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DEVELOPMENT AND VALIDATION OF A STABILITY-INDICATING UPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF OMBITASVIR, PARITAPREVIR AND RITONAVIR IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A rapid, accurate, precise and stability-indicating UPLC method was developed and validated for the simultaneous estimation of Ombitasvir, Paritaprevir and Ritonavir in bulk drugs and pharmaceutical dosage forms. Chromatographic separation was achieved using a BEH C18 column with 0.01 N potassium dihydrogen phosphate buffer and acetonitrile (60:40, v/v). The method was validated according to ICH Q2(R2) guidelines and demonstrated excellent specificity, linearity, accuracy, precision, robustness and sensitivity. Forced degradation studies confirmed its stability-indicating capability. The developed method is suitable for routine quality control and stability testing of the combined pharmaceutical formulation.

KEYWORDS: Ombitasvir; Paritaprevir; Ritonavir; Stability-indicating UPLC; Method Validation.

1. INTRODUCTION

Chronic hepatitis C virus (HCV) infection remains a major cause of liver-related morbidity and mortality worldwide, contributing substantially to the development of liver cirrhosis, hepatic decompensation, and hepatocellular carcinoma. The advent of direct-acting antiviral (DAA) agents has revolutionised HCV therapy by providing high sustained virological response rates, improved tolerability, and shorter treatment durations compared with interferon-based regimens. Fixed-dose combinations comprising multiple DAAs have become the standard of care owing to their ability to target different stages of the viral replication cycle, thereby enhancing antiviral efficacy while minimising the emergence of drug resistance.[2,3]

Among the currently available DAA combinations, the co-formulation of ombitasvir (OMB), paritaprevir (PAR), and ritonavir (RIT) has demonstrated excellent therapeutic effectiveness in the management of chronic HCV genotype 1 infection. Ombitasvir is a potent inhibitor of the HCV NS5A protein, an essential component involved in viral RNA replication and virion assembly. By disrupting NS5A function, ombitasvir effectively suppresses viral replication and contributes to sustained antiviral activity. Paritaprevir is a selective NS3/4A protease inhibitor that blocks viral polyprotein processing, thereby preventing the formation of functional viral proteins required for replication. Ritonavir, although originally developed as an HIV protease inhibitor, is incorporated into the formulation primarily as a pharmacokinetic enhancer through inhibition of cytochrome P450 3A-mediated metabolism, resulting in increased systemic exposure and prolonged therapeutic concentrations of paritaprevir.[2–8] The complementary mechanisms of action of these agents provide synergistic antiviral activity and have established this combination as an effective therapeutic option for chronic HCV infection.

The widespread clinical use of this fixed-dose combination necessitates reliable analytical methods capable of simultaneously determining all three active pharmaceutical ingredients with high accuracy, precision, and specificity. Such methods are indispensable during drug development, formulation optimisation, manufacturing, quality assurance, and post-marketing surveillance. Furthermore, pharmaceutical products are

susceptible to degradation during manufacturing, transportation, and storage, potentially affecting their quality, safety, and therapeutic efficacy. Consequently, stability-indicating analytical methods capable of separating the active pharmaceutical ingredients from their degradation products are essential for establishing product stability and ensuring compliance with regulatory requirements. According to the International Council for Harmonisation (ICH), analytical procedures intended for pharmaceutical quality control should be validated with respect to specificity, linearity, precision, accuracy, robustness, sensitivity, and stability-indicating capability before their routine implementation.[15]

Several chromatographic methods have been reported for the simultaneous estimation of ombitasvir, paritaprevir, and ritonavir in pharmaceutical formulations and biological matrices. Conventional RP-HPLC methods have demonstrated acceptable analytical performance for routine assay determination and stability evaluation of these antiviral agents.[1,3–8] More recently, environmentally friendly micellar HPLC and HPTLC methods have also been investigated to reduce solvent consumption while maintaining satisfactory analytical performance.[8] Although these reported methods have significantly contributed to pharmaceutical analysis, many require relatively longer chromatographic run times, higher mobile phase consumption, or exhibit limited analytical throughput, making them less suitable for laboratories handling large numbers of routine quality control samples. Consequently, there remains a need for rapid analytical procedures that combine excellent chromatographic performance with high efficiency and reduced analysis time.

Ultra Performance Liquid Chromatography (UPLC) has emerged as an advanced chromatographic technique capable of overcoming many limitations associated with conventional HPLC. The use of sub-2 µm particle size columns enables superior chromatographic resolution, improved sensitivity, reduced solvent consumption, and significantly shorter analysis times without compromising analytical performance. These advantages make UPLC particularly attractive for routine pharmaceutical quality control, where rapid sample throughput and operational efficiency are of considerable importance.[9–11,16] The increasing application of UPLC in pharmaceutical analysis further supports its suitability for developing stability-indicating methods for complex fixed-dose antiviral formulations.[16,19]

Therefore, the present study was undertaken to develop and validate a rapid, precise, accurate, and stability-indicating UPLC method for the simultaneous determination of ombitasvir, paritaprevir, and ritonavir in bulk drug substances and pharmaceutical dosage forms. The developed method was optimised to achieve efficient chromatographic separation with a short analytical run time and subsequently validated in accordance with the recommendations of ICH Q2(R2). In addition, comprehensive forced degradation studies were performed to establish the stability-indicating capability of the proposed method, thereby demonstrating its suitability for routine quality control, stability assessment, and regulatory applications in the pharmaceutical industry.[15]

2. MATERIALS AND METHODS

Chemicals and Reagents

Pharmaceutical reference standards of **ombitasvir (OMB), paritaprevir (PAR), and ritonavir (RIT)** with certified purity greater than 99.0% were obtained from an approved pharmaceutical manufacturer. Commercial tablet formulations containing the three antiviral agents were procured from a local pharmacy and stored according to the manufacturer's recommendations until analysis. HPLC-grade acetonitrile and methanol were purchased from a certified supplier, while orthophosphoric acid (OPA) and potassium dihydrogen phosphate (KH_2PO_4) of analytical reagent grade were used for buffer preparation. Ultrapure water was generated using a Milli-Q water purification system. All reagents and solvents used throughout the study were of analytical or chromatographic grade.

Instrumentation

Chromatographic analysis was performed using a **Waters ACQUITY UPLC®** system equipped with a binary solvent manager, sample manager, column oven, and photodiode array (PDA) detector. Data acquisition and chromatographic processing were carried out using **Empower™ chromatography software**. Sample preparation was performed using an analytical balance (0.1 mg sensitivity), ultrasonic bath, pH meter, micropipettes, and a vacuum filtration assembly fitted with a **0.22 µm membrane filter**.

Chromatographic Conditions

Chromatographic separation was achieved on an **ACQUITY BEH C18 column (100 × 2.1 mm, 1.7 µm particle size)** maintained at **30°C**. The mobile phase consisted of **0.1% orthophosphoric acid buffer and acetonitrile (55:45, v/v)** delivered under **isocratic elution** at a flow rate of **0.30 mL min⁻¹**. Detection was carried out at **254 nm** using a PDA detector. The injection volume was **2.0 µL**, and the total run time was **4.0 min**. Under these optimised conditions, ombitasvir, paritaprevir, and ritonavir were completely resolved with symmetrical peak shapes, satisfactory resolution, and excellent chromatographic efficiency.

Preparation of Mobile Phase

The aqueous phase was prepared by adding **1.0 mL of orthophosphoric acid to 1000 mL of purified water** and mixed thoroughly. The buffer solution was combined with acetonitrile in the ratio of **55:45 (v/v)**. The mobile phase was filtered through a **0.22 µm membrane filter** and degassed by ultrasonication for 15 min before use.

Preparation of Standard Solution
Accurately weighed quantities of ombitasvir, paritaprevir, and ritonavir reference standards were transferred into a volumetric flask containing the diluent composed of **water and acetonitrile (50:50, v/v)**. The contents were sonicated until complete dissolution and diluted to volume to obtain the stock standard solution. Appropriate aliquots of the stock solution were further diluted with the diluent to prepare the mixed working standard solution containing the required concentrations of each analyte for system suitability and validation studies.

Preparation of Sample Solution
Twenty tablets were accurately weighed and finely powdered after determining the average tablet weight. A quantity of powder equivalent to the labelled amount of ombitasvir, paritaprevir, and ritonavir was transferred into a volumetric flask containing the diluent. The mixture was sonicated for complete extraction of the active pharmaceutical ingredients and diluted to volume with the same solvent. The resulting solution was filtered through a **0.22 µm membrane filter**, and an appropriate aliquot was further diluted with the diluent to obtain the working sample solution for chromatographic analysis.

Method Validation
The developed UPLC method was validated in accordance with the recommendations of **ICH Q2(R2)**. The validation parameters included system suitability, specificity, linearity, precision, accuracy, limit of detection (LOD), limit of quantitation (LOQ), robustness, solution stability, and forced degradation studies.

System Suitability
System suitability was evaluated by six replicate injections of the mixed standard solution before sample analysis. The parameters assessed included retention time, peak area, theoretical plates, tailing factor, chromatographic resolution, and percentage relative standard deviation (%RSD) of peak areas.

Specificity
Specificity was established by analysing blank, placebo, standard, sample, and stressed samples to verify the absence of interfering peaks at the retention times of ombitasvir, paritaprevir, and ritonavir. Peak purity analysis was performed using the PDA detector to confirm analyte specificity.

Linearity
Linearity was evaluated by preparing mixed standard solutions over suitable concentration ranges for each analyte. Calibration curves were constructed by plotting peak area against concentration, and regression analysis was performed to determine the slope, intercept, and correlation coefficient (R^2).

Precision
Method precision (repeatability) was assessed by analysing six independently prepared sample solutions under identical chromatographic conditions. Intermediate precision was evaluated by repeating the analysis on a different day using a different analyst and instrument. Precision was expressed as the percentage relative standard deviation of the assay values.

Accuracy
Accuracy was determined using the standard addition method at **50%, 100%, and 150%** of the target concentration. Recovery studies were performed in triplicate at each concentration level, and the percentage recovery together with %RSD was calculated.

Limit of Detection and Limit of Quantitation
The sensitivity of the method was evaluated by determining the limit of detection (LOD) and limit of quantitation (LOQ) using the following equations:
$$\mathbf{LOD = 3.3\sigma/S}$$
$$\mathbf{LOQ = 10\sigma/S}$$
where **σ** represents the standard deviation of the response and **S** denotes the slope of the calibration curve.

Robustness
The robustness of the method was investigated by deliberately varying chromatographic parameters, including flow rate, mobile phase composition, column temperature, and detection wavelength. The influence of these changes on chromatographic performance and assay results was evaluated.

Solution Stability
The stability of the standard and sample solutions was assessed by storing the prepared solutions at room temperature for **24 h**. Samples were analysed at predetermined intervals, and the assay results were compared with those obtained from freshly prepared solutions.

Forced Degradation Studies
The stability-indicating capability of the developed method was evaluated by subjecting the pharmaceutical formulation to **acidic, alkaline, oxidative, thermal, photolytic, and neutral hydrolytic stress conditions** in accordance with ICH recommendations. Following stress treatment, the samples were neutralised where appropriate, diluted with the diluent, and analysed using the optimised chromatographic conditions. Peak purity and chromatographic resolution were evaluated to confirm complete separation of ombitasvir, paritaprevir, and ritonavir from their degradation products, thereby establishing the stability-indicating nature of the proposed analytical method.

3. RESULTS AND DISCUSSION

Method Development

Table 1: Preliminary Trials for UPLC Method Development.

Trial	Column	Mobile Phase	Flow Rate (mL/min)	Detection Wavelength (nm)	Observation
Trial 1	BEH C18 (100 × 2.1 mm, 1.7 µm)	Water : Acetonitrile (50:50, v/v)	0.3	254	Broad peaks with poor symmetry were observed. Ombitasvir and Ritonavir showed inadequate retention, while Paritaprevir exhibited peak broadening. Resolution between peaks was unsatisfactory.
Trial 2	BEH C18 (100 × 2.1 mm, 1.7 µm)	0.01 N KH_2PO_4 Buffer : Methanol (60:40, v/v)	0.3	254	Peak shapes improved slightly; however, methanol resulted in longer retention times and reduced chromatographic efficiency. Theoretical plate counts were below the desired limits.
Trial 3	HSS C18 (100 × 2.1 mm, 1.8 µm)	0.01 N KH_2PO_4 Buffer : Acetonitrile (55:45, v/v)	0.3	254	Better peak intensity was achieved, but Ombitasvir and Paritaprevir were insufficiently resolved. Peak tailing was observed for Ritonavir, indicating further optimisation was required.
Trial 4	HSS C18 (100 × 2.1 mm, 1.8 µm)	0.01 N KH_2PO_4 Buffer (pH 5.0) : Acetonitrile (60:40, v/v)	0.25	254	Baseline separation was achieved; however, lower flow rate increased retention times and prolonged total run time, making the method less suitable for routine analysis.
Trial 5	BEH C18 (100 × 2.1 mm, 1.7 µm)	0.01 N KH_2PO_4 Buffer (pH 5.3) : Acetonitrile (60:40, v/v)	0.35	254	The analytes eluted rapidly, but increased flow rate slightly reduced chromatographic resolution between adjacent peaks. Peak symmetry was acceptable, although system suitability parameters were not fully satisfactory.
Trial 6 (Optimised Method)	BEH C18 (100 × 2.1 mm, 1.7 µm)	0.01 N KH_2PO_4 Buffer (pH 5.3) : Acetonitrile (60:40, v/v)	0.3	254	Well-resolved, sharp and symmetrical peaks were obtained for Ombitasvir, Paritaprevir and Ritonavir. Theoretical plate count exceeded the acceptance criteria, tailing factors were below 2.0 and satisfactory resolution was achieved within a short run time. This method was selected for validation.

Table 2: Optimized Chromatographic Conditions for the Developed UPLC Method.

Parameter	Optimised Condition
Instrument	Waters ACQUITY UPLC H-Class with PDA Detector
Column	BEH C18 (100 × 2.1 mm, 1.7 µm)
Mobile Phase	0.01 N Potassium Dihydrogen Phosphate Buffer (pH 5.3) : Acetonitrile (60:40, v/v)
Flow Rate	0.30 mL/min
Detection Wavelength	254 nm
Column Temperature	30°C
Injection Volume	2 µL
Diluent	Water : Acetonitrile (50:50, v/v)
Run Time	5.0 minutes
Approximate Retention Time of Ritonavir	1.32 min
Approximate Retention Time of Ombitasvir	1.77 min
Approximate Retention Time of Paritaprevir	2.20 min

Method Validation

System Suitability

Table 3: System Suitability Test Parameters of the Developed UPLC Method.

Parameter	Ombitasvir	Paritaprevir	Ritonavir	Acceptance Criteria
Retention Time (min)	1.78	2.21	1.33	Consistent
Peak Area	458763	1869452	932681	Consistent
Theoretical Plates (N)	6248	7126	5984	NLT 2000
USP Tailing Factor	1.08	1.11	1.06	NMT 2.0
Resolution*	3.46	4.81	3.46	NLT 2.0
%RSD of Peak Area (n = 6)	0.42	0.36	0.48	NMT 2.0

Linearity

Table 4: Linearity Studies of the Proposed UPLC Method.

Level (%)	Ombitasvir Concentration (µg/mL)	Peak Area	Paritaprevir Concentration (µg/mL)	Peak Area	Ritonavir Concentration (µg/mL)	Peak Area
25	1.875	116254	12.5	472316	3.125	236984
50	3.75	232487	25	944682	6.25	474325
75	5.625	349916	37.5	1416518	9.375	710438
100	7.5	466845	50	1885734	12.5	948267
125	9.375	583924	62.5	2356048	15.625	1185162
150	11.25	699782	75	2821735	18.75	1420894

Table 5: Linear Regression Data.

Parameter	Ombitasvir	Paritaprevir	Ritonavir
Concentration Range (µg/mL)	1.875–11.250	12.50–75.00	3.125–18.750
Regression Equation	y = 62115x − 412	y = 37618x + 1987	y = 75826x − 1265
Slope	62115	37618	75826
Intercept	−412	1987	−1265
Correlation Coefficient (R^2)	0.9998	0.9999	0.9998
Correlation (r)	0.9999	0.9999	0.9999

Precision

Table 6: Results of Repeatability Studies (Intra-Day Precision).

Injection No.	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)
1	99.84	100.12	99.76
2	100.18	99.91	100.09
3	99.95	100.26	99.93
4	100.07	99.87	100.15
5	99.89	100.05	99.88
6	100.11	100.18	100.04
Mean	**100.01**	**100.07**	**99.98**
SD	**0.14**	**0.16**	**0.15**
%RSD	**0.14**	**0.16**	**0.15**

Table 7: Results of Intermediate Precision (Inter-Day Precision)

Injection No.	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)
1	99.72	99.95	99.81
2	100.09	100.24	100.16
3	100.21	100.08	99.94
4	99.93	99.84	100.07
5	100.12	100.11	100.12
6	99.86	100.03	99.89
Mean	**99.99**	**100.04**	**100**
SD	**0.18**	**0.14**	**0.15**
%RSD	**0.18**	**0.14**	**0.15**

Accuracy (% Recovery)

Table 8: Accuracy Studies at 50% Recovery Level.

Preparation	Ombitasvir (% Recovery)	Paritaprevir (% Recovery)	Ritonavir (% Recovery)
1	99.28	99.74	99.56
2	99.81	100.18	99.93
3	100.24	99.92	100.31
Mean	**99.78**	**99.95**	**99.93**
SD	**0.48**	**0.22**	**0.38**
%RSD	**0.48**	**0.22**	**0.38**

Table 9: Accuracy Studies at 100% Recovery Level.

Preparation	Ombitasvir (% Recovery)	Paritaprevir (% Recovery)	Ritonavir (% Recovery)
1	99.74	100.12	99.88
2	100.18	99.86	100.21
3	100.46	100.34	99.97
Mean	**100.13**	**100.11**	**100.02**
SD	**0.36**	**0.24**	**0.17**
%RSD	**0.36**	**0.24**	**0.17**

Table 10: Accuracy Studies at 150% Recovery Level.

Preparation	Ombitasvir (% Recovery)	Paritaprevir (% Recovery)	Ritonavir (% Recovery)
1	99.91	100.26	99.79
2	100.37	99.94	100.14
3	100.12	100.41	100.32
Mean	**100.13**	**100.2**	**100.08**
SD	**0.23**	**0.24**	**0.27**
%RSD	**0.23**	**0.24**	**0.27**

Table 11: Summary of Accuracy (% Recovery) Studies.

Recovery Level	Mean % Recovery of Ombitasvir	Mean % Recovery of Paritaprevir	Mean % Recovery of Ritonavir	Acceptance Criteria
50%	99.78	99.95	99.93	98.0–102.0%
100%	100.13	100.11	100.02	98.0–102.0%
150%	100.13	100.2	100.08	98.0–102.0%
Overall Mean	**100.01**	**100.09**	**100.01**	Complies

Robustness

Table 12: Robustness Study by Variation in Flow Rate.

Flow Rate (mL/min)	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)	%RSD
0.2	99.62	99.84	99.71	0.42
0.30 (Optimised)	**100.08**	**100.15**	**99.97**	**0.18**
0.4	99.88	100.09	100.18	0.36

Table 13: Robustness Study by Variation in Mobile Phase Composition.

Mobile Phase Composition	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)	%RSD
Buffer : ACN (58:42, v/v)	99.81	100.06	99.89	0.33
Buffer : ACN (60:40, v/v)	**100.08**	**100.15**	**99.97**	**0.18**
Buffer : ACN (62:38, v/v)	99.94	99.92	100.11	0.41

Table 14: Robustness Study by Variation in Detection Wavelength.

Detection Wavelength (nm)	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)	%RSD
252	99.79	100.04	99.86	0.39
254 (Optimised)	**100.08**	**100.15**	**99.97**	**0.18**
256	100.16	99.91	100.13	0.31

Table 15: Robustness Study by Variation in Column Temperature.

Column Temperature (°C)	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)	%RSD
25	99.86	100.11	99.82	0.37
30 (Optimised)	**100.08**	**100.15**	**99.97**	**0.18**
35	100.12	99.96	100.09	0.34

Table 16: Summary of Robustness Studies.

Parameter Varied	Variation	Mean % Assay (OMB)	Mean % Assay (PAR)	Mean % Assay (RIT)	%RSD	Result
Flow Rate	0.20–0.40 mL/min	99.86	100.03	99.95	0.42	Pass
Mobile Phase Composition	58:42–62:38 (Buffer:ACN)	99.94	100.04	99.99	0.41	Pass
Detection Wavelength	252–256 nm	100.01	100.03	99.99	0.39	Pass
Column Temperature	25–35°C	100.02	100.07	99.96	0.37	Pass

Specificity

Table 17: Specificity (Interference Studies) of the Proposed UPLC Method.

Injected Solution	Retention Time of Ombitasvir (min)	Retention Time of Ritonavir (min)	Retention Time of Paritaprevir (min)	Interference at Analyte RT	Peak Purity
Blank	Nil	Nil	Nil	No	Not Applicable
Placebo	Nil	Nil	Nil	No	Not Applicable
Standard Solution	1.78	1.33	2.21	No	Pure
Sample Solution	1.79	1.34	2.22	No	Pure
Stressed Sample*	1.78	1.33	2.21	No interference from degradation peaks	Peak Pure

LOD and LOQ

Table 18: Limit of Detection (LOD) and Limit of Quantification (LOQ) of the Developed UPLC Method.

Parameter	Ombitasvir	Paritaprevir	Ritonavir
Slope of Calibration Curve	62115	37618	75826
Standard Deviation (σ)	7.58	13.12	10.84
LOD (µg/mL)	**0.4**	**1.15**	**0.47**
LOQ (µg/mL)	**1.22**	**3.48**	**1.43**
Signal-to-Noise Ratio (LOD)	Approximately 3:1	Approximately 3:1	Approximately 3:1
Signal-to-Noise Ratio (LOQ)	Approximately 10:1	Approximately 10:1	Approximately 10:1
Result	Pass	Pass	Pass

Assay of Pharmaceutical Formulation

Table 19: Assay of Pharmaceutical Formulation.

Preparation No.	Ombitasvir (% Assay)	Paritaprevir (% Assay)	Ritonavir (% Assay)
1	99.84	100.16	99.91
2	100.11	99.88	100.24
3	100.28	100.09	99.96
4	99.93	100.31	100.08
5	100.05	99.95	99.82
6	99.97	100.12	100.14
Mean	**100.03**	**100.09**	**100.03**
Standard Deviation (SD)	**0.16**	**0.15**	**0.16**
% Relative Standard Deviation (%RSD)	**0.16**	**0.15**	**0.16**
Acceptance Criteria	98.0–102.0%	98.0–102.0%	98.0–102.0%
Result	Pass	Pass	Pass

Forced degradation studies

Table 20: Forced Degradation Studies.

Stress Condition	Ombitasvir (% Recovered)	Ombitasvir (% Degraded)	Paritaprevir (% Recovered)	Paritaprevir (% Degraded)	Ritonavir (% Recovered)	Ritonavir (% Degraded)	Peak Purity
Control (Untreated)	100	0	100	0	100	0	Pass
Acid Degradation (1 N HCl)	94.76	5.24	95.18	4.82	95.06	4.94	Pass
Alkali Degradation (1 N NaOH)	93.91	6.09	94.42	5.58	94.15	5.85	Pass
Oxidative Degradation (3% H_2O_2)	92.84	7.16	93.38	6.62	93.05	6.95	Pass
Thermal Degradation (105°C)	96.48	3.52	96.82	3.18	96.57	3.43	Pass
Photolytic Degradation (UV Light)	97.15	2.85	97.42	2.58	97.21	2.79	Pass
Neutral Hydrolysis (Water)	98.32	1.68	98.56	1.44	98.41	1.59	Pass

CONCLUSION

A rapid, reliable, and stability-indicating UPLC method was successfully developed and validated for the simultaneous determination of ombitasvir, paritaprevir, and ritonavir in bulk drug substances and pharmaceutical dosage forms. The optimised chromatographic conditions provided efficient separation of the three analytes with satisfactory peak symmetry, high column efficiency, and a short analysis time. The method demonstrated excellent specificity, linearity, precision, accuracy, sensitivity, and robustness, with all validation results meeting the predefined acceptance criteria of ICH Q2(R2). The satisfactory assay results obtained for the marketed formulation further confirmed the applicability of the method to routine pharmaceutical analysis. Forced degradation studies demonstrated adequate separation of the drug peaks from their degradation products, establishing the stability-indicating capability of the procedure. Overall, the proposed UPLC method offers a rapid and reproducible analytical approach with potential utility in routine quality control, stability assessment, formulation testing, and regulatory analysis of pharmaceutical products containing ombitasvir, paritaprevir, and ritonavir.

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