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Quantitative Determination of Favipiravir Tablets by Ultraviolet-Visible Spectrophotometry

Patsachon Poonsawat[1], Sivaporn Wongpayoon[1] and Phurit Thanarangsarit[2]*
[1]Pharmacy Student, Faculty of Pharmaceutical Sciences, Huachiew Chalermprakiet University, Thailand
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Huachiew Chalermprakiet University, Thailand
*Corresponding Author's E-mail: stamphurit@hotmail.com

Rationale

Nowadays, due to the worldwide outbreak of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection or generally known as the coronavirus disease-2019 (COVID-19), favipiravir has been repurposed and also indicated as one of first-line therapy in some countries, including Thailand. Based on the clinical practice guideline, favipiravir is recommended in case of symptomatic COVID-19 without pneumonia and no risk factors for severe disease.

Japanese Pharmacopoeia (JP) with support from other pharmacopoeias has developed an official method for assaying favipiravir and favipiravir tablets, using high-performance liquid chromatography (HPLC). In addition, validated HPLC method was also developed for the analysis of favipiravir in pharmaceutical products and human plasma. However, HPLC was realized to be a costly and time-consuming method.

Recently, using of UV-visible spectrophotometric method for the determination of favipiravir in pharmaceutical formulations has been reported in previous studies. Ethanol, ethanol and water (5 in 100 mL for standard stock solution), and deionized water only were used as solvent. Since favipiravir is slightly soluble in water and ethanol, selection of suitable solvent was a key step for further preparation and dilution of standard and sample solutions.

To ensure that favipiravir was dissolved completely in a consistent component of the solvent, in this study, a validated UV-visible spectrophotometric method using a cosolvent system was developed for quantification of favipiravir in tablet dosage form.

Research Objectives

To develop and validate a UV-visible spectrophotometric method for the estimation of favipiravir in tablet formulation.

Methodology

Preparation of stock standard solution

Favipiravir standard was weighed accurately about 10 mg into a 100-mL volumetric flask and 40 mL of ethanol : water (1:1, v/v) was then added. The flask was swirled vigorously for 10 min or until the standard was completely dissolved. Finally, adjusted to the volume with the same solvent to obtain a favipiravir stock standard solution at concentration of 100 µg/mL.

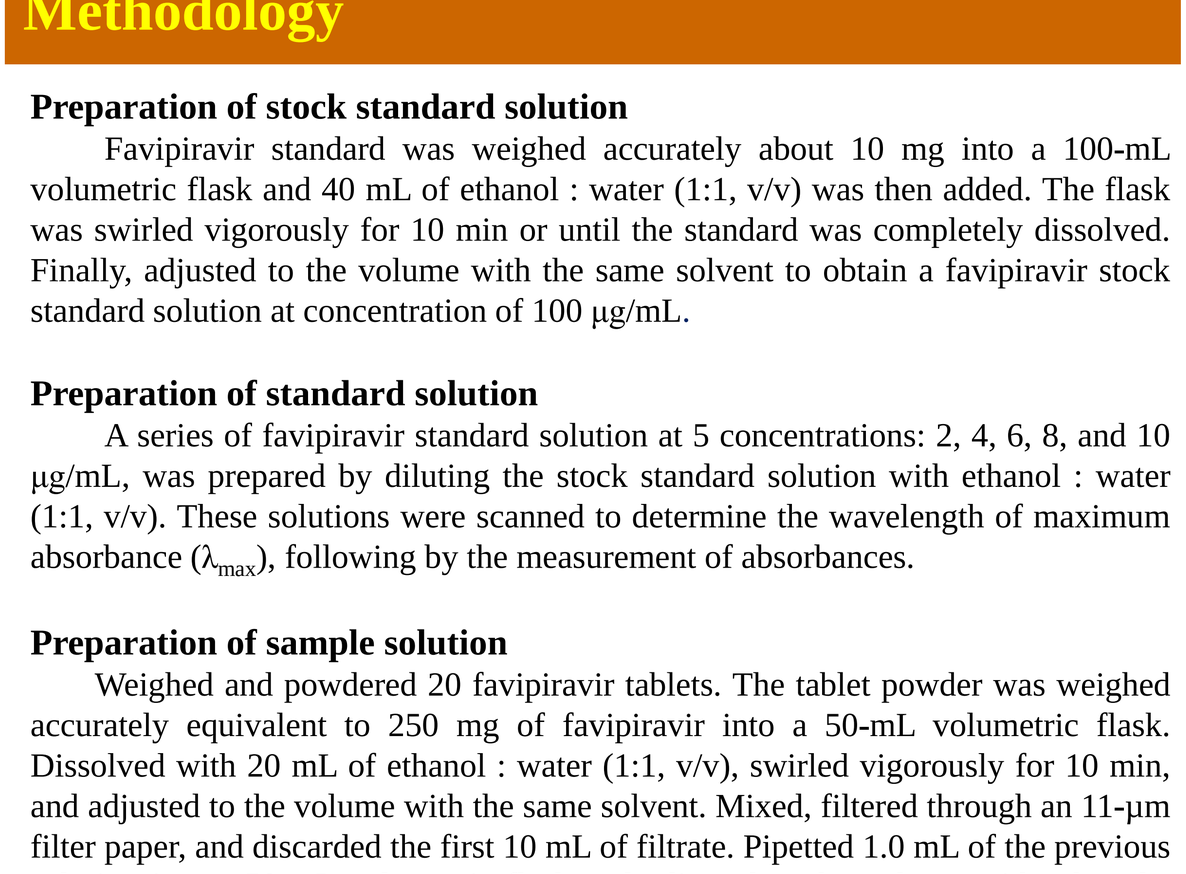
Preparation of standard solution

A series of favipiravir standard solution at 5 concentrations: 2, 4, 6, 8, and 10 µg/mL, was prepared by diluting the stock standard solution with ethanol : water (1:1, v/v). These solutions were scanned to determine the wavelength of maximum absorbance (λ_{max}), following by the measurement of absorbances.

Preparation of sample solution

Weighed and powdered 20 favipiravir tablets. The tablet powder was weighed accurately equivalent to 250 mg of favipiravir into a 50-mL volumetric flask. Dissolved with 20 mL of ethanol : water (1:1, v/v), swirled vigorously for 10 min, and adjusted to the volume with the same solvent. Mixed, filtered through an 11-µm filter paper, and discarded the first 10 mL of filtrate. Pipetted 1.0 mL of the previous solution into a 50-mL volumetric flask and adjusted to the volume with ethanol : water (1:1, v/v) to finally obtain a sample solution containing 100 µg/mL of favipiravir.

Method validation (ICH and AOAC guideline)



Assay of favipiravir tablets

Referred to the preparation of sample solution, 100 µg/mL of favipiravir was prepared in triplicate. Firstly, the tablet powder was weighed accurately equivalent to 50 mg of favipiravir into a 50-mL volumetric flask. Then, 20 mL of ethanol : water (1:1, v/v) was added, swirled vigorously for 10 min, and adjusted to the volume with the same solvent. After quantitative filtration, 5.0 mL of the filtrate was diluted to 50.0 mL with ethanol : water (1:1, v/v). Finally, diluted 3.0 mL of this solution to 50.0 mL with ethanol : water (1:1, v/v) and measured the absorbance at λ_{max}. Calculated the content of favipiravir per tablet by the absorptivity (a) obtained from linear regression analysis.

For the acceptance criteria, favipiravir tablets contain not less than 95.0% and not more than 105.0% of the labeled amount.

Results

Method validation

All validation parameters and results are displayed in Table 1 and Figure 1.

Table 1 ***Method validation results of favipiravir***

Parameters	Acceptance criteria	Result	Conclusion
Specificity	Characteristics of UV spectra and λ_{max} are resemble	λ_{max} = 227 nm **(Fig. 1)**	**PASSED**
Linearity	r ≥ 0.995	y = 0.042x + 0.0152 r = 0.9998	**PASSED**
Range	Concentration range that gives a linear response	2 – 10 µg/mL	-
Accuracy	%Recovery = 98 – 102	100.2 (average)	**PASSED**
Precision	%RSD ≤ 1.3	1.28	**PASSED**

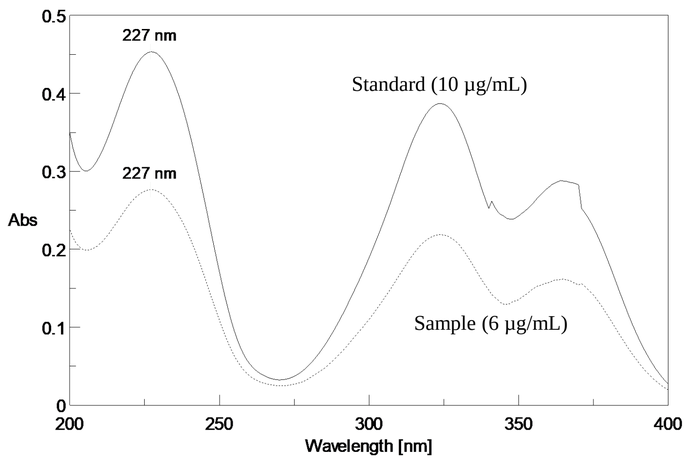


Fig. 1 ***Overlay UV absorption spectra of standard favipiravir at 10 µg/mL (solid line), and sample solution at 6 µg/mL (dash line).***

Assay of favipiravir tablets

Sample solution of 200-mg favipiravir tablets at 6 µg/mL was prepared in triplicate and determined for the absorbances at 227 nm. Based on the calculation using regression equation, the amount of favipiravir (mg/tablet) and percent labeled amount (%L.A.) were displayed in Table 2.

Table 2 ***Assay result of favipiravir tablets (n = 3)***

No.	Label claim (mg)	Amount found (mg)	%L.A.
1	200	190.5	95.27
2	200	191.2	95.60
3	200	193.2	96.59
	Average		**95.82**

Discussion and Conclusion

In this study, UV-visible spectrophotometric method which used to quantify the content of favipiravir in tablet formulation was modified from recent studies. Jyothi, *et al.* (2021) had introduced a simple, precise, and accurate UV spectrophotometric method for the estimation of favipiravir. Unfortunately, using of this validated method to analyze the marketed products was not applicable. As mentioned earlier, ethanol : water (1:1, v/v) was a suitable solvent in terms of cosolvent property with consistent ratio for the preparation of favipiravir standard and sample solutions. For method validation results, referred to ICH guideline, all parameters including specificity, linearity and range, accuracy, and precision were evaluated and also met the acceptance criteria. Interestingly, our study showed good linearity of the method with r ≥ 0.995 over the concentration range of 2 – 10 µg/mL, lower than a previous study result which was reported in the range of 10 – 60 µg/mL for both UV and HPLC technique (Bulduk, 2021, pp. 57-65). This finding suggested higher sensitivity of developed method for favipiravir detection.

For favipiravir assay, although the %L.A. of faviravir (in triplicate) were in range of 95.0 – 105.0%, all values as well as the average %L.A. were near the lower limit criteria. Thus, more brands of commercially available favipiravir tablets should be tested to confirm the performance of this analytical method.

In conclusion, the developed UV-visible spectrophotometric method in this study was considered to be simple, specific, linear, accurate, precise and sensitive for the determination of favipiravir. Moreover, this analytical method was fully validated as per ICH guideline and successfully applied for the estimation of favipiravir in tablet formulation. Hence, this method can be used in routine quantitative analysis for the quality control of favipiravir tablets.

References

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