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REVIEW ARTICLE

A Review on Various Novel Analytical Methods Reported on Favipiravir Estimation

Harshitha M*[1], Sowmya H G[2], Naveen Kumar G S[3]

[1] *Student, Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, Bharathinagara, Mandya district, Karnataka, India*
[2] *Assistant professor, Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, Bharathinagara, Mandya district, Karnataka, India*
[3] *Head of department, Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, Bharathinagara, Mandya district, Karnataka, India.*

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Abstract:
The ongoing and interdependent tasks associated with research and development, quality control, and quality assurance encompass the generation and validation of analytical methods. These methods play a crucial role in risk management and equivalency assessments, aiding in the formulation of product-specific acceptability standards and ensuring consistent outcomes. Validation processes determine the appropriateness of analytical methods for their intended purposes. A comprehensive literature review reveals that Favipiravir can be analyzed individually or in combination with other medications using analytical techniques such as UV spectroscopy, RP-HPLC, and HPTLC. The parameters, including accuracy, precision, robustness, and other aspects of analytical validation, were scrutinized in line with ICH guidelines. The identified techniques are applicable to both bulk and tablet dosage forms of Favipiravir, given their straightforward, sensitive, and reproducible nature. The review also elucidates the applicability and limitations of various published analytical techniques for Favipiravir analysis. Researchers engaged in Favipiravir studies stand to gain significant insights from this comprehensive review.

Keywords: Favipiravir; Quantification; Validation; RP-HPLC; HPTLC, COVID-19.

1. Introduction

Favipiravir, a widely recognized medication for influenza, is currently under investigation for its potential in treating COVID-19, representing the first orally administered antiviral for mild to moderate cases of the disease. Research conducted in China, Japan, and Russia has indicated its effectiveness in treating COVID-19. Developed by Japan's Toyama Chemical, Favipiravir is a pyrazine carboxamide derivative known for inhibiting various RNA viruses. Initially identified as a minimally cytotoxic, selective inhibitor of influenza virus replication, Favipiravir targets the RdRp catalytic region, impeding viral replication and reducing infection. As a prodrug, Favipiravir undergoes phosphorylation and ribosylation to form its active state, Favipiravir ribofuranosyl-5'-triphosphate (Favipiravir-RTP). This active form binds to RNA-dependent RNA polymerase, mimicking guanosine and adenosine, preventing primer extension and inhibiting viral replication. Clinical studies highlight Favipiravir's teratogenic properties, rendering it unsuitable for use during pregnancy. Orally administered, the medication achieves peak concentration within two hours, with a brief half-life of two to five hours. Favipiravir exhibits a plasma protein binding capability of 54%. Favipiravir is chemically identified as 6-fluoro-3-hydroxypyrazine-2 carboxamide. Presenting as a pale-yellow powder in crystalline solid form, it exhibits solubility in organic solvents like N, N-Dimethyl Formamide and methanol, as well as in DMSO, NAOH, and deionized water. With a molecular formula of C5H4FN3O2, a molecular weight of 157.1g/mol, and a melting point ranging from 187 to 193°C [2], Favipiravir is characterized by these chemical and physical attributes.

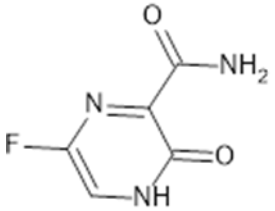

Figure 1 Structure of Favipiravir

* Corresponding author: Harshitha M

The main aim of this review is to critically evaluate and present all the recent analytical methods reported for the estimation of Faviparivar in bulk and tablet dosage forms.

2. Analytical Methods Reported on Favipiravir

- Sayyed Nazifa Sabir Ali et al. (2022) reported a UV-spectroscopic method was developed to quantify Favipiravir in both bulk and pharmaceutical dosage forms. The chosen solvent for UV examination was water, and the solution was scanned in the UV range (200-400nm) with a concentration range of 2–10µg/ml. The λmax value was determined. The RP-HPLC method utilized an inertsil ODS-3V C18 column (150mm X 4.6mm X 5µ) with a mobile phase of buffer pH 3.5 acetonitrile (90:10), a flow rate of 1.0ml/min, and PDA detection at 358nm. Validation of the UV method included assessments for linearity, precision, accuracy, repeatability, and stability in accordance with ICH criteria, with all parameters meeting acceptable limits. The established UV and RP-HPLC procedures were deemed accurate, sensitive, repeatable, and precise, making them suitable for routine Favipiravir analysis in the pharmaceutical industry. Forced degradation studies showed water hydrolysis to be the least detrimental (3.57% degradation), in contrast to acid hydrolysis (39.64% breakdown) [3]

- Sandip D Firke et al. (2021) reported a UV-spectroscopic method was developed to quantify Favipiravir in both bulk and pharmaceutical dosage forms. The chosen solvent for UV examination was water, and the solution was scanned in the UV range (200-400nm) with a concentration range of 2–10µg/ml. [4]
- Karthikeyan Ramadoss et al. (2023) validated a UV method for quantifying Favipiravir (400mg) in tablet and bulk forms, employing ethanol: water (30:70) as the solvent. The method demonstrated linearity in the 2–10µg/ml range, with a determined λmax of 231nm and an r2 value of 0.9987 for the calibration curve. Precision, determined by percentage RSD values for intraday and interday measurements, was within acceptable limits. Accuracy testing on a commercial tablet formulation showed percentage purity between 98 and 103%, confirming the method's accuracy and correctness. The suggested approach proved successful for the quantitative estimation of Favipiravir in tablet formulations [5]
- Girija Bhavar et al. (2023) devised and validated an ultraviolet spectrophotometric method for quantifying favipiravir, following ICH principles. Utilizing 0.1N HCL as the solvent, the analysis was conducted at 323nm. The linear calibration curve spanned the concentration range of 1 to 25µg/ml, adhering to Beer–Lambert's law with a correlation coefficient (r2) of 0.9992. Thorough validation, in accordance with ICH regulations, encompassed range, recovery study, LOD, LOQ, accuracy, and precision. The method demonstrated accuracy through percentage RSD values below 2%, and recoveries ranged from 98% to 102%. No interference from tablet excipients was observed, and the approach was deemed precise, accurate, robust, and specific. Successfully implemented in medicine dosage forms, the suggested UV method is suitable for routine favipiravir analysis [6].
- P Chiranjeevi et al. (2022) aimed to develop and validate a UV spectroscopy method for assaying favipiravir in pharmaceutical and pure dosage forms. Standard and working solutions were prepared using acetonitrile, with subsequent examination of various concentration aliquots. The established method demonstrated accuracy and sensitivity within the 4–24µg/ml range, without interference from formulation excipients. The linear equation Y=0.037x-0.027, with a correlation coefficient (r2) of 0.999, was utilized in multivariate analysis. Precision findings revealed accuracy at each level, with % RSD below 2%. Recovery experiments confirmed the method's accuracy, and the developed methodology's correctness was indicated by high recovery values. Robustness and ruggedness studies highlighted the method's increased sensitivity [7].
- Ibrahim Bulduk et al. (2020) introduced a fast, accurate, and precise high-performance liquid chromatography (HPLC) approach for routine quality monitoring of favipiravir in pharmaceutical formulations. Utilizing a C18 column, a mobile phase of 50mM potassium dihydrogen phosphate (pH 2.3) and 90:10v/v acetonitrile, a flow rate of 1ml/min, and UV detection at 323nm, the method demonstrated outstanding linear connection between peak area. The developed method proved to be robust, accurate (recovery, 99.19–100.17%), precise (low interday and intraday RSD values), sensitive (limits of detection and quantification), and specific. The approach has been effectively utilized for measuring favipiravir in medication formulations, providing a rapid, economical, and accurate solution for analysis [8].
- Safa M. Megahed et al. (2019) have introduced a reliable, sensitive, and environmentally friendly fluorescence-detection HPLC method for the determination of favipiravir (FAV). The fractional factorial design was employed to screen parameters influencing chromatographic results, and the Box-Behnken design optimized critical method parameters. The optimal chromatographic conditions involved a mobile phase consisting of 0.1% phosphoric acid solution and isopropanol (98.2% v/v) at a flow rate of 0.8ml/min and a temperature of 35°C. The Eclipse plus® C18 (100mm x 4.6mm X 3.5µm) column was used, and the fluorescence detector detected emission at 432nm and excitation at 361nm. A linear response within the 20-240ng/ml range was observed, with a limit of 6.11mg/ml. The method exhibited a mean recovery percentage of ±0.59 for the pharmaceutical formulation of FAV, and its sensitivity enabled determination in spiked human plasma within a 40–240ng/ml range. The integration of quality by design and green chemistry contributed to the development of an environmentally friendly technique [9].

- Rambabu Gundla et al. (2021) developed and validated a precise, accurate, linear, robust, and stability-indicating HPLC technique for identifying degrading impurities in favipiravir film-coated tablets. Utilizing an Inert sustain AQ-C18 (250 × 4.6 mm, 5-µm particle) column, acetonitrile and water (50:50, v/v) in mobile phase B, and KH2 PO4 buffer (pH 2.5 ± 0.05) and acetonitrile (98:2, v/v) in mobile phase A, the method successfully separated all contaminants. Chromatographic conditions were optimized at a flow rate of 0.7ml/min, UV detection at 210nm, injection volume of 20µL, and column temperature of 33°C. The method was verified based on the Q2 (R1) International Conference on Harmonization guidelines. Recovery study and linearity ranges were established, and the technique's validation results indicated r2=0.9995-0.9999 and 98.6–106.2% recovery and linearity for all detected contaminants, respectively. Precision findings showed relative standard deviation below 5% [10].
- Ibraam E. Mikhail et al. (2021) developed and verified two new straightforward, environmentally friendly, and sensitive methods for determining FAV using solvent-free micellar LC and spectrofluorimetric techniques. Variables such as pH, buffering, solvent type, and additional surfactants were investigated to enhance FAV native fluorescence. The maximum sensitivity for FAV fluorescence was observed at 436nm in Britton-Robinson buffer (pH 4) within the concentration range of 20–350ng/ml. Another HPLC technique, utilizing a C18-RP (5 µm, 250 × 4.6 mm) stationary phase and solvent-free mobile phase, was verified over a range of concentrations of 10-100µg/ml, with FAV eluting in 3.8 minutes. The methods were successfully applied to determine FAV in spiking human plasma samples and marketed tablet dosage forms, demonstrating eco-friendliness based on two contemporary greenness metrics (AGREE and GAPI) [11].
- Patil Aishwarya Balu et al. (2021) employed high-performance liquid chromatography (HPLC) to estimate the dosage form and bulk of favipiravir. The separation process utilized a mobile phase of methanol: water (0.05% triethylamine) at a ratio of 70:30, flowing at a rate of 0.8ml/min through a C18 column with UV detection at 360nm. The favipiravir calibration curve spanned the concentration range of 20–100µg/ml, displaying a linear response directly correlated with its concentration within the 10-100µg/ml range. Repeatability and intermediate precision, indicated by the percentage RSD, were both below 2%. The method's accuracy was confirmed by a respectable percentage recovery of 99.7%, coupled with its short run time (15 min), retention time (2.34), and mobile phase flow rate (0.8 ml/min), making it an effective tool for antiretroviral measurement. Its potential application extends to future research in various matrices, such as plasma, and for quality control analysis [12].
- Vijay Borkar et al. (2022) achieved the validation of Favipiravir in tablet and pure form through a rapid and accurate reverse-phase high-performance liquid chromatographic technique. Using a 50:50v/v mixture of HPLC grade water and methanol as the mobile phase, chromatography occurred on a Kromasil 100-5-C18 column (300×3.9 mm, 5 µm) at a flow rate of 1.0ml/min, with detection at 221nm. The medication was retained for 3.325 ±0.25 minutes. The technique demonstrated linear results within the Favipiravir concentration range of 20–100µg/ml, with precision less than 2.0% RSD. Both intra- and inter-day variations confirmed the accuracy of the system, meeting ICH criteria. The LOQ was 0.44µg/ml, and the LOD was 0.15µg/ml, validating the method for various factors and meeting ICH guidelines [13].
- Srivani Bathula et al. (2023) developed a high-performance liquid chromatographic method to validate favipiravir in both bulk and medicinal dosage forms. The separation used a methanol: phosphate buffer (35:65) v/v mobile phase at a flow rate of 1.0ml/min on a symmetrical ODS C18 column (4.6X250mm, 5µm) with UV detection at 235nm, resulting in a run time of less than 8min. Favipiravir's retention time was found to be 2.276 minutes, and the calibration plot displayed linearity over the concentration range of 6–14µg/ml. Limits of quantification and detection were 3.6 and 1.2mg/ml, respectively. The method demonstrated accuracy, linear recovery within the 98.0-102% range, and precision within acceptable limits. Resilience and robustness tests were successfully passed, and the analytical method displayed linearity within the target concentration range of 6-14ppm for Favipiravir [14].
- Nandeesha Itigimatha et al. (2022) explored Favipiravir (FVP), a pyrazine analogue, renowned for its antiviral efficacy against various viruses, including its potential as a COVID-19 treatment candidate. Despite its absence in formal pharmacopoeias, a rapid, precise, and accurate isocratic high-performance liquid chromatography (HPLC) method was developed for routine pharmaceutical quality control. The method employed a C18 column to achieve separation in dosage forms. The mobile phase, composed of 50mM potassium dihydrogen phosphate (pH 2.3) and acetonitrile (90:10, v/v) at a flow rate of 1ml/minute, facilitated a 15-minute run duration. Linear correlation (r2 = 0.9999) was established between peak area and Favipiravir concentration (10–100mg/ml). The method proved to be robust, accurate (recovery, 99.19–100.17%), precise (interday and intraday RSD values < 0.4% and 0.2%, respectively), sensitive (detection and quantification limits of 1.20mg/mL and 3.60mg/mL, respectively), and specific, effectively quantifying Favipiravir in medication formulations [15].
- Srinivas lingabathula et al. (2021) presented a validated stability-indicating gradient RP-HPLC technique for the quantitative measurement of peramivir and favipiravir. Utilizing an isocratic elution technique on an inertsil ODS column with a mobile phase of acetonitrile and 0.1% orthophosphoric acid (70:30), the method demonstrated accurate quantification. The technique showed linearity between 10 and 150µg/ml for Favipiravir and 10 and 100µg/ml for Peramivir, with correlation coefficients exceeding 0.999. Accuracy was confirmed through impurity-spiked solutions and percentage recovery values (Favipiravir: 100.154–100.624%, Peramivir: 99.512–99.918%). Precision studies yielded RSD values within acceptable limits, validating the accuracy and reliability of the developed method [16].

- Keerthi. G et al. (2022) introduced a novel RP-HPLC technique for the sensitive quantification of Favipiravir in bulk and pharmaceutical dosage form, with rivaroxaban as the internal standard. Employing acetonitrile and water as the mobile phase on an Enable C18 column, the separation occurred at 296nm with a flow rate of 1ml/min. The method was validated over a concentration range of 5-25µg/mL, exhibiting LOD and LOQ values of 2.17µg/mL and 6.58µg/mL, respectively. The technique proved to be resilient, linear, specific, accurate, and precise, making it applicable for the quantification of Favipiravir in pharmaceutical dosage forms. Method validation, as per ICH Q2 (R1) recommendations, affirmed the method's selectivity, sensitivity, linearity, accuracy, repeatability, and robustness [17].
- Jyoti shinde et al. (2022) detailed the development and validation of an RP-HPLC method for the estimation of favipiravir in both bulk and tablet forms. Employing quality by design principles, initial screening investigations involved measuring the organic phase concentration and buffer pH using the central composite method. Optimization through numerical and graphic optimization on retention duration, peak asymmetry, and theoretical plates led to selecting the acetonitrile: water (80:20, %v/v) mobile phase at 1ml/min flow rate and 323nm wavelength. Repeatability, intraday precision, and interday precision exhibited percentage RSD values of 0.97, 0.88, and 0.65, respectively. LOD and quantification were determined as 316.5µg/ml and 104.44µg/ml. The expanded HPLC analytical QBD concept provided optimal performance and design space. Method validation confirmed compliance with permissible bounds, offering a valuable, future-proof practical knowledge base with benefits such as rapid analysis, convenient FAP quantification, and environmental friendliness for both bulk drugs and pharmaceutical formulations [18].
- Santhosh Illendula et al. (2023) utilized RP-HPLC to estimate favipiravir in both marketed pharmaceutical dosage form and API form. Employing ODS HG-5 RP C18, 5µm, 15cmX4.6mm chromatogram, the mobile phase included methanol and phosphate buffer (0.02M, pH 3.6) at a flow rate of 1.0ml/min, with the ideal wavelength set at 255nm. Repeatability and intermediate precision %RSD values were 0.462, 0.44, and 0.593, respectively. Recovery fell within the Favipiravir tolerance range. LOD and LOQ were determined as 5.004µg/ml and 15.164µg/ml, respectively. The method, cost-effective and straightforward, was suitable for routine quality control testing, offering benefits like quick turnaround time, easy sample preparation, and reduced retention and run times [19].
- Ramarao N et al. (2021) presented a straightforward, sensitive, fast, precise, accurate, and robust isocratic HPLC and UV spectroscopic method for favipiravir determination and quantification. Utilizing a Shim-Pack GIST C18 column with a mobile phase mixture of 10mM potassium dihydrogen orthophosphate buffer (pH 4.0) and acetonitrile (90:10, v/v) at 1.0ml/min flow rate, elution occurred at 30°C with UV detection at 315nm. The calibration plot displayed optimal regression over a concentration range of 10–60µg/ml, with LOD and LOQ at 0.18 and 0.53µg/ml, respectively. Recovery studies confirmed accuracy (99.47–100.80%), and repeatability demonstrated the procedure's precision, falling within acceptable bounds. The method, with a retention time of 4.622 minutes, was effectively applied to commercially available Favipiravir tablet formulations, emphasizing economy and environmental friendliness [20].
- Subhadip Chakraborty et al. (2023) devised and assessed UV Spectrophotometric (zero order, first order, area under the curve) and RP-HPLC methods to estimate favipiravir in its pharmaceutical dosage form. Green solvent mixture (methanol, ethanol, and water, 25:35:40 v/v/v) served as the mobile phase and diluent. Method A, a zero-order spectrophotometric technique, demonstrated a correlation coefficient of 0.99962, with LOD and LOQ at 0.18 and 0.55µg/ml, respectively. Method B, a first-order spectrophotometric method, exhibited a correlation coefficient of 0.9964, with LOD and LOQ at 0.64 and 1.96µg/ml. Method C, the area under the curve spectrophotometric method, showed a correlation coefficient of 0.9986, with LOD and LOQ at 0.32 and 0.96µg/ml. Method D, an RP-HPLC approach, presented retention times of 7.216min, flow rates of 0.80ml/min, and isocratic mode. All methods demonstrated high recovery and repeatability with %RSD < 2 [21].
- Hoda M. Marzouk et al. (2021) developed and validated a stability-indicating HPLC-DAD method for determining favipiravir, exploring its stability under various stress scenarios. Employing a Zorbax C18 column and isocratic elution, the mobile phase consisted of phosphate buffer (pH 3.5±0.05) with 0.1% (w/v) sodium salt heptane sulphonic acid methanol-acetonitrile (62:28:10) at a flow rate of 1.0ml/min. The diode array detector signal for FAV was observed at 321nm. The method, efficient, precise, and targeted, identified FAV even in the presence of forced degradation products. A thorough investigation revealed FAV susceptibility to oxidative deterioration, base hydrolysis, and acid hydrolysis. The method was successfully employed for in-vitro dissolution monitoring and pharmaceutical formulation assessment, indicating its applicability as a stability-indicating method in quality control laboratories [22].
- Sonu A. Varma et al. (2021) designed and validated a stability-indicating RP-HPLC method for the estimation of favipiravir in pharmaceutical dosage form in accordance with ICH recommendations. The mobile phase comprised a 0.1% v/v solution of orthophosphoric acid and acetonitrile (77:23). The method demonstrated a retention period of 5.6 minutes at a flow rate of 1ml/min. A forced degradation study covering acid, base, oxidative, photo, and thermal degradation confirmed the degradation results within acceptable bounds. The RP-HPLC method exhibited robustness, accuracy, linearity, and precision, complying with ICH guidelines. With good linearity (correlation coefficient r2 = 0.9989) over the concentration range of 10–30µg/ml, the method was deemed suitable for routine analysis, stability studies, and quality control of favipiravir [23].
- Aydinoglu Marinelli et al. (2023) addressed the growing interest in using the broad-spectrum antiviral favipiravir for COVID-19 treatment. They developed a straightforward, rapid, and precise Reverse-Phase High-Performance Liquid

Chromatography (RP-HPLC) method for favipiravir (FVP) measurement in pharmaceutical formulations. The ACE 5 C18 column (250mm × 4.6mm, 5µm) executed the method, utilizing a mobile phase composition of 10mM phosphate buffer (pH = 2.5): methanol (80:20, v/v) at a flow rate of 0.6mL/min. Method validation established parameters such as linearity (0.5 to 100µg/mL) with a regression coefficient (r2) of 0.99998. Precision recovery yields ranged from 99.9 to 101.4% for three concentrations. The method exhibited a limit of quantification of 0.02µg/mL and a limit of detection of 0.05µg/mL. Precision experiments demonstrated inter-day and intra-day relative standard deviation of less than 2%. Robustness assessments, varying mobile phase ratio, detecting wavelength, and flow rate, showed stability. Chromatographic analysis determined a pKa value of 5.03 ± 0.02 for FVP, and the study provides valuable insights into the spectral and chromatographic properties of FVP [24].

- Roshdy E. Saraya et al. (2022) introduced a sensitive, simple, and high-performance thin-layer chromatography (TLC) method for simultaneous determination of favipiravir, molnupiravir, and ritonavir. Silica gel 60F254 TLC plates, using methylene chloride, ethyl acetate, methanol, and 25% ammonia as the mobile phase (6:3:4:1, v/v/v/v), were employed. Densitometric detection at 289nm revealed retention factors of 0.22, 0.42, and 0.63 for favipiravir, molnupiravir, and ritonavir, respectively. The method exhibited linearity in the ranges of 2.75–100.00µg/mL for ritonavir and 3.75–100.00µg/mL for molnupiravir and favipiravir. Detection limits were 1.12, 1.21, and 0.89µg/mL, respectively. This innovative technique is the first to concurrently determine these three antiviral medications, demonstrating its applicability in quality control. Greenness measures were employed to evaluate the method, and the study showcased its effectiveness in determining the drugs simultaneously in a single dosage form using artificially prepared capsules [25].

The literature review can be summarized as follows:

Reference	Method used	Key Findings
[3]	UV Spectrophotometry & HPLC	Developed methods for Favipiravir quantification; Validation parameters established.
[4]	UV Spectrophotometry & HPLC	Validated methods for dosage forms; Robustness and precision confirmed.
[5]	HPLC	Developed HPLC method for assay determination; System found accurate and within limits.
[6]	HPLC	Validated HPLC method for dosage forms; Precision and accuracy within acceptable limits.
[7]	HPLC	Developed and validated HPLC method; Applied in quality control analysis.
[8]	HPLC	Established HPLC method for bulk and tablet dosage; Precise, accurate, and linear results.
[9]	HPLC	HPLC method for bulk and dosage forms; Linearity, accuracy, and precision verified.
[10]	HPLC	Developed HPLC method for bulk and dosage forms; Linearity and precision validated.
[11]	HPLC	Validated HPLC method for bulk and dosage forms; Linearity and precision confirmed.
[12]	HPLC	Developed HPLC method for dosage forms; Robust and accurate for routine analysis.
[13]	HPLC	Validated HPLC method for tablet dosage form; Precision and accuracy within limits.
[14]	HPLC	Developed HPLC method for bulk and dosage forms; Precise and linear analysis.
[15]	HPLC	Established HPLC method for pharmaceutical dosage forms; Linear, accurate, and sensitive.
[16]	Gradient RP-HPLC	Confirmed stability-indicating technique; Accuracy and reliability demonstrated.
[17]	RP-HPLC	Developed sensitive RP-HPLC method; Validation per ICH guidelines; Suitable for pharmaceuticals.
[18]	RP-HPLC	Developed RP-HPLC method using quality by design; Validated for bulk and tablet dosage forms.
[19]	RP-HPLC	Estimated favipiravir in marketed forms and API; Low-cost, straightforward method.
[20]	HPLC-DAD	Developed stability-indicating HPLC-DAD method; Suitable for routine quality control.
[21]	RP-HPLC	Simple, accurate RP-HPLC method developed; Suitable for routine analysis.
[22]	RP-HPLC & UV	Developed and validated RP-HPLC and UV methods; Stability studies demonstrated.
[23]	RP-HPLC	Stability-indicating RP-HPLC method developed and validated.
[24]	RP-HPLC	Developed RP-HPLC method for FVP in pharmaceuticals; Validation parameters established.
[25]	TLC	Developed TLC method for simultaneous determination; First technique for these antiviral medications.

3. Discussion

The literature review reveals a comprehensive exploration of analytical methods for the quantification of Favipiravir across various studies. UV Spectrophotometry and High-Performance Liquid Chromatography (HPLC) emerged as the predominant techniques, showcasing their efficacy in providing accurate and reliable results. UV Spectrophotometry, particularly at wavelengths such as 236nm and 227nm, demonstrated simplicity and sensitivity, while HPLC methods consistently exhibited precision, linearity, and robustness. Several studies highlighted the validation of methods for pharmaceutical dosage forms, emphasizing their applicability in real-world scenarios. The Quality by Design (QBD) approach and Stability-Indicating methods underscored the commitment to ensuring the reliability and robustness of the analytical techniques. Furthermore, the use of green solvents in some studies aligns with the contemporary emphasis on environmentally friendly practices in pharmaceutical analysis. The application of these methods extended beyond bulk drug analysis to pharmaceutical formulations, contributing to quality control processes in the industry. Studies also explored the simultaneous determination of Favipiravir with other antiviral medications, demonstrating versatility in addressing complex analytical challenges

4. Conclusion

In conclusion, the literature review consolidates evidence on the diverse analytical strategies employed for Favipiravir quantification, providing a comprehensive understanding of their respective strengths and applications. UV Spectrophotometry and HPLC methods, in particular, stand out as robust tools for routine analysis and quality control in pharmaceutical settings. The continuous refinement of methodologies, adherence to validation guidelines, and exploration of green practices showcase the adaptability of these techniques in the rapidly evolving landscape of pharmaceutical analysis. As Favipiravir gains prominence in antiviral therapy, the validated methods presented in these studies offer valuable contributions to ensuring the drug's accurate and reliable quantification in various formulations and dosage forms

References

[1] Chaudhari P, Waghmare S. An Overview on Analytical Estimation of Favipiravir. Intl J of Pharm Res and Applications.2022 Jun;7(3):2456-4494.

[2] Pruthvi Shree V, Zaranappa. A Review of the Analytical methods for the determination of Favipiravir. Intl J of Pharm Sci and Res. 2022 May;14(5):2060-2075.

[3] Arji SR, Eranki SS, Kadimi A, Sarella PN, Mangam VT. Development and validation of an HPLC method for the simultaneous estimation of salbutamol, theophylline and ambroxol in tablet dosage form. International Journal of Science and Research Archive. 2023;10(2):634-45.

[4] Sandip D Firke, UV Spectroscopic Method Development and Validation for Estimation of Potent Antiviral Drug Favipiravir. Int j of Pharma and Res. 2021 Jul;14(5): 2320-5148.

[5] Ramadoss K, Meerasa SS, Satyapal AK, Vijayakumar A, Venugopal V. Quantitative analysis of favipiravir in bulk and pharmaceutical dosage forms using UV visible spectrophotometer. J of med pharma and allied sciences. 2023 April;12(2):4410.

[6] Bhavar G. development and validation of UV spectrophotometric method for estimation of favipiravir. Eur Chem Bull. 2023;12(5):259-269.

[7] Chiranjeevi P, Varaprasad Rao, Bala Naga Priya M, Sireesha P. UV-Spectrophotometric method development and validation of Favipiravir in pure and formulation. UGC Care Grp J. 2022 Jul;52(6):0378-4568.

[8] Ibrahim Bulduk. Comparison of HPLC and UV Spectrophotometric methods for quantification of favipiravir in pharmaceutical formulations. Iran J of pharma Res. 2021; 20(3):57-65.

[9] Megahed S, Habib A, Hammad S, Kamal A. Chemometric approach based on factorial and box-Behnken designs for determination of Anti coronavirus drug; Favipiravir in bulk and spiked human plasma by green HPLC method. Turkish J of Anal Chem. 2021 Dec 12; 3(2):70-8.

[10] Vemuri DK, Gundla R, Konduru N, Mallavarapu R, Katari NK. Favipiravir (SARS-CoV-2) degradation impurities: Identification and route of degradation mechanism in the finished solid dosage form using LC/LC–MS method. Biomed Chromatogr. 2022 Jun;36(6):5363.

[11] Ibraam E. Mikhail, Heba Elmansi, Fathallah Belal, Adel Ehab Ibrahim. Green micellar solvent – free HPLC and Spectrofluorimetric determination of favipiravir as one of COVID-19 antiviral regimens. Micro chem J. 2021 March 15; 165:106189.

[12] Balu PA, Paresh MS. Stability-indicating RP HPLC method development for estimation of favipiravir in bulk and pharmaceutical dosage form. World J of Pharma Res. 2021 Oct 20;10(14):1444-65.

[13] Borkar V, Shahare H, Chandrmore K, Rkhibe V, Amruta B, Vidhate S, Patil C, Jain S. Development and Validation of RP-HPLC Method for Estimation of Favipiravir in Bulk and Its Pharmaceutical Dosage Form. (IJFANS) Int J of Food and Nutr Sci. 2022;11(2): 2319-1775.

[14] Bathula S, Sammaiah G, Warangal T. RP-HPLC method development and validation for determination of favipiravir in pure substances and marketed tablet dosage form. Int J Of Adv Res in Med & Pharma Sci (IJARMPS). 2023 Aug;8(4):2455-6998.

[15] Nandeesha Itigimatha, Kailash S, Chadchan, Basappa C. Yallur, Manjunatha D. Hadagali. New analytical methods for the determination of new Anti-viral drug Favipiravir: A potential therapeutic drug against COVID-19 virus, in bulk and dosage forms. Pharma Che J. 2023;56(10):5610-1419.

[16] Lingabathula S, Jain N. Stability Indicative and Cost-Effective Analytical Method Development and Validation Favipiravir and Peramivir in Bulk and Pharmaceutical Dosage Form by Using RP-HPLC. Int J Appl Pharm. 2021;13(4):265-71.

[17] Keerthi G, Ravi Kumar. P, Padmavathi. Y. Development and validation of RP-HPLC Method for quantitative estimation of Favipiravir in bulk and pharmaceutical dosage form. YMER. 2022 Jun;21(6):0044-0477.

[18] Shinde J, Sharma PK, Sharma J. Development and Validation Of RP-HPLC Method For Estimation of Favipiravir API and Its Tablet Dosage Form Using Quality by Design Approach. J of Pharma Neg R. 2023 Jan;13(8):115-26.

[19] Nayak AB, Sree PP, Illendula S, Suresh BD, Rao K N. A new analytical method development and validation for the quantitative determination of favipiravir in bulk and pharmaceutical dosage form by RP-HPLC method. Res gate. 2023 Feb;22(2):0044-0477.

[20] Nadendla R, Abhinandana P. a Validated High-Performance Liquid Chromatographic Method for the Quantification of Favipiravir by PDA Detector. Int J Life Sci Pharma Res. 2021;11(2):1818.

[21] Chakraborty S, Mondal S. a Green Eco-friendly Analytical Method Development, Validation, and Stress Degradation Studies of Favipiravir in Bulk and Different Tablet Dosages Form by UV-Spectro-photometric and RP-HPLC Methods with their Comparison by Using ANOVA and in-vitro Dissolution Studies. Int J of Pharma Invt. 2023 Apr 1;13(2):290-305.

[22] Marzouk HM, Rezk MR, Gouda AS, Abdel-Megied AM. A novel stability-indicating HPLC-DAD method for determination of favipiravir, a potential antiviral drug for COVID-19 treatment; application to degradation kinetic studies and in-vitro dissolution profiling. Micro chem J. 2022 Jan 1; 172:106917.

[23] Sonu A. Varma and Priyanka Yadav, Stability indicating HPLC Method Development and Validation for Estimation of Favipiravir in Pharmaceutical Dosage Form. WJPPS. 2021;10(5):1749-1760.

[24] Aydinoglu Marinelli, Sabriye, Bozyel, Metin. Favipiravir determination in pharmaceutical formulation via HPLC chromatographic approach. Iran J Chem Eng 2023;42(4):1099-1110.

[25] Roshdy E. Saraya, Sami El Deeb, Baher I. Salman, Adel Ehab Ibrahim. Highly sensitive High-performance thin layer chromatography method for the simultaneous determination of molnupiravir, favipiravir, and ritonavir in pure forms and pharmaceutical formulations. J Sep Sci. 2022; 45:2582-2590.

Author's short biography

Harshitha M

Harshitha M is a determined and accomplished individual holding a Bachelor of Pharmacy (B.Pharm) degree and currently pursuing a Master of Pharmacy (M. Pharm). Academic journey reflects a deep-rooted passion for pharmaceutical sciences, marked by her unwavering commitment to the field..

Sowmya HG

Sowmya, a dedicated professional, holds an M. Pharm degree and currently serving as an Assistant Professor in the Department of Pharmaceutical Analysis at Bharathi College of Pharmacy, Bharathi Nagar, Karnataka. With a passion for pharmaceutical education, Sowmya contributes to shaping aspiring pharmacists' futures. The role involves imparting theoretical and practical insights, fostering a dynamic learning environment. Sowmya's commitment to continuous learning and research makes a significant impact, positioning them as a valued member of the faculty at Bharathi College

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Naveen Kumar GS

Naveen Kumar, an accomplished professional with an PhD, currently serves as an HOD in the Department of Pharmaceutical Analysis at Bharathi College of Pharmacy, Bharathi Nagar, Karnataka. Beyond teaching, Naveen Kumar actively contributes to the academic landscape through the publication of articles, showcasing a dedication to advancing pharmaceutical knowledge. Simultaneously, as a mentor, Naveen Kumar provides guidance to students, fostering their academic and research growth. This tri-fold role, encompassing teaching, publication, and guidance, exemplifies Naveen Kumar's commitment to both imparting knowledge and nurturing the next generation of pharmacists at Bharathi College