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Pharmaceutical Quality Evaluation of Vonoprazan Film Coated Tablets: A Newly Approved and Launched First-in-Class Potassium Competitive Acid Blocker Marketed in Bangladesh

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Abstract

Context: Vonoprazan fumarate is the first-in-class innovative P-CAB (potassium-competitive acid blocker) authorized and launched in the Bangladeshi pharmaceutical market in June 2023. There is no study yet on the pharmaceutical quality of Vonoprazan fumarate products manufactured and marketed in Bangladesh. Systematic assessment of pharmaceutical quality parameters is a crucial part of the continuous quality improvement and monitoring of pharmaceutical products. It is also an outstanding component of pharmacovigilance and post-marketing surveillance. **Objective:** This study aims to assess the physicochemical quality parameters of different marketed brands of Vonoprazan fumarate available in Bangladesh. As part of quality factors, uniformity of weight, hardness, moisture content, disintegration time, identification, dissolution, and potency test were considered in the present study. **Methodology:** Five brands of samples of Vonoprazan fumarate tablets were randomly chosen and purchased from different pharmacies located in Dhaka, Bangladesh. Multiple *in vitro* tools were used to predict and scrutinize the collected medication formulations to assess and ensure product quality and patient safety. Among others, USP (United States Pharmacopeia), Apparatus 2 (Paddle System), and HPLC (High-Performance Liquid Chromatography) were used for dissolution and potency evaluation, respectively. These tests were considered to measure the actual drug content and physical properties, as well as to forecast how specific products will behave *in vivo*. **Results:** During this investigation, it was found

that the tested results of the five brands of Vonoprazan fumarate tablets complied with the quality specifications described in USP 43-NF 38 (United States Pharmacopeia 43-National Formulary 38). **Conclusion:** All five tested samples from the five distinct brands met the acceptability standards. The products may meet patients' demands and provide the intended therapeutic effects.

Subject Areas

Public Health

Keywords

Vonoprazan Tablets, Potassium-Competitive Acid Blocker (P-CAB), Proton Pump Inhibitor (PPI), Pharmaceutical Quality Assessment, High-Performance Liquid Chromatography (HPLC)

1. Introduction

Vonoprazan fumarate has emerged as a novel, highly efficacious, and long-lasting P-CAB (potassium-competitive acid blocker) that acts through competitive binding and blocking the H^+/K^+-ATPase enzyme of the stomach's parietal cells [1] [2]. The chemical name of Vonoprazan fumarate is 1-[5-(2-Fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyrrol-3-yl]-N-methylmethanamine monofumarate and the alternative names are TAK 438, TAK-438 and Takecab. Vonoprazan has been approved to treat adult patients suffering from a gastric acid-related disorder, such as reflux esophagitis, duodenal ulcer, or gastric ulcer, for the avoidance of recurrence of a gastric or duodenal ulcer when taking low-dose aspirin or NSAIDs (non-steroidal anti-inflammatory drugs). Additionally, it is used as a supplement to annihilate *Helicobacter pylori* among those who have *H. pylori* gastritis, eradicate duodenal ulcers, gastric ulcers, idiopathic thrombocytopenic purpura, and gastric MALT (mucosa-associated lymphatic tissue) lymphoma [3]-[6].

Although PPIs (proton pump inhibitors) have been widely used for GI (gastrointestinal) acid suppression for a long time, some distinct properties of Vonoprazan, such as its rapid onset of action [4] without prior activation [7] and its independence on pH and meal [8], make it prove to be superior to PPIs. Further, the PPIs are insufficient to effectively inhibit nocturnal acid secretion because their inhibitory impact on acid secretion is not properly sustained for up to 24 hours. Still, in such cases, Vonoprazan comes up as a beacon of hope to overcome the situations [7].

The longer half-life of Vonoprazan is the crucial contributing factor for the eradication of *Helicobacter Pylori* in gastric-related disease [9]-[11]. Due to its numerous excellent properties, Vonoprazan has gained global attention in treating gastric acid-related disorders and Bangladesh is not beyond this. Though Vonoprazan was first approved in Japan in 2015 and in Bangladesh, it was approved in 2023 [12]. Currently, about 22 pharmaceutical companies are manufacturing Vonoprazan

in Bangladesh. Literature review showed works like method development for Vonoprazan content analysis [13] [14], bio-equivalence study with Vonoprazan [15], and so on. However, there is no study available on the quality profiles of Vonoprazan that are being manufactured and marketed in Bangladesh. Therefore, this study aims to perform the first-ever pharmaceutical quality evaluation tests of Vonoprazan in Bangladesh.

2. Materials

2.1. Sample Collection

Vonoprazan film-coated tablets were randomly selected and purchased based on their availability in the local retail pharmacy outlets in Dhaka, Bangladesh. It was done to ensure that the study sampling reflects the products that the consumers most commonly access. Since only five brands were selected, this study does not represent every manufacturer. However, this random selection helped to minimize selection bias and provided a realistic assessment of the quality of these products in the local market. The purchased samples were then coded (coded as Sample 1, Sample 2, Sample 3, Sample 4, and Sample 5) and evaluated for various physicochemical quality attributes, including their potency.

2.2. Chemicals and Reagents

Acetonitrile, Triethylamine, Orthophosphoric acid, and Milli-Q water were used in this study.

3. Solution Preparations

3.1. Preparation of Buffer at pH = 6.3

One milliliter of phosphoric acid was added into a 1000 mL beaker containing 900 mL Milli-Q water and mixed well. The solution was adjusted with triethylamine to a pH of 6.3 and volume to 1000 mL with Milli-Q water. pH of the prepared buffer solution was measured and adjusted using a pH meter (Horiba Scientific LAQUA F-72, Japan). Finally, this solution was filtered through a 0.45 µm membrane filter and degassed before use.

3.2. Preparation of Mobile Phase

Acetonitrile and buffer were mixed at a ratio of 30:70 to prepare 3000 mL of mobile phase. The mobile phase was filtered through a membrane filter and sonicated before use.

3.3. Preparation of Diluent

Acetonitrile and Milli-Q water were mixed at a ratio of 5:95 to prepare 5000 mL of diluent.

3.4. Preparation of Standard Solution for Assay

13.40 mg of Vonoprazan Fumarate (which is equivalent to 10.0 mg of Vonoprazan)

working standard was taken in a 100 mL volumetric flask. Sixty milliliters of diluent was added into the volumetric flask, and then the content was sonicated for about 10 minutes. The flask was cooled to room temperature, and the volume was made up to the mark of the flask with diluent. Finally, 1.5 mL was vialed up after filtering through a 0.45 μm PTFE (Poly Tetra Fluoro Ethylene) filter.

3.5. Preparation of Standard Solution for Dissolution

13.40 mg of Vonoprazan Fumarate (which is equivalent to 10.0 mg of Vonoprazan) working standard was taken in a 100 mL volumetric flask. Sixty milliliters of Milli-Q water was added and then sonicated for about 10 minutes. It was cooled at room temperature and 5 mL of this solution was transferred into a 25 mL volumetric flask and Milli-Q water was added up to the mark of the volumetric flask. Finally, 1.5 mL was vialed up after filtering through a 0.45 μm PTFE filter.

3.6. Preparation of Sample Solution for Dissolution

Dissolution Sample preparation was carried out separately for five of the test samples. For each of them, the following procedure was followed.

The dissolution test was carried out utilizing USP Apparatus 2 (Paddle System) according to the method delineated in USP 43-NF 38. Milli-Q water was used as a dissolution medium. The temperature was set at 37˚C.

3.7. Preparation of Sample Solution for Assay

Sample 1A: 142.53 mg powdered Vonoprazan Fumarate tablets sample and 60 mL diluent were taken into a 100 mL volumetric flask, and the flask was placed into a sonicator for sonication for about 10 minutes. The mixture was cooled at room temperature, and then diluent was added up to the mark of the volumetric flask. Finally, 1.5 mL was vialed up through a 0.45 μm PTFE filter. Similarly, Sample 1B was prepared for the present study where the sample weight was 142.65 mg.

For further samples, the preparation procedure was the same, except for the changes in sample weights. Those samples (2A, 2B, 3A, 3B, 4A, 4B, 5A, and 5B) had 123.45 mg, 123.67 mg, 144.96 mg, 145.67 mg, 100.7 mg, 100.2 mg, 133.34 mg, 134.65 mg sample weights, respectively.

4. Methods

Vonoprazan is yet under review and was not included in any version of USP, BP, or other accessible compendia at the time when the tests were carried out. Nevertheless, the general quality parameters or specifications for assay, as well as all the tests conducted throughout this research work, were carried out by following the general chapters (chapters: 621, 631, 701, 711, 730, 851, and 905) of USP 43-NF 38.

4.1. Visual Inspection and Description

Sample 1: White color, oval-shaped film-coated tablet having both sides plain and

free from foreign particles. Sample 2: White color, round-shaped film-coated tablet, and both sides biconvex. Free from foreign particles. Sample 3: White color, round-shaped film-coated tablet having one side plain and the manufacturer's logo embedded on the other side. Free from foreign particles. Sample 4: White color, round-shaped film-coated tablet having both sides plain and free from foreign particles. Sample 5: White color, round-shaped film-coated tablet, both sides plain and both sides are slightly biconvex. Final Evaluation: the visual appearance of all the samples was acceptable.

4.2. Test for Uniformity of Weight

4.2.1. Average Weight per Tablet

Twenty tablets were taken to calculate the average weight of individual tablets. The claimed weight of Vonoprazan in each tablet was 10 mg. The authors of the present study used standard analytical balance (Radwag AS82/220.R2, Poland) for measuring the perfect weight of each tablet. Each tablet was weighed and the weight was recorded. Finally, the average weight was calculated.

4.2.2. Uniformity of Weight

To know the uniformity of weight of the tablets of various samples, the positive deviation, the negative deviation in weight of the tablets, and the percent of relative standard deviation were calculated using Microsoft Excel.

The following formulas were used for positive and negative deviation calculation purposes:

$$\text{Positive deviation} = \frac{\text{Highest weight of tablet} - \text{Average weight of tablets}}{\text{Average weight of tablets}}$$

$$\text{Negative deviation} = \frac{\text{Lowest weight of tablet} - \text{Average weight of tablets}}{\text{Average weight of tablets}}$$

4.3. Hardness Test Procedure

Hardness testing is an important quality aspect. In the present study, six tablets were taken for hardness testing using a hardness tester (Dr. Schleuniger Pharmatron, Switzerland). Each tablet was positioned properly into the tester and subsequently, the force was applied onto the tablet. The required force to break the tablet was recorded and the average value (in kg) was taken as a result of the hardness of the tablets.

4.4. Moisture Content Test Procedure

A 2 g sample was taken on a weighing pan of automatic moisture balance (Radwag PMC 210, Poland), the temperature was set at 105˚C, and the operation was started. The reading of moisture balance was taken when the value was stable.

4.5. Disintegration Time Test Procedure

The disintegration test was carried out according to the specification provided in

the USP 43-NF 38. A Disintegration tester (Labindia 1000, India) was used to accomplish the test and Milli-Q water was used as a disintegration medium. Firstly, the disintegration beaker was filled up with sufficient medium and waited to raise the temperature to 37.0˚C of the disintegration tester. Then, six tablets were taken and one tablet was poured into each tube and a disc was added to each tube. The operation was started and observed. Disintegration was considered to be achieved when no residue, except fragments of the tablet, remains on the screen of the test apparatus. Disintegration time was recorded and the average time was used as the disintegration time of the tablets.

4.6. Identification Test Procedure

Identification of Vonoprazan in Vonoprazan tablet formulations was done by chromatographic analysis. When the prepared sample's chromatogram shows a prominent Vonoprazan peak at the retention time, the Vonoprazan is deemed to have been detected.

4.7. Dissolution Test Procedure

The dissolution of Vonoprazan Fumarate tablets was tested after method validation was carried out to determine accuracy, precision, linearity, range, system suitability, and specificity.

Dissolution media (Milli-Q water as required) was poured into six of the dissolution vessels of the Dissolution Tester (Electrolab Inspire 8, India) and the heater was turned on to achieve 37˚C temperature. When the temperature was achieved, one tablet was placed in each of the six dissolution vessels. For every brand, the device was operated with a paddle system for 45 minutes at 75 rpm. Subsequently, after the specified time, a sample solution was collected from the midzone of dissolution vessels. After filtering the solution through filter papers, it was vialed through a 0.45 μm PTFE disc filter. Finally, dissolution test solutions were tested with the aid of HPLC. The following formula was used for the calculation of % dissolution:

$$\%\ \text{Dissolved} = \frac{Au \times Ws \times 5 \times 500\ \text{mL} \times Pstd \times 100}{As \times 100 \times 25 \times 10 \times 100 \times \text{Factor}(1.34)}$$

where,

Au = Peak area of sample solution;

As = Peak area of standard solution;

Ws = Weight (mg) of working standard taken;

$Pstd$ = Potency of working standard in percentage (%).

4.8. Potency Evaluation of Vonoprazan Tablets

High-Performance Liquid Chromatography (Shimadzu LC-2030C 3D Plus Prominence-1, Japan) after proper validation was used for the assay. A stainless-steel column (15 cm × 4.6 mm) having C8 packing was used for the HPLC analysis. The flow rate was 0.80 mL/min and the injection volume was 10 μL. Run time was 15

minutes and the column temperature was maintained at 40˚C. A PDA (photodiode array) detector was used to detect the active pharmaceutical ingredient (Vonoprazan) at 230 nm. The Assay result was calculated by using the following formula:

$$\text{Content of Vonoprazan per tablet} = \frac{A_{spl} \times W_{std} \times 100 \text{ ml} \times Pstd \times Aw}{A_{std} \times 100 \text{ ml} \times W_{spl} \times F \times 100}$$

$$\text{Stated Potency} = \frac{\text{Content}}{\text{label Claim}} \times 100$$

where,

A_{Spl} = Peak area of sample solution;

A_{std} = Peak area of standard solution;

W_{Std} = Weight (mg) of working standard taken;

W_{Spl} = Weight (mg) of sample taken;

$Pstd$ = Potency of working standard in percentage (%);

Aw = Average weight (mg) of tablet;

F = Factor of Vonoprazan Fumarate to Vonoprazan = 1.34.

5. Statistical Analysis

The data were analyzed using Microsoft Excel 2013 (MS Excel 2013). Mean, standard deviation (SD), and relative standard deviation (RSD) were calculated using the functions = AVERAGE (A_2:A_3), = STDEV.S (A_2:A_3), and = (STDEV (A2:A3)/AVERAGE (A2:A3)) × 100, respectively, where A_2 and A_3 indicate the cell number of MS Excel.

6. Results and Discussions

Continuous quality management is the precondition for manufacturing good quality pharmaceutical products with sustainable market demand. Generic pharmaceutical products must adhere to a similar quality, effectiveness, and safety profile compared to the innovator's product. This study focused on conducting the pharmaceutical quality assessment tests of Vonoprazan following the general chapters (chapters: 621, 631, 701, 711, 730, 851, and 905) of USP 43-NF 38. In the absence of a specialized USP monograph for Vonoprazan fumarate, there is no other way than to follow the general chapters though they do not fully reflect the utmost uniqueness in procedures for analysis of a specific drug product such as Vonoprazan fumarate. In this paper, the mean and, when applicable, the RSD (relative standard deviation) in percentage were used to express the results of different quality parameters.

6.1. Uniformity of Weight Test

Uniformity of the tablet and its drug content weight is the precondition for obtaining therapeutic outcomes from patient care with drug therapy avoiding untoward effects. Tablet contents and content uniformity are very critical quality attributes of solid dosage forms since they may affect the patient' safety and effectiveness

[16]. Weight variation of individual tablets affects their content uniformity. The differences in the weight of individual tablets impact the consistency of their content, which can lead to production batch failures that incur significant financial losses. Extreme inter-tablet weight variations have even resulted from marketed product recalls also [17]. Therefore, the maintenance of uniformity of weight of each tablet in every representative batch must be ensured by the manufacturer. Sometimes, weight variation tests are utilized indirectly to confirm that a drug product's dosage units consistently contain the prescribed dosage of the medicine [18]. In this study, the positive and negative deviation of each tablet of the five test samples was within ±7.5% of the average tablet weight and thus the tested samples complied with the quality specifications (positive and negative deviation should be within ±7.5% of average weight) stated in USP. The results of the test are placed in Table 1, which confirms the consistency of tablet wights.

Table 1. Test results for uniformity of weight of five brands of Vonoprazan fumarate film-coated tablets (n = 20) marketed and manufactured in Bangladesh.

Brands code	The mean weight of tablets	RSD (%)
Sample 1	142.56	2.95
Sample 2	123.88	3.47
Sample 3	145.32	2.86
Sample 4	102.16	3.82
Sample 5	133.06	3.19

6.2. Hardness Test

The mechanical strength of tablets is a crucial property for the effective advancement and production of solid pharmaceutical products, especially tablets. Inadequate mechanical strength can lead to problems like patients and regulating authorities seeing tablets as being of low quality because of undesirable looks like chipping, lamination, and dustiness, and problems like incorrect dosage due to drug loss during shipping and handling [19]. As a result, the potency may be affected by the lower or higher hardness of the tablets [20]. So, the manufactured tablets must have the optimum mechanical strength to be counted as a good-quality pharmaceutical product. This study revealed that none of the five test samples from five

Table 2. Hardness test results of different Vonoprazan fumarate film-coated tablets (n = 6) marketed and manufactured in Bangladesh.

Brands code	Mean hardness (kg/cm^2)	RSD (%)
Sample 1	7.43	0.472
Sample 2	6.02	0.544
Sample 3	7.09	0.372
Sample 4	6.66	0.324
Sample 5	6.85	0.354

different brands had a hardness of less than 6 kg/cm^2 (shown in Table 2) which complies with the quality specification (6 to 12 kg/cm^2 for film-coated tablets) stated in British pharmacopeia.

6.3. Moisture Content Test

Moisture content is considered a very critical and influential parameter of pharmaceutical products. The characteristics of aged tablets made through the wet granulation method showed significant variation based on the moisture levels within the granules. Moisture content in drug formulation may affect the stability of the drug products through hydrolysis and alterations in the crystal habit of solids. The more moisture they contained, the more influence it had on their properties. Research findings imply that two controllable variables-tablet crushing strength and moisture content influence tablet friability. At higher crushing strengths and ideal moisture concentrations, tablet friability can be significantly decreased [21]. It was discovered that tablets with a high initial moisture content become harder during storage which means hardness increases upon storage. A tablet with increased hardness may lengthen the time for its disintegration which affects the pattern and times of drug release from the dosage form and finally may affect the onset of drug action. Tablets along with reduced levels of primary moisture content are not significantly influenced during storage [22]. In this work, it was found that none of the five test samples from five different individual brands had a moisture content of more than 3.0% at 105˚C temperature (shown in Table 3), which indicates the optimum level of moisture content in the tablets of all studied brands.

Table 3. Moisture content of Vonoprazan fumarate film-coated tablets (n = 6) marked as different brands in Bangladesh.

Brands code	Mean moisture content (%)	RSD (%)
Sample 1	1.13	1.545
Sample 2	2.36	0.758
Sample 3	1.56	1.608
Sample 4	1.96	1.291
Sample 5	1.86	0.927

6.4. Disintegration Time Test

The physical process of mechanically breaking down a tablet or granulated particle into smaller pieces is known as disintegration [23]. Disintegration occurs in two stages after the liquid has soaked into and penetrated the tablet's surface pores. Two things happen: first, the tablet breaks up into tiny granules, and then the granule disintegration or disaggregation takes place [24]. Disintegration affects the initial steps of drug release from its dosage form and mostly influences the rate of drug dissolution. Disintegration facilitates drug absorption by inducing the surface area of active drugs and it is the prerequisite for the bioavailability of the API (active pharmaceutical ingredients) [25] [26]. In this analysis, it was observed that

none of the five test samples of five different brands had a disintegration time of more than 30 minutes in Milli-Q water at 37˚C temperature which indicates the good disintegration time profile of Vonoprazan fumarate film-coated tablets (shown in Table 4). This finding implicitly indicates effective *in vivo* predicted disintegration of the investigated drug products, which is crucial for the initial drug release rate from the tablet and may enhance the drug dissolution rate upon contact with biological fluids.

Table 4. Test results for disintegration time of Vonoprazan fumarate film-coated tablets (n = 6) marked as different brands in Bangladesh.

Brands code	Disintegration time (minutes)
Sample 1	11
Sample 2	7
Sample 3	10
Sample 4	8
Sample 5	10

6.5. Identification Test

Anticipating the presence of pure substances or contaminants is the first step towards quantifying and purifying a material and eliminating surplus. For pharmaceutical quantitative analysis, it is very important to identify the API and excipients separately before quantifying. Potency analysis is crucial to ensure the accurate dose of a drug in a particular dosage form or a specified unit dose. But before quantifying the actual drug content in a pharmaceutical formulation, it must be ascertained that the substance is the desired drug substance. For this type of assurance, an identification test is considered as a benchmark. In this research, before conducting the dissolution and potency evaluation the authors of the present study conducted the identification test for vonoprazan comparing the retention time (3.7 min) of Vonoprazan sample chromatogram (Figure 1) with that of the Vonoprazan reference standard chromatogram (Figure 5). Vonoprazan was thus properly identified in each of the six tested samples of five different brands (shown in Table 5), which indicated that patients are taking the right drug labeled on the drug product.

Table 5. Identification of Vonoprazan fumarate film-coated tablets (n = 2) marked as different brands in Bangladesh.

Brands code/standard	Mean retention time (minutes)	RSD (%)
Standard	3.777	0.056
Sample 1	3.767	0.019
Sample 2	3.779	0.056
Sample 3	3.772	0.3
Sample 4	3.776	0.393
Sample 5	3.86	0.784

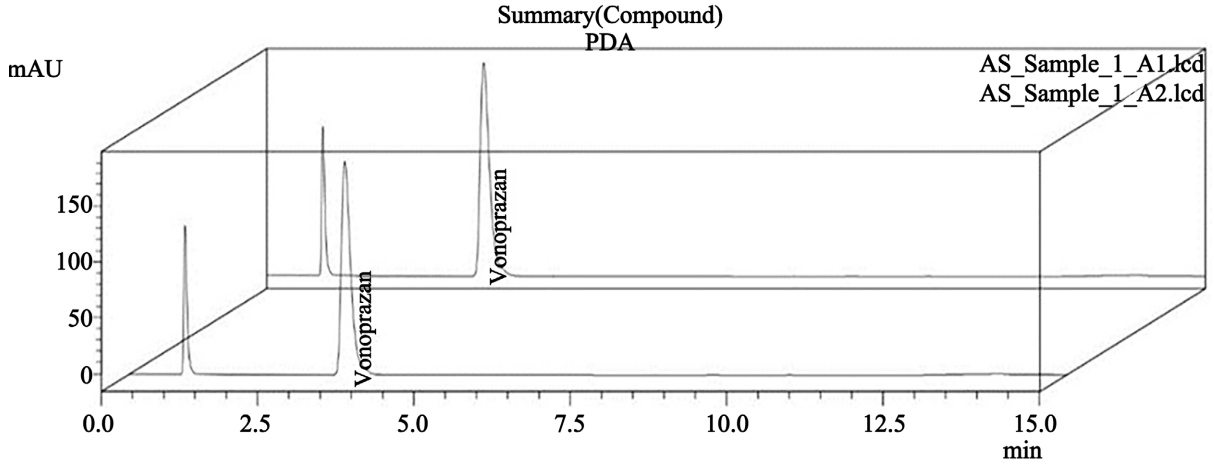

Figure 1. Chromatogram of Vonoprazan fumarate of Sample 1 (two replicates) confirms the identification of Vonoprazan.

6.6. Dissolution Test

When developing and approving a generic dosage form of a particular drug, *in vitro* dissolution testing is considered a crucial technique. Dissolution test is commonly used to ensure the quality and stability of both oral and non-oral dose forms. In another case, it can be utilized to forecast how specific products will behave *in vivo* [27] [28]. Additionally, dissolution testing is crucial in determining bio-equivalence investigations regarding scale-up and post-approval modifications [29] [30]. Without compromising the caliber of the pharmaceutical items, regulatory bodies work to lessen the weight of regulations and avoid needless human studies. A significant part of this sort of work is the dissolution testing of generic medication items [31]. In the present study, authors conducted a dissolution test of Vonoprazan fumarate film-coated tablets with six replicates (**Figure 3**, a representative figure) for each brand. The investigated five different brands manufactured in Bangladesh showed the percentage of dissolution within the acceptance range which was not less than 75% (**Table 6**). The dissolution test results of all the studied samples thus complied with the USP specifications suggesting that the active ingredient in the studied brands will achieve the expected dissolution in the patients' stomach and result in the distribution of the drug in the bloodstream of the patient to impart its action properly. The dissolution rate was calculated using a chromatogram of standard for dissolution (**Figure 2**) and a chromatogram of samples such as Sample 1 for dissolution (**Figure 3**) and others (not shown).

Table 6. Dissolution of Vonoprazan fumarate film-coated tablets (n = 6) marked as different brands in Bangladesh.

Brands code/standard	Mean dissolution rate (%)	RSD (%)
Sample 1	89.36	4.592
Sample 2	95.86	0.867
Sample 3	96.47	1.493
Sample 4	89.32	2.023
Sample 5	78.6	5.554

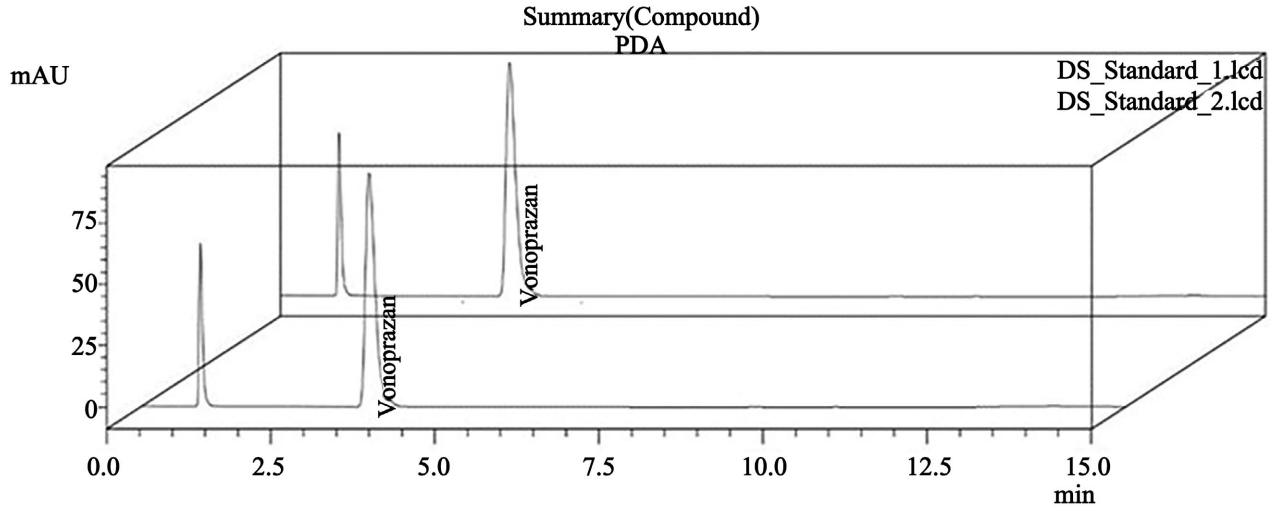

Figure 2. Chromatogram of the standard Vonoprazan fumarate recorded for its dissolution profile.

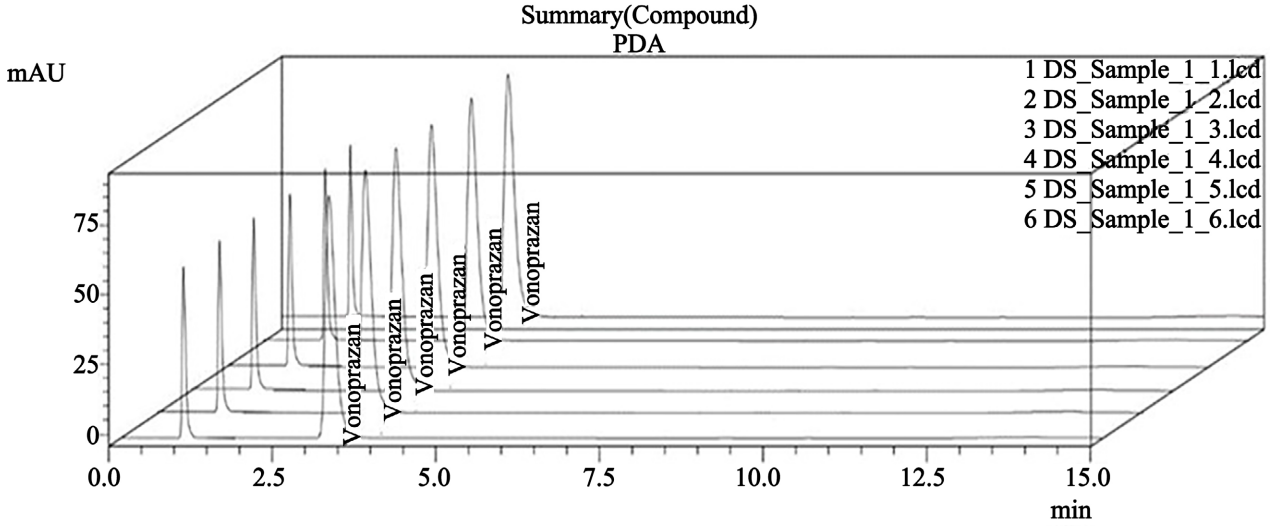

Figure 3. Chromatogram of Vonoprazan fumarate sample-1 (six replicates) recorded for its dissolution profile.

6.7. Potency Test

Potency analysis of the selected brands of Vonoprazan fumarate film-coated tablets was carried out by the validated HPLC method as stated in the method section of this manuscript. **Figure 5** shows the chromatogram of the Vonoprazan fumarate reference standard. It indicates that Vonoprazan fumarate appears at a retention time of about 3.7 minutes. **Figure 1** and **Figure 4** are the chromatograms of Vonoprazan fumarate table Sample 1A and Sample 1B, respectively. Peaks at about 3.7 minutes in these figures indicate that Sample 1A and Sample 1B contain Vonoprazan. Other samples also show similar chromatograms (figures are not shown). The content of the Vonoprazan in each sample was calculated utilizing the chromatogram of the Vonoprazan reference standard for potency (**Figure 5**) and Vonoprazan samples such as **Figure 1** and **Figure 4** and using the formula stated under the method section in this paper. The mean potency of each sample was determined from two

replicates of HPLC measurements. The results and RSD values are presented in Table 7. Chromatograms of the remaining samples are not shown to save pages of the journal.

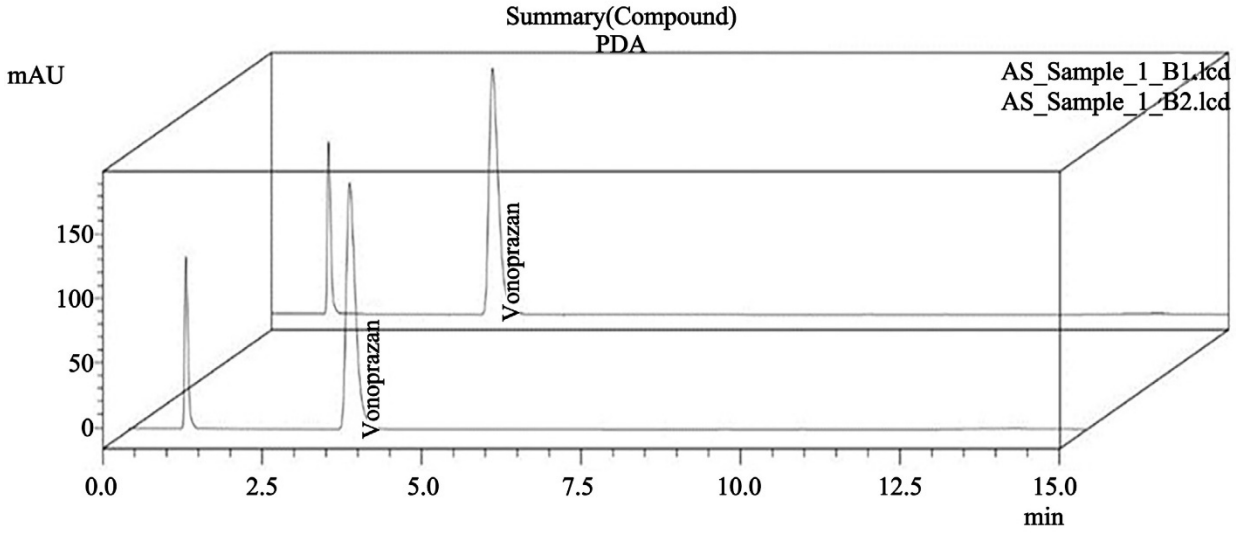

Figure 4. Chromatogram of Vonoprazan fumarate Sample 1A (two replicates).

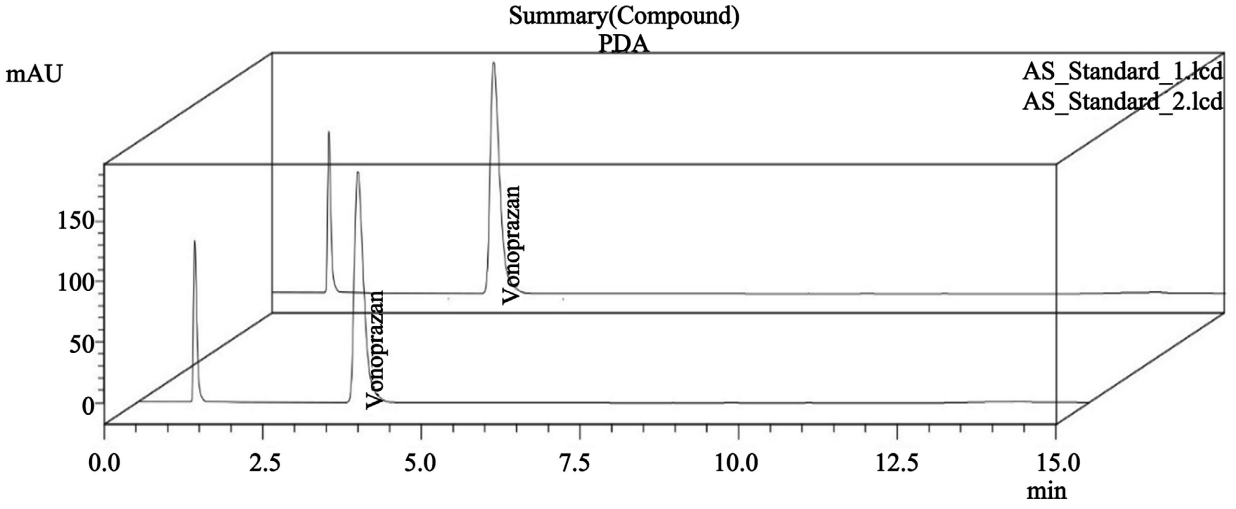

Figure 5. Chromatogram of Vonoprazan fumarate reference standard for potency.

Table 7. Potency and RSD of Vonoprazan fumarate film-coated tablets (n = 2) marked as different brands in Bangladesh.

Brands code/standard	Mean potency (%)	RSD (%)
Sample 1	99.55	0.071
Sample 2	100.8	0.281
Sample 3	100.1	0.283
Sample 4	101.6	0.139
Sample 5	101.95	0.624

In most cases, an upsurge in toxicity occurs along with a rise in therapeutic potency but the therapeutic ratio does not always alter [32]. Drug potency is also related to AMR (antimicrobial resistance) in the case of antimicrobial drugs. AMR may develop if an individual takes an antimicrobial medicine with sub-therapeutic potency within the specified time frame. According to certain research, inadequate quality control procedures and incompetent regulatory agencies may also contribute to the release of inferior or overrated pharmaceutical items onto the market [33]. So, potency evaluation before and after launching a drug into the market and at rational intervals is crucial for ensuring patient safety. In this study, each of the five samples from five different brands was shown to have the content of Vonoprazan within the range of 90% - 110% (**Table 7**), which fairly complies with the regulatory specification for film-coated tablets stated in USP 43-NF 38. These results suggest that each of the studied brands has enough abundance of its active ingredient to impart pharmacological action and cure patients.

This *in vitro* study highlights the need for continuous quality management and broader evaluations. However, *in vivo* studies could further aid in a deeper assessment of the quality of those drugs. Such efforts can enhance patient care, promote public confidence, and support sustainable pharmaceutical markets.

7. Conclusion

Finally, it can be summarized that all of the five tested samples from five different brands manufactured and marketed in Bangladesh have passed the acceptance quality criteria and the products may satisfy the patients' needs with desired therapeutic outcomes. All of the brands studied here have proven that the manufacturer can manufacture the desired quality and world-class pharmaceutical products in Bangladesh. Monitoring the drug products' quality involves evaluating different aspects of their quality and disseminating the information gathered. The results of the current study may help in this regard. Although the studied products revealed a good state of quality, manufacturers must pay strong attention to preserving all the quality features of their products to ascertain the effectiveness and safety of manufactured products for the best utilization of patients' money with excellent therapeutic outcomes. Additionally, regulatory bodies must exercise greater caution and maintain strict pressure on manufacturers to safeguard the production of high-quality pharmaceutical products.

8. Limitations

Due to financial and resource constraints, the products of Vonoprazan fumarate of only five brands out of the 22 available were studied in this research. The products of only 10 mg strength were studied, as this strength is common in all of the manufacturers' products, but it would have been better if we could have included the products with various dosage strengths. There was no specialized USP monograph existed for Vonoprazan fumarate, necessitating reliance on standard USP chapters. Although general chapters offer effective guidelines and useful recommendations,

they do not fully reflect the utmost uniqueness.

9. Future Directions

This analysis only focused on *in vitro* test parameters. Extensive *in vivo* analysis is required to ensure the proper safety, efficacy, and overall therapeutic effectiveness of those products. This study was conducted with self-funding. Later, if we get enough funds for research, then we will investigate more physicochemical quality parameters using other sophisticated analytical tools, various *in vivo* analyses will be conducted and Vonoprazan fumarate from all available brands will be included.

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This study was conducted with self-funding.

Authors' Contributions

Shahriyar Tonmoy conducted this study. Md. Ataur Rahman helped in planning and conducting the study with the necessary supervision during the work. Md. Ataur Rahman also wrote the initial draft of the manuscript. Besides giving suggestions from time to time to the members of the research team, Md. Rafiquzzaman comprehensively reviewed and edited the manuscript to bring it to the publishable standard and format. Every author contributed to the background of the work and participated in literature work, editing, and preparation of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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