International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

Analytical Method and Validation for Estimation of Vonoprazan in Pharmaceutical Dosage Form – A Review

Mr. C.A. Shaik Fayaaz Ahamed*[1], M.Hariharan[2], G.Hemamalini[2], M.Harshath Nowfaldeen[2], M.Hemalatha[2], R.Hemnath[2]

*[1] *Associate Professor Department Of Pharmaceutical Analysis,* [2] *B.Pharm Final Year.*
Aadhibhagawan College Of Pharmacy, Rantham, Thiruvannamalai, Tamilnadu.

Date of Submission: 05-09-2025 Date of Acceptance: 15-09-2025

ABSTRACT:
Vonoprazan is a first in class potassium competitive acid blocker (P-CAB) approved by the U.S. Food and Drug Administration(FDA) for the treatment of helicobacter pylori infection in adults. H+\K+ATP ase proton pump,vonaprazan compatetively and reversibely blocks potassium binding on the proton pump,resulting in more rapid,potent and sustained acid suppression. Additionally , vonoprazan shows promise in managing PPI-resistance gastroesophageal reflux disease (GIRD). Peptic ulcer in the combination regimens for helicobacter pylori eradication. Vonopazan offers faster onset of action, prolonged acid suppression and improved patient outcomes compared to PPI'S. clinical trails have demonstrated higher eradication rates with vonoprazan – based triple therapy, even in patients with clarithromycin resistant strains, which is a key advantages in reducing progression of chronic gastritis to gastric cancer. In long term studies are warranted to establish its role in reducing gastric cancer. While vonoprazan has not been directly linked to COVID-19 outcomes, its pharmacological properties suggest potential utility in supporting gastrointestinal management in infected patient. Its stability in acidic environments and independence from metabolic variability provide advantages in critically ill patients, including those receiving multiple medications during COVID-19 treatment. Vonoprazan offers faster onset of action, prolonged acid suppression, and improved patient outcomes compared to PPI's. with its favorable pharmacokinetic profile and safety data, vonoprazan represent a significant advancement in the treatment of acid-related diseases, though long term safety evaluation and border clinical use are still under investigation.

KEYWORDS: Vonoprazan Fumarate; Helicobacter pylori; Gastric cancer; Proton pump inhibitors; potassium-competitive acid blockers; COVID-19.

I. AIM:

The aims of vonoprazan analysis methods include developing and validating stability-indicating HPLC, UHPLC, HPTLCe forms by using that are simple, accurate, sensitive and reliable.

II. INTRODUCTION:

2.1 Analytical chemistry:

Analytical chemistry may be defined as the science and art of determining composition of Materials in term of the element of composition and quantitative analysis of the substance and Chemical species.Analytical chemistry can be broken down into two general areas of analysis.

- Qualitative analysis.
- Quantitative analysis

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

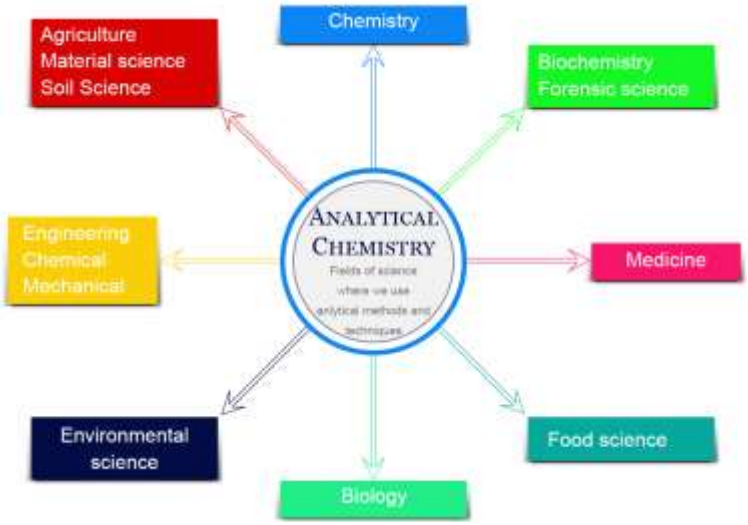

Fig: 1 Analytical Chemistry

2.2 Analytical method development:

Analytical method development and validation are essential components in the processes of drug discovery, development, and pharmaceutical manufacturing. Rooted in analytical chemistry, method development encompasses techniques for identifying, separating, and quantifying the chemical constituents of medicinal compounds.

The primary goal of analytical method development is to confirm the identity, purity, potency, and physical properties of drugs, including factors like bioavailability and stability. This process ensures that analytical methods are suitable fo evaluating drugs, particularly the active pharmaceutical ingredient (API).

2.3 Validation:

Validation is the documented process of demonstrating that a procedure, process, equipment, Material, activity, or system consistently produces the intended outcome. According to ISO, validation involves verifying through examination and objective evidence That specific requirements for an intended use have been met. The FDA defines validation as the process of generating documented proof that provides strong Assurance a particular process will consistently yield a product that meets its predetermined Specifications and quality standards.

Fig: 2 Validation

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

III. DRUG PROFILE:

3.1 Drug Name:

Vonoprazan is classified as a potassium-competitive acid blocker (PCAB).PCABs inhibit the gastric H^+ /K^+ -ATPase enzyme system by competing with potassium ions, reducing gastric acid secretion.

3.2 Structure:

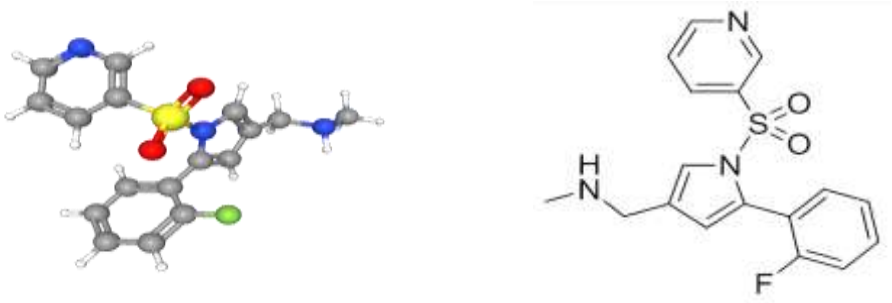

Fig: 3 Structure Of Vonoprazan

3.3 Physio-chemical Properties:

- **Chemical Name:** 5-(2-Fluorophenyl)-N-methyl-1-(3-pyridinylsulfonyl)-1H-pyrrole-3-methanamine 2-Butenedioate.
- **Brand Name:** Voquezna.
- **Molecular Formula:** $C_{17}H_{16}FN_3O_2S$
- **Melting Point:** 194.8°C
- **Boiling Point:** ~ 530 °C (± 60 °C) at 760 mmHg
- **Bioavailability:** 85-95%
- **Half- Life:** 7.7 hours

3.4 Mechanism Of Action:

Vonoprazan is a potassium-competitive acid blocker (PCAB) that inhibits the H^+, K^+-ATPase enzyme system in a potassium-competitive manner. Through this mechanism, vonoprazan suppresses basal and stimulated gastric acid secretion at the secretory surface of gastric parietal cells. Although both classes of drugs inhibit the H^+, K^+-ATPase, the mechanism of action of PCABs differs from that of proton-pump inhibitors (PPIs). PPIs form a covalent disulphide bond with a cysteine residue on the H^+, K^+-ATPase, which leads to the inactivation of the enzyme, while PCABs interfere with the binding of K^+ to the H^+, K^+-ATPase.

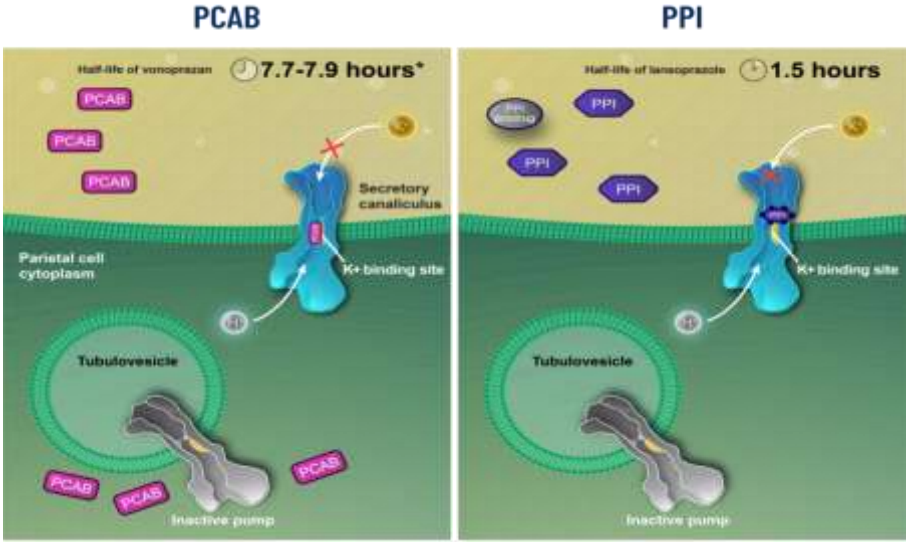

Fig: 4 Mechanism action Of Vonoprazan

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

IV. SPECTROSCOPY:

Spectroscopy is a key method employed in physics and chemistry to investigate the interaction of matter with electromagnetic radiation. From uncovering the mysteries of atoms and molecules to identifying illnesses through MRI, spectroscopy influences numerous fields in science and healthcare. This article explores thoroughly the meaning of spectroscopy, its fundamental principles, distinctions from comparable techniques, and its extensive uses.

Spectroscopy is the scientific technique used to investigate how various substances absorb, emit, or scatter electromagnetic radiation, including light. In simple terms, it entails dissecting radiation into its individual wavelengths to gain insights into the structure and characteristics of matter. The way to pronounce spectroscopy is spek-TRAW-skuh-pee. In organic chemistry, spectroscopy is essential for determining molecular structure, whereas in physics, it aids in elucidating the basic behavior of energy and matter. In chemistry, spectroscopy denotes analytical methods that assess how molecules respond to different types of radiation. This can disclose information regarding chemical makeup, functional groups, and bonding. In physics, spectroscopy typically targets atomic and subatomic phenomena, including energy states, electron motion, and the spectral emissions or absorptions of various elements. This helps in grasping the physical laws that control the universe.

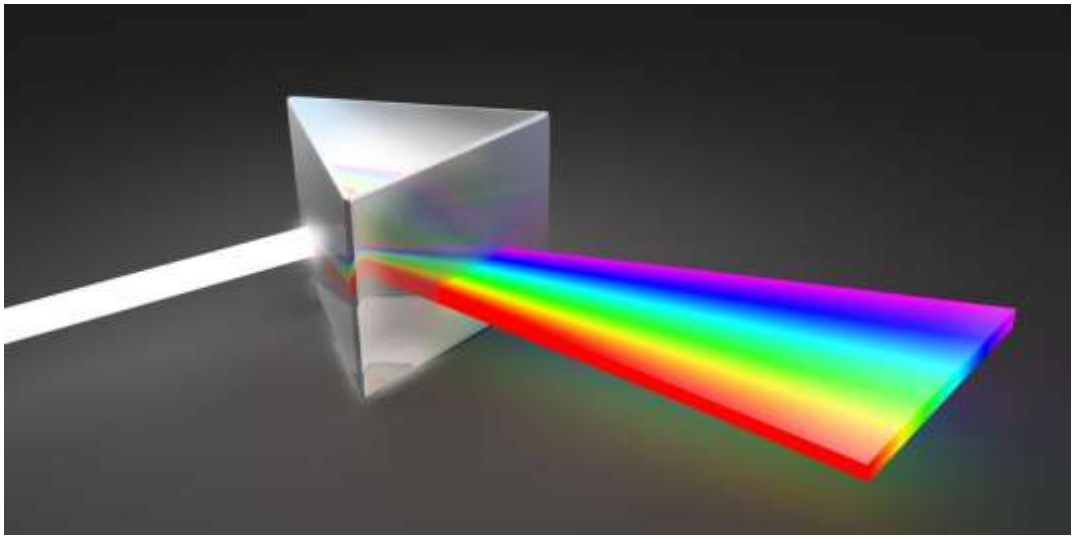

Fig: 5 Spectroscopy

4.1 UV –Spectroscopy:

UV spectroscopy, or ultraviolet-visible (UV-Vis) spectroscopy, is an analytical technique used to measure the absorption of ultraviolet and visible light by a substance. It is based on the principle that when molecules are exposed to UV or visible light, electrons can absorb energy and transition from a lower energy level to a higher one. These electronic transitions typically occur between bonding, anti-bonding, and non-bonding orbitals, such as π to π* and n to π* transitions, which are common in compounds containing double bonds, lone pairs, or conjugated systems.

The amount of light absorbed by a compound is measured and plotted as a spectrum, typically showing absorbance versus wavelength. The peak of maximum absorbance, called λ_max, is characteristic of the compound's electronic structure. The intensity of absorbance follows the Beer–Lambert law, which relates absorbance (A) to concentration (c), path length (l), and molar absorptivity (ε) through the equation: $A = \varepsilon cl$. This relationship makes UV-Vis spectroscopy useful for both qualitative and quantitative analysis.

Applications of UV spectroscopy are broad and include determining the concentration of solutions, identifying functional groups, checking the purity of compounds, and studying reaction kinetics. It is also commonly used in biological studies to analyze DNA and proteins, which have characteristic absorption at 260 nm and 280 nm, respectively. While the technique is fast, non-destructive, and easy to perform, it is limited to compounds that absorb in the UV-visible range, and interpretation can be challenging when spectra have

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

overlapping peaks or are influenced by the solvent or pH conditions.

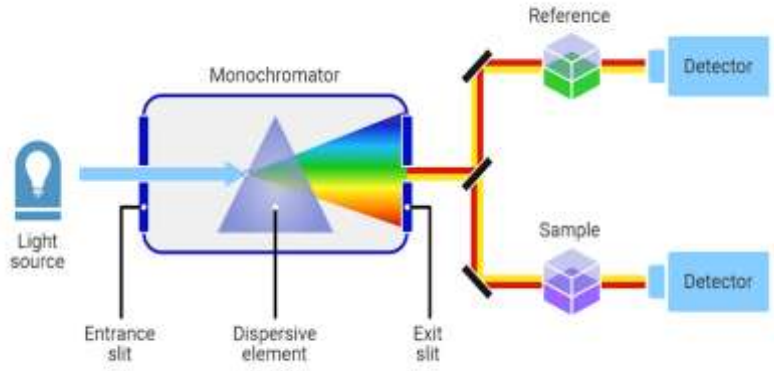

Fig: 6 UV - Spectroscopy

4.2 Ultra Performance Liquid Chromatography:

Ultra Performance Liquid Chromatography (UPLC) is an advanced form of liquid chromatography that allows for faster, more efficient, and higher-resolution separation of chemical compounds compared to traditional High Performance Liquid Chromatography (HPLC). It operates on the same basic principle as HPLC—separating compounds based on their interaction with a stationary phase and a mobile phase—but utilizes smaller particle sizes (typically less than 2 µm) in the column packing material. These smaller particles increase the surface area for interactions, which leads to better separation and sharper peaks in a shorter amount of time.

UPLC systems operate at much higher pressures (up to 15,000 psi or more) than conventional HPLC, which typically operates at pressures up to 6,000 psi. This increased pressure is necessary to push the mobile phase through the tightly packed columns. As a result, UPLC achieves faster analysis times, improved sensitivity, and better resolution, making it ideal for high-throughput laboratories and applications requiring precise quantification or trace analysis.

The technique is widely used in pharmaceutical development, environmental testing, food safety, clinical research, and biochemical analysis. Despite its advantages, UPLC requires specialized equipment that can withstand high pressures, and the cost of columns and instrumentation is generally higher than traditional HPLC. Nonetheless, its speed, efficiency, and ability to handle complex samples have made it a valuable tool in modern analytical chemistry.

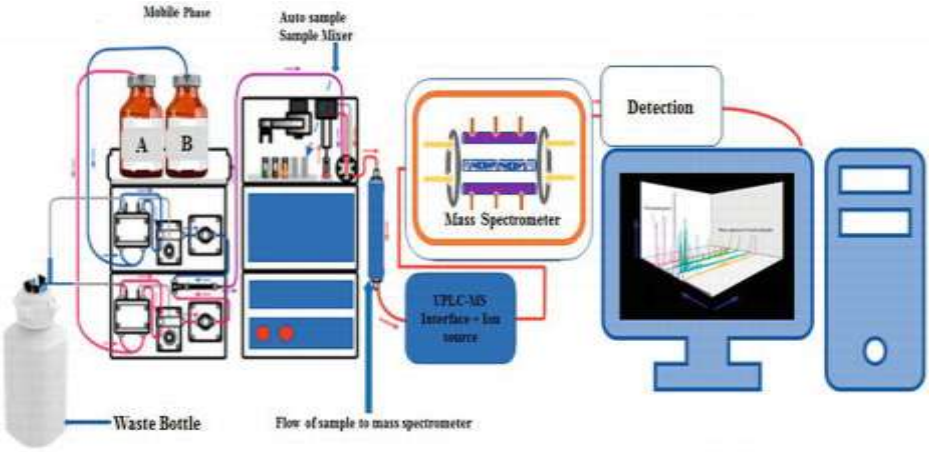

Fig: 7 UPLC

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

4.3 HIGH PERFORMANCE THIN LAYER CHROMATOGRAPHY:

High Performance Thin Layer Chromatography (HPTLC) is an enhanced version of traditional Thin Layer Chromatography (TLC), designed to provide better resolution, sensitivity, and reproducibility for the separation and analysis of complex mixtures. Like TLC, HPTLC works on the principle of the separation of components based on their different affinities toward the stationary phase (usually a thin layer of silica gel coated on a glass, plastic, or aluminum plate) and the mobile phase (a suitable solvent or mixture of solvents). However, HPTLC employs more sophisticated instrumentation, finer particle sizes in the stationary phase, and automated sample application and detection systems.

One of the key features of HPTLC is the use of precoated plates with uniform, smaller particle sizes (typically 5–10 µm), which significantly improves the separation efficiency and sensitivity compared to conventional TLC. Sample application is done precisely using an automatic applicator, which ensures consistent sample size and position. After development in a controlled chamber, the plates are often dried and visualized under UV light or by using chemical reagents. Detection and quantification are carried out using densitometers or scanners, which can measure the intensity of spots accurately and provide a digital readout.

HPTLC is widely used in the pharmaceutical, food, herbal, cosmetic, and environmental industries for qualitative and quantitative analysis. It is especially useful for analyzing multiple samples simultaneously, identifying compounds in complex mixtures, checking the purity of substances, and performing stability studies. The advantages of HPTLC include low operating costs, the ability to analyze many samples in parallel, minimal sample preparation, and visual as well as instrumental documentation. However, it requires careful method development and precise control of experimental conditions to ensure reproducibility and accuracy.

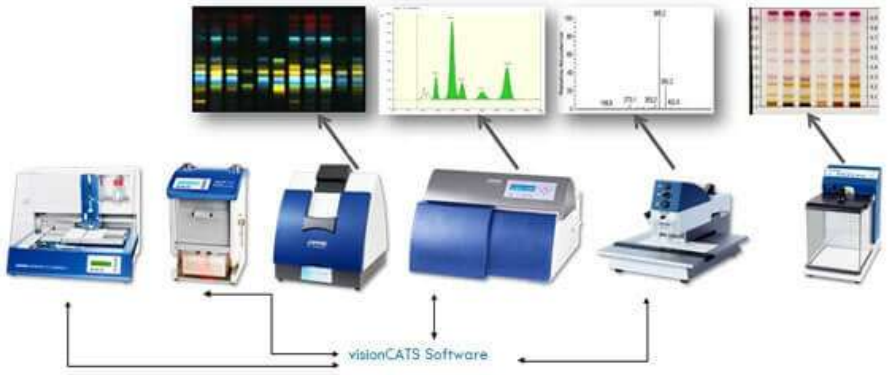

Fig: 8 HPTLC

4.4 HIGH PERFORMANCE LIQUID CHROMATOGRAPHY:

High Performance Liquid Chromatography (HPLC) is an advanced analytical technique used to separate, identify, and quantify components in a mixture. It operates on the principle of differential partitioning of analytes between a mobile phase (liquid solvent) and a stationary phase (typically a packed column). As the sample is injected into the system, it is carried by the mobile phase through the stationary phase, where different compounds interact differently with the column material based on their polarity, size, or chemical properties. These differences cause the compounds to elute at different times, known as retention times, allowing for their separation and analysis.

HPLC systems consist of several key components: a solvent reservoir, a high-pressure pump, an injector, a chromatographic column, a detector, and a data system. The pump generates the high pressure needed to push the solvent through the tightly packed column, enabling faster and more efficient separations compared to traditional liquid chromatography. The detector (such as UV-Vis, fluorescence, or mass

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

spectrometry) identifies and quantifies the separated compounds as they exit the column. HPLC is highly versatile and is widely used in pharmaceuticals, environmental analysis, food and beverage testing, and clinical diagnostics. It is especially valuable for drug purity testing, content uniformity, and stability studies. There are various types of HPLC based on the nature of the stationary and mobile phases, including reverse-phase HPLC, normal-phase HPLC, ion-exchange HPLC, and size-exclusion HPLC.

The main advantages of HPLC include high resolution, sensitivity, reproducibility, and the ability to analyze both volatile and non-volatile compounds. However, it requires expensive equipment, trained personnel, and careful method development to achieve accurate and reliable results.

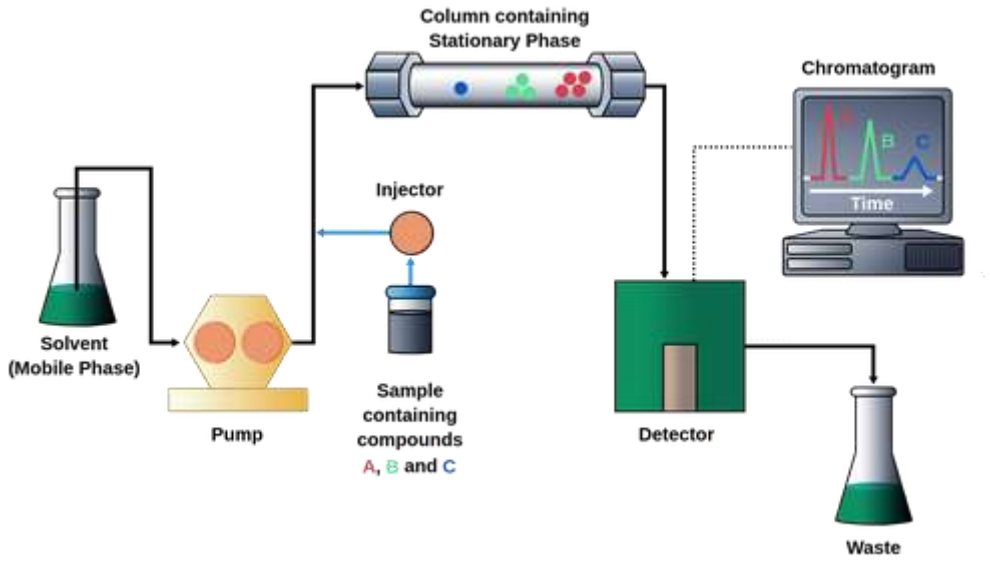

Fig: 9 HPLC

V. MATERIALS AND METHOD:

5.1 High-Performance Thin Layer Chromatography For Vonoprazan:

High-performance thin layer chromatography method was developed and validated for analysis of vonoprazan fumarate. An Alkaline forced degradation kinetic study was performed to find out probable rate of degradation of vonoprazan fumarate.

S.No	Stationary phase	Mobile phase	Absorbance	Rf value
1.	Aluminum packed TLC plates precoated with silica gel 60F254.	Methanol: Toluene: triethylamine (6: 4: 0.1 v/v/v)	267nm	0.43±0.1

Table: 1 HPTLC of Vonoprazan

5.2 UV-Spectroscopy For Vonoprazan:

UV-spectrophotometric technique for determining vonoprazan fumarate, a first-in-class potassium-competitive acid blocker, in bulk and tablet medicinal dosage form was developed and validated.

S.No	Stationary phase	Mobile phase	Wavelength	Results
1.	Column C18 and C8.	Phosphate buffer (50:50v/v).	Wave length : 230nm	LOD: 0.24µg/ml LOQ: 0.70µg/ml Recovery: 99.48 ± 0.3 47 % RSD: less than 2.

Table: 2 UV-Spectrum of Vonoprazan

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 177-185 www.ijprajournal.com ISSN: 2456-4494

5.3 Ultra-Performance Liquid Chromatography For Vonoprazan:

Ultra performance liquid chromatography method can uses reverse phase chromatography, often employing a C18 column, (50×2.1mm). used for quality control including related substances analysis and drug content estimation and therapeutic drug monitoring and in bioequivalence studies.

S.No	Stationaryphase	Mobilephase	Flow rate/ Detection/ Wavelength	Results
1.	C18 column (2.1× 50 mm, 1.7 µm) using gradient elution.	0.2%formicacidin acetonitrile and 0.1% ammonium hydroxide and 10 mmol/Lammonium formate in deionized water.	Flowrate:0.4ml/min Detection : uv Wavelength:230nm	Percision: 1.1%-14.6% Accuracy: 0.0%-14.7%

Table: 3 UPLC of Vonoprazan

5.4 High - Performance Liquid Chromatography For Vonoprazan:

HPLC offers high sensitivity, specificity, and accuracy, making it an ideal method for analyzing Vonoprazan. The technique involves separating, identifying, and quantifying the analyte based on its interactions with the stationary and mobile phases.

S.No	Stationary phase	Mobile phase	Absorbance	Rf value
1.	Aluminum packed TLC plates precoated with silicagel60F254.	Methanol: Toluene: triethylamine(6: 4: 0.1 v/v/v)	267nm	0.43±0.1

Table: 4 HPLC of Vonoprazan

5.5 Reversed-Phase High-Performane Liquid Chromatography Of Vonoprazan:

Rapid, simple, and sensitive reversed - phase HPLC-UV method of analysis for Vonoprazan in pharmaceutical formulation. Effective chromatographic separation was achieved using Agilent with isocratic elution of the mobile phase composition. pH, retention time, column temperature are obtained as per ICH.

S.No	Stationary phase	Mobile phase	Flow rate/ Detection/ Retention Time	Results
1.	Agilent 5 HC C18 – (150X4.6mm, 5µm) with isocratic elution of the mobile phase.	Buffer (0.01M potassium dihydrogen phosphate (1.36 g/L) and 0.02M sodium dihydrogen phosphate (2.4 g/L) in 900ml water.	Column Temperature:35°C Detection : uv Wavelength:225nm Flow rate:1.0ml/min Retention:3.3min	LOD:0.182 µg/ml LOQ:0.552 µg/ml Recovery: 99.64% Linearity: 10-50ug/ml As per ICH

Table: 5 RP-HPLC of Vonoprazan

VI. CONCLUSION:

The analytical evaluation of vonoprazan tablets plays a critical role in maintaining product quality and therapeutic reliability. Advanced techniques such as Uv spectrophotometry, HPLC, and LC-MS/MS have demonstrated high sensitivity and selectivity for both bulk drug and formulated dosage forms. Method validation in accordance with ICH Q2(R1) ensures accuracy, precision, linearity, and robustness, thereby establishing

scientific credibility for routine quality control. Furthermore, validated methods contribute to dissolution profiling, stability assessments, bioequivalence studies, and regulatory submissions. Thus, developing and optimizing robust analytical methods for vonoprazan supports not only routine pharmaceutical analysis but also long-term clinical and industrial applications.

REFERENCES:

[1]. Echizen H: The First-in-Class Potassium-Competitive Acid Blocker, Vonoprazan Fumarate: Pharmacokinetic and Pharmacodynamic Considerations. Clin Pharmacokinet. 2016 Apr;55(4):409-18. doi: 10.1007/s40262-015-0326-7.

[2]. Sugano K: Vonoprazan fumarate, a novel potassium-competitive acid blocker, in the management of gastroesophageal reflux disease: safety and clinical evidence to date. TherapAdvGastroenterol. 2018 Jan 9;11:1756283X17745776. doi: 10.1177/1756283X17745776. eCollection 2018.

[3]. Kiyotoki S, Nishikawa J, Sakaida 1: Efficacy of Vonoprazan for Helicobacter pylori Eradication. Intern Med. 2020 Jan 15;59(2):153-161. doi: 10.2169/internalmedicine.2521-18. Epub 2019 Jun 27.

[4]. FDA Thailand Product Information: Vocinti (vonoprazan fumarate) oral tablets [Link].

[5]. FDA Approved Drug Products:VOQUEZNA TRIPLE PAK (vonoprazan tablets; amoxicillin capsules; clarithromycin tablets), co-packaged for oral use and VOQUEZNA DUAL PAK (vonoprazan tablets; amoxicillin capsules) co-packaged for oral use.

[6]. FDA Approved Drug Products: VOQUEZNA (vonoprazan) tablets, for oral use (November 2023).

[7]. FDA Approved Drug Products: VOQUEZNA (vonoprazan) tablets, for oral use (July 2024).

[8]. Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet 1: 1273-1275, 1983. – PubMed.

[9]. Marshall BJ, Armstrong JA, McGechie DB, Glancy RJ. Attempt to fulfil Koch's postulates for pyloric Campylobacter. Med J Aust 142: 436-439, 1985. – PubMed.

[10]. Morris A, Nicholson G. Ingestion of Campylobacter pyloridis causes gastritis and raised fasting gastric pH. Am J Gastroenterol 82: 192-199, 1987. – PubMed.

[11]. Asaka M, Kato M, Kudo M, et al. . Atrophic changes of gastric mucosa are caused by Helicobacter pylori infection rather than aging: studies in asymptomatic Japanese adults. Helicobacter 1: 52-56, 1996. – PubMed.

[12]. Rokkas T, Pistiolas D, Sechopoulos P, Robotis I, Margantinis G. The long-term impact of Helicobacter pylori eradication on gastric histology: a systematic review and meta-analysis. Helicobacter 12 (Suppl 2): 32-38, 2007. – PubMed.

[13]. 13.Polk DB, Peek RM Jr. Helicobacter pylori: gastric cancer and beyond. Nat. Rev. Cancer 2010; 10: 403–414. - PMC – PubMed.

[14]. Thrift AP, Wenker TN, El-Serag HB. Global burden of gastric cancer: epidemiological trends, risk factors, screening and prevention. Nat. Rev. Clin. Oncol. 2023; 20: 338–349. – PubMed.

[15]. Hooi JKY, Lai WY, Ng WK et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology 2017; 153: 420–429. – PubMed.

[16]. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C. Global burden of gastric cancer attributable to Helicobacter pylori . Int. J. Cancer 2015; 136: 487–490. – PubMed.

[17]. Ma JL, Zhang L, Brown LM et al. Fifteen-year effects of Helicobacter pylori, garlic, and vitamin treatments on gastric cancer incidence and mortality. J. Natl. Cancer Inst. 2012; 104: 488–492. - PMC – PubMed.