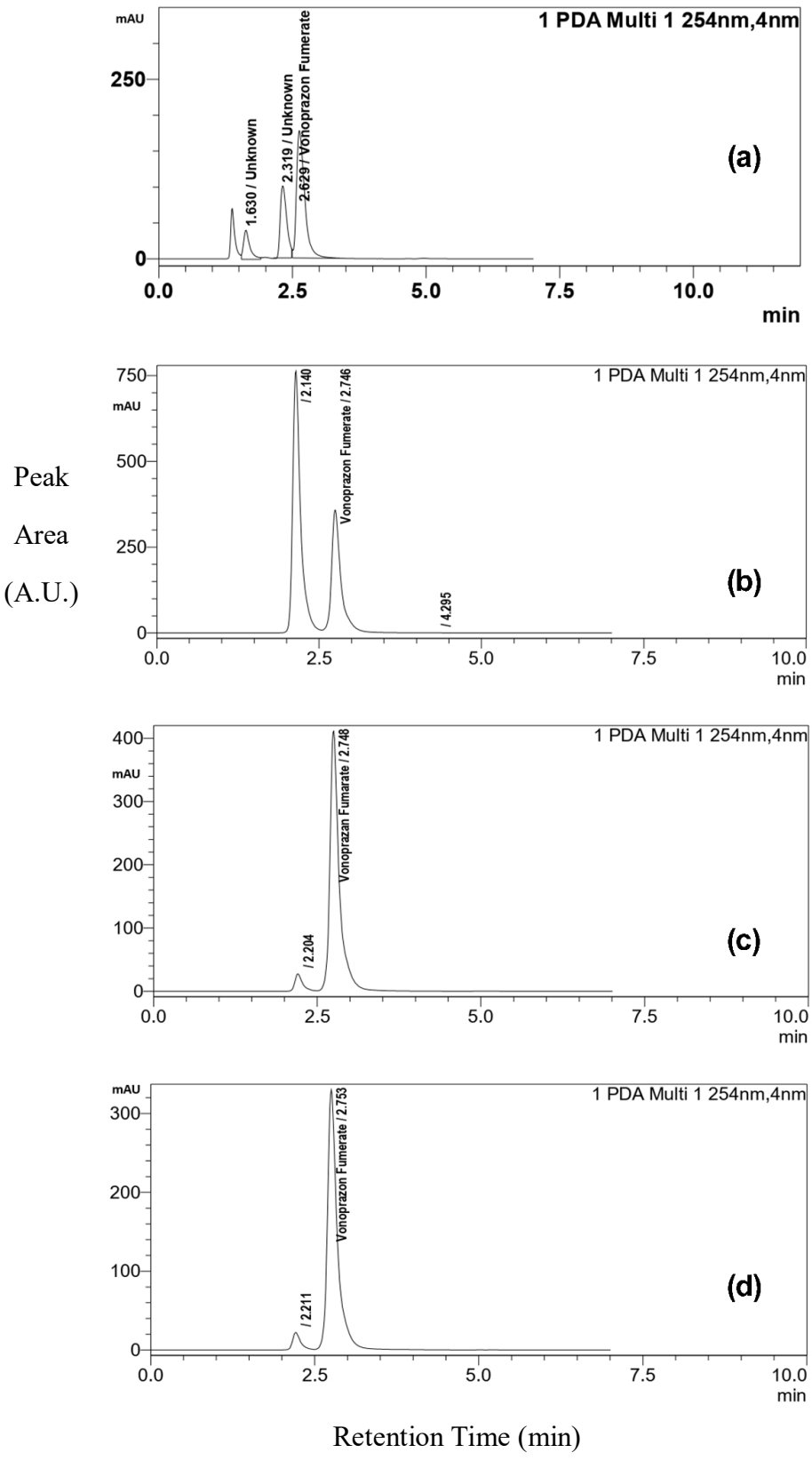

Fig. 4: Chromatogram representing the forced degradation of vonoprazan fumarate. (a) Alkaline medium; (b) Oxidative stress; (c) Photodegradation; (d) Thermal degradation.

Table 3: Summary of forced degradation of VF.

Stressed conditions	Time duration (hrs)	Sample recovery (%)	Degradation (%)
Thermal degradation	0	100	0
	1	98.4	1.60
	2	97.02	2.98
	3	96.44	3.56
Photodegradation	0	100.00	0
	1	97.39	2.61
	2	95.8	4.20
	3	94.43	5.57
Chemical degradation			
Oxidative stress	0	100.00	0
	1	97.51	2.49
	2	95.95	4.05
	3	94.78	5.22
Alkaline hydrolysis	0	100.00	0
	1	84.16	15.84
	2	74.69	25.31
	3	66.88	33.12
Acidic hydrolysis	0	100.00	0
	1	99.95	0.05
	2	99.93	0.07
	3	99.89	0.11

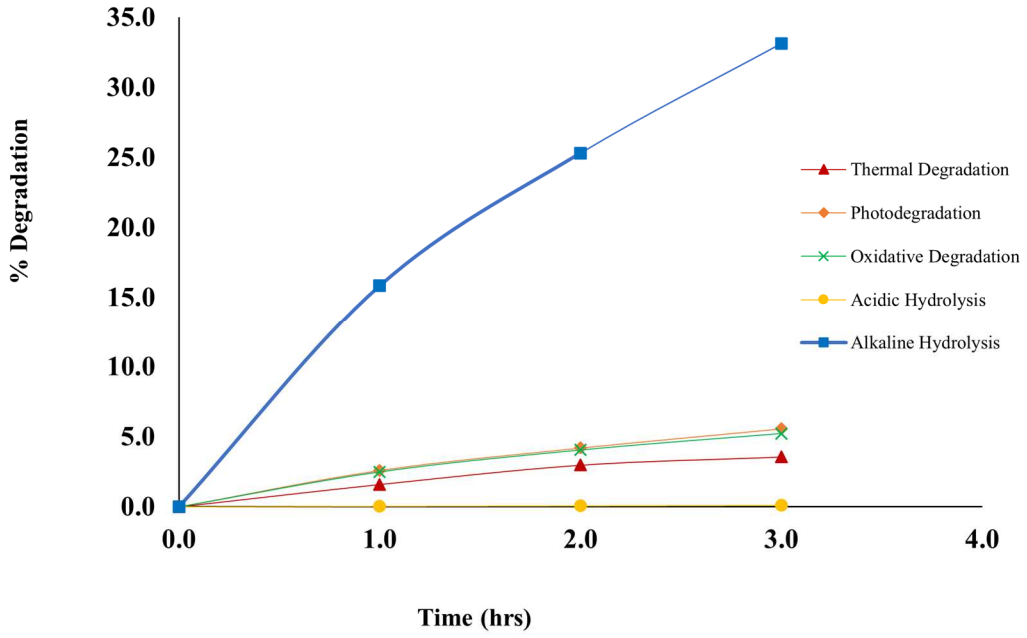

Fig. 5: Degradation (%) of vonoprazan fumarate over time in forced conditions.

DISCUSSION

Method validation

Method validation is the most significant parameter in the design of an analytical protocol with accurate and precise quantification of the analyte or drug sample (Rao, 2018). In this study, VF was estimated using a validated HPLC method. The HPLC method validation was performed in accordance with the ICH Q2 (R1) guideline (ICH, 2005). The method was found to be linear, with a regression correlation (r2) close to 1. The data show that the % recovery ranges and the % RSD values confirm the

method's precision and greater system suitability for the estimation of VF, along with column performance parameters, including proper peak integration, as indicated by the number of theoretical plates and the tailing factor obtained from the chromatograms. Method robustness was assessed by applying minor intended variations to the procedure parameters, such as flow rate, pH and wavelength, with no significant changes observed.

The DL and QL of the method confirmed that it was robust and could be used efficiently for the determination of VF. Method specificity was carried out to observe the interference in terms of retention time (tR) between the sample and other components including excipients, impurities and degradation products. The method Precision was also assured by performing intra-day testing of VF samples for repeatability. As per the standard limit, the %RSD value confirmed the method precision & repeatability for the determination of VF with greater system suitability in Intra-Day analysis. Ruggedness was also determined by quantifying the active per tablet. The results demonstrated consistent assay values with acceptable %RSD, confirming that the method is robust and reproducible under normal operational conditions complied with ICH Q2(R1) guidelines (Borman and Elder, 2017). Therefore, the developed analytical method can be useful for analyzing VF in both pure and finished dosage forms.

Forced degradation studies

Force degradation studies are crucial for stability testing and for identifying the specificity of degradation products/impurities (Kogawa *et al*., 2016; Wu *et al*., 2024). The parameters investigated in forced degradation studies include the physicochemical stability and characterization of drug degradation products in the formulations (Reynolds *et al*., 2002; Blessy *et al*., 2014). The oxidative stress, thermal degradation and photodegradation studies of VF show comparatively lesser extent of degradation which shows relative stability of VF when exposed to UV light, high temperatures and oxidative environment. However, chemical degradation of VF shows significant degradation when exposed under acidic, alkaline and oxidative. The forced degradation study revealed that VF is highly susceptible to degradation in alkaline media and resistant to degradation under acidic hydrolysis. However, the detailed stability profile and characterization of degradation products still require further investigation.

CONCLUSION

A simple, robust and cost-effective chromatographic analytical method is developed to analyze the newly formulated fast-dispersible Vonoprazan fumarate tablets and implemented for the stability studies of the Vonoprazan fumarate according to the ICH guidelines. The method validation was carried out in accordance with various standard validation parameters. The method showed reproducibility within ±2%. This method can also be used to quantify vonoprazan and detect all possible degradation products in fast-dispersible tablets. The forced degradation studies show that Vonoprazan fumarate is highly susceptible to degradation under alkaline hydrolysis, while showing greater stability in the acidic solution. The oxidative stress, photodegradation and thermal degradation of Vonoprazan fumarate show lower degradation, indicating relative stability of VF under stressed conditions.

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None.

Authors' contributions

Atta-Ur-Rehman: Participated in the study, conducted experiments and analyzed data; Farya Zafar: Provided significant intellectual input during the editing and refining of the manuscript; Kiran Qadeer: Provided substantial intellectual input during the drafting and revision of the manuscript, contributed to the analysis and interpretation of data; Huma Ali: Participated in data collection, evaluating and interpreting and contributed significantly in the interpretation and manuscript preparation.

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Data availability statement

Data will be available from the corresponding author upon request.

Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Abdelazim AH, Abdel-Fattah A, Osman AO, Abdel-Kareem RF and Ramzy S (2023). Spectrophotometric quantitative analysis of aspirin and vonoprazan fumarate in recently approved fixed-dose combination tablets using ratio spectra manipulating tools. *J. AOAC Int.*, **106**: 490-495.

Aboras SI, Ahmed AR, Belal TS, Elbordiny HS (2025). A tri-hued and sustainable assessment of HPLC for the concurrent determination of multi-purpose binary and ternary vonoprazan combinations: Application to combined dosage forms and simulated gastric juice. *Microchem. J.*, **6**: 113882.

Abuothman M, Deeb AA, Hailat M, Abuyaman O, Aldoqum HM (2024). A novel fast analytical method for the determination of N-nitroso vonoprazan in vonoprazan tablets and raw materials using LC-ESI-MS/MS. *Int. J. Environ. Anal. Chem.,* **9**: 1-10.

Ali NA, El-Gindy AE, Wahba ME, Mostafaa AE (2025). Ecofriendly chromatographic method for the separation and quantification of vonoprazan fumarate, a novel potassium competitive acid blocker with amoxicillin

and clarithromycin which are effective in the treatment of Helicobacter pylori. *Acta Chromatographica.,* 1-13.

Alzaghal NM, El-Mossalamy ESH and El-Sayed GO (2024). Method development and validation for estimation of vonoprazan by RP-HPLC method in bulk and tablets dosage form. *Egyp. J. Chem.*, **67**(2):145-159.

Anusha K and Sowjanya GA (2024). Reliable RP-UPLC-TUV Method for simultaneous estimation of clarithromycin, amoxicillin and vonoprazan in co-packed pharmaceutical dosage forms: Method development and validation with stability indicating properties. *Int. J. App. Pharm*., **16**(2): 351-357.

Blessy MR, Patel RD, Prajapati PN and Agrawal YK (2014). Development of forced degradation and stability indicating studies of drugs—A review. *J. Pharm. Anal.,* **4**(3): 159-165.

Cayman Chemical, "Safety data sheet of Vonoprazan Fumarate," (2022) [Online]. Available: https://www.caymanchem.com/product/24200/vonoprazan-(Fumarate).

El Hamd MA, El-Maghrabey M, Magdy G, Soltan OM, Abdelrahman KS, Obaydo RH, Mahdi WA, Alshehri S, Abu-Hassan AA (2024). Factorial design-aided derivatization-free fluorimetric ultrasensitive assay of vonoprazan with application in uniformity of dosage units and plasma samples analysis: Comprehensive and comparative greenness and whiteness assessment. *Microchem. J.*, **205**: 111320.

Howden CW, Katz P, DeVault KR, Metz DC, Tamene D, Smith N, Hunt B, Chang YM, Spechler SJ (2025). Integrated analysis of vonoprazan safety for symptomatic gastro-oesophageal reflux disease or erosive oesophagitis. *Aliment. Pharmacol. Ther.,* **61**(5): 835-851.

Borman P and Elder D. (2017). Q2 (R1) validation of analytical procedures: Text and methodology. ICH quality guidelines: An implementation guide, 127-166

ICH, Q1A(R2) (2003) Stability testing of new drug substances and products - Step 5, European Medicines Agency.

ICH Q10 (2005). International Conference on Harmonization (ICH) of technical requirements for registration of pharmaceuticals for human use.

Iram F, Iram H, Iqbal AZ and Husain A (2016). Forced degradation studies. *J. Anal. Pharm. Res.*, **3**(6): 00073.

Kogawa C, Ana Salgado RN and Herid (2016). Impurities and Forced Degradation Studies: A Review. *Curr. Pharm. Anal.*, **12**(1): 18-24.

Liu L, Cao N, Ma X, Xiong K, Sun L and Zou Q (2016). Identification, characterization and high-performance liquid chromatography quantification of process-related impurities in vonoprazan fumarate. *J. Sep. Sci.,* **39**(7): 1232-1241.

Mahgoub H, Ragab MA, Tarek S, Maher HM (2024). An eco-friendly liquid chromatographic analysis of the triple therapy protocol of amoxicillin, metronidazole and vonoprazan for H. pylori eradication: Application to combined dosage forms and simulated gastric fluid. *BMC Chemistry.*, **18**(1): 106.

Mori H and Suzuki H (2019). Role of acid suppression in acid-related diseases: Proton pump inhibitor and potassium-competitive acid blocker. *J. Neurogastroenterol. Motil.,* **25**: 6-14.

Parmar MS, Shah DA, Chhalotiya UK (2025). Stability indicating HPTLC–densitometric method for estimation of vonoprazan fumarate. *Drug* Dev. Ind. Pharm.*,* **51**(6): 546-554.

Qiao Y, Huang J, XU Y, Zhao J and Wang Q (2018). Determination of vonoprazan pyroglutamate and vonoprazan fumarate by HPLC. *China Pharmacist.*, **12**: 535-538.

Qiao Y, Zhao J, Yue X, Zhang Y, Zhang R, Xu Y, Tang X, Liu X and Wang Q (2017). Study on pharmacokinetics and bioequivalence of Vonoprazan pyroglutamate in rats by liquid chromatography with tandem mass spectrometry. *J. Chromatogr. B*., **1059**: 56-65.

Rao TN (2018). Validation of analytical methods. In: M. Stauffer, ed., *Calibration and Validation of Analytical Methods—A Sampling of Current Approaches*, 25th ed., Intech Open, London UK, pp.131-41.

Reynolds DW, Facchine KL, Mullaney JF, Alsante KM, Hatajik TD and Motto MG (2002). Conducting forced degradation studies. *Pharm. Technol.,* **26**(2): 48-56.

Saraya RE, Hassan YF, Eltukhi WE and Salman BI (2022). Ultra-sensitive fluorimetric method for the first estimation of vonoprazan in real human plasma and content uniformity test. *J. Fluoresc.*, **32**(5): 1725-1732.

Wu J, Zhang H, Zhao H, Qin B, Lou T, Yu Y, Huang L, Cheng J and Zhao H (2024). Validation of an ion-pair reverse phase high-performance liquid chromatography method for the detection of major components and related substances in diquafosol sodium eye drops. *ACS Omega*., **9**(9): 10160-10168.

Yoneyama T, Teshima K, Jinno F, Kondo T and Asahi S (2016). A validated simultaneous quantification method for vonoprazan (TAK-438F) and its 4 metabolites in human plasma by the liquid chromatography-tandem mass spectrometry. *J. Chromatogr. B*., **1015**: 42-49.

Zhang MM, Wang MD, Yang SY, Hu JQ, Zhu BQ, Wei YK, Zhang CL, Long EW (2025). The efficacy and safety of vonoprazan-based high-dose dual therapy for eradication of Helicobacter pylori: A systematic review and meta-analysis. *J Infect Public Health.*, **18**(7): 102768.