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# METHOD DEVELOPMENT AND VALIDATION OF SIMULTANEOUS ESTIMATION OF TEZACAFTOR AND IVACAFTOR IN BULK DRUGS BY RP-HPLC

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**Abstract:**
*A rapid, precise, and accurate reversed-phase high-performance liquid chromatography (RP-HPLC) method has been developed for the simultaneous estimation of tezacaftor and ivacaftor in bulk drugs. Chromatographic separation was performed on an Agilent Eclipse C18 ODS column (4.6 mm × 150 mm, 5 µm) using a mobile phase of triethylamine (TEA) and methanol (30:70 v/v) at a flow rate of 1.0 mL/min, with detection at 298 nm. The retention times of tezacaftor and ivacaftor were 2.46 and 4.38 min, respectively. The method showed linear responses over the concentration ranges of 10-50 µg/mL for tezacaftor and 15-75 µg/mL for ivacaftor. Method precision for the assay was below 2.0% RSD. Stress degradation studies were performed in accordance with the ICH guidelines.*

***Keywords:*** *Tezacaftor, ivacaftor, RP-HPLC, validation, and estimation.*

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## 1. INTRODUCTION:

High-performance liquid chromatography (HPLC) is a technique used to analyze drug substances and drug products and to determine and quantify known and unknown impurities at low levels [1]. The Food and Drug Administration (FDA) also trusts the purity analysis method using HPLC for its high accuracy and reproducibility [2].

Tezacaftor is a cystic fibrosis transmembrane conductance regulator (CFTR) corrector medication. It is practically insoluble in neutral to acidic media, exhibits negligible pH-dependent solubility improvements, and its high pKa underscores its neutral, uncharged state under biological conditions. IUPAC name for tezacaftor is 1-(2,2-difluoro-2H-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2--2-yl)-1H-indol-5-yl} cyclopropane-1-carboxamide [3].

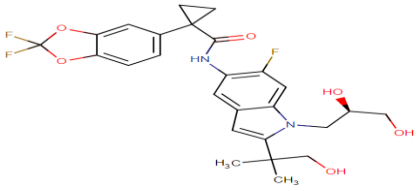

**Fig 1: Structure of tezacaftor**

Ivacaftor is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator. It is used either as monotherapy or in combination with other agents to treat cystic fibrosis. It plays a key role in improving the function of defective CFTR proteins, thereby addressing the underlying cause of the disease in eligible individuals. The IUPAC name for ivacaftor is N-(2,4-di-tert-butyl-5-hydroxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxamide. It is practically insoluble in water, showing very low aqueous solubility. Its solubility tends to increase in organic solvents and at higher pH values, reflecting pH-dependent solubility behavior [4].

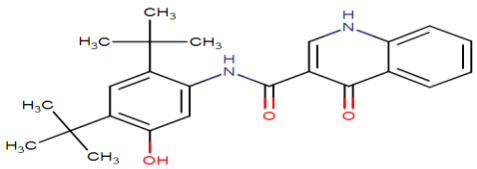

**Fig 2: Structure of ivacaftor**

In the present study, the simultaneous estimation of tezacaftor and ivacaftor was performed using RP-HPLC.

## 2. MATERIALS AND METHODS

### 2.1. Materials

Tezacaftor and ivacaftor gift samples obtained from the pharma train were used for the study. All the solvents and reagents used were of HPLC grade.

### 2.2. Equipment

Chromatographic separation studies were carried out on a Waters 2695 with a UV detector in isocratic mode and the analytical reversed-phase Agilent Eclipse C18 column (4.6 x 150mm, 5µm). The results were acquired and processed by the Empower software. Membrane filters with 0.45 µm pore size were used to filter the mobile phase.

### 2.3. Methods

#### 2.3.1. Preparation of the tezacaftor and ivacaftor standard & sample solutions:

**Standard solution preparation:**

Accurately weigh and transfer 20 mg of tezacaftor and 30 mg of ivacaftor working standard into a clean, dry 100 ml volumetric flask. Add about 7 mL of diluent, sonicate until completely dissolved, and bring the volume to the mark with the same solvent (stock solution). Further pipette 1.5 ml of the above stock solutions into a 10ml volumetric flask and dilute up to the mark with diluent [5].

#### 2.3.2. System suitability:

The tailing factor for the peaks of tezacaftor and ivacaftor in the standard solution should not exceed 2.0. Theoretical plates for the tezacaftor and ivacaftor peaks in the standard solution should be at least 2000. The resolution for the tezacaftor and ivacaftor peaks in the standard solution should be at least 2 [6].

#### 2.3.3. Mobile phase optimization:

Initially, the mobile phases tested were methanol: ortho-phosphoric acid buffer, methanol: phosphate, TEA: methanol, and acetonitrile: methanol, with various pH values and proportions. Finally, the mobile phase was optimized to 0.1% TEA in methanol at a 30:70 (v/v) ratio [7].

#### 2.3.4. Selection of wavelength:

The UV spectra of 10 µg/ml tezacaftor and 10 µg/ml ivacaftor in diluents were recorded over the 200nm to 400nm range. From the UV spectrum, the wavelength was selected as 298 nm. At this wavelength, both drugs show good absorbance [8].

#### 2.3.5. Assay

Inject 20 µL of the standard and sample into the chromatographic system, measure the areas of the Tezacaftor and Ivacaftor peaks, and calculate the %Assay using the formulae [9].

$$\% Assay = \frac{AT}{AS} * \frac{WS}{DS} * \frac{DT}{WT} * \frac{Average\ weight}{Label\ Claim} * \frac{P}{100} * 100$$

Where,

AT = average area counts of sample preparation.

AS = average area counts of standard preparation.

WS= Weight of working standard taken in mg.
P= Percentage purity of working standard
LC = Label Claim mg/ml.

**2.3.6. Linearity:**
Inject each level into the chromatographic system and measure the peak area for each. Plot a graph of peak area versus concentration (on the X-axis, concentration, and on the Y-axis, peak area) and calculate the correlation coefficient [10].

**2.3.7. Precision:**
The standard solution was injected six times, and the area was measured for each injection in HPLC. The %RSD for the area of six replicate injections was within the specified limits.

**2.3.8. Intermediate precision/ruggedness:**
To assess the method's intermediate precision, precision was evaluated on different days. The standard solutions, prepared with precision, were injected six times the other day, and the HPLC measured the areas for all six injections. The %RSD for the area of six replicate injections was within the specified limits [11].

**2.3.9. Accuracy:**
Inject the standard solution, accuracy 50%, accuracy 100%, and accuracy 150% solutions. Calculate the amounts found and added for tezacaftor & ivacaftor, and the individual and mean recovery values [12].

**2.3.10. Determination of LOD and LOQ:**
The solutions were prepared, injected three times, and the areas for all three injections were measured by HPLC. The %RSD for the area of six replicate injections was within the specified limits [13].

**2.3.11. Robustness:**
As part of robustness testing, deliberate changes in flow rate and mobile phase composition were made to evaluate their impact on the method.

**Flow rate was varied from 0.9 ml/min to 1.1ml/min.**
A standard solution of 30 ppm tezacaftor & 45 ppm ivacaftor was prepared and analyzed at various flow rates, including the method flow rate. Upon evaluation of the above results, it can be concluded that the variation in flow rate significantly affected the method.

**Change in the mobile phase composition.**
On evaluation of the above results, it can be concluded that the variation in 10%. Organic composition in the mobile phase significantly affected the method. Hence, it indicates that the method is robust even to changes in the mobile phase of ±10 [14].

**2.3.12. Degradation studies**
The ICH guideline entitled stability testing of new drug substances and products requires that stress testing be carried out to elucidate the inherent stability characteristics of the active substance. This work aimed to perform stress degradation studies on the tezacaftor and ivacaftor using the proposed method [15].

**Hydrolytic degradation under acidic conditions:**
Pipette 1.5 ml of the above solution into a 10ml volumetric flask, and 3 ml of 0.1N HCl was added. Then, the volumetric flask was kept at 60ºC for 24 hours, neutralized with 0.1 N NaOH, and made up to 10 mL with diluent. Filter the solution through 0.44 µ syringe filters and place in vials.

**Hydrolytic degradation under alkaline conditions:**
Pipette 1.5 ml of the above solution into a 10ml volumetric flask, then add 3ml of 0.1N NaOH to the 10ml volumetric flask. Then, the volumetric flask was kept at 60ºC for 24 hours, neutralized with 0.1N HCl, and made up to 10 mL with diluent. Filter the solution through 0.44 µ syringe filters and place in vials.

**Thermal-induced degradation:**
A tezacaftor and ivacaftor sample was placed in a Petri dish and heated in a hot-air oven at 1100 °C for 3 hours. Then the sample was taken, diluted with diluents, and injected into the HPLC and analyzed.

**Oxidative degradation:**
Pipette 1.5 ml of the stock solution into a 10ml volumetric flask, and add 1ml of 30% w/v hydrogen peroxide to a 10ml volumetric flask; make up to the mark with diluent. The volumetric flask was then kept at room temperature for 15 min. Filter the solution through 0.45 µ syringe filters and place in vials.

**Photo degradation:**
Pipette 1.5 ml of the stock solution into a 10ml volumetric flask, expose it to sunlight for 24hrs, and make up the volume to the mark with diluent. Filter the solution through 0.45 µ syringe filters and place in vials [16].

## 3. Results and Discussion

### 3.1. Method development

**Optimization of chromatographic conditions:**
Instrument used: Waters HPLC with an auto sampler and UV detector.
Temperature: Ambient(25° C)
Mode of separation: Isocratic mode
Column: Agilent Eclipse column (4.6 x 150mm, 5µm)
Mobile phase: 0.1% TEA: Methanol (30: 70)
Flow rate: 1 ml per min
Wavelength: 298 nm
Injection volume: 10 L

Run time: 10 min.

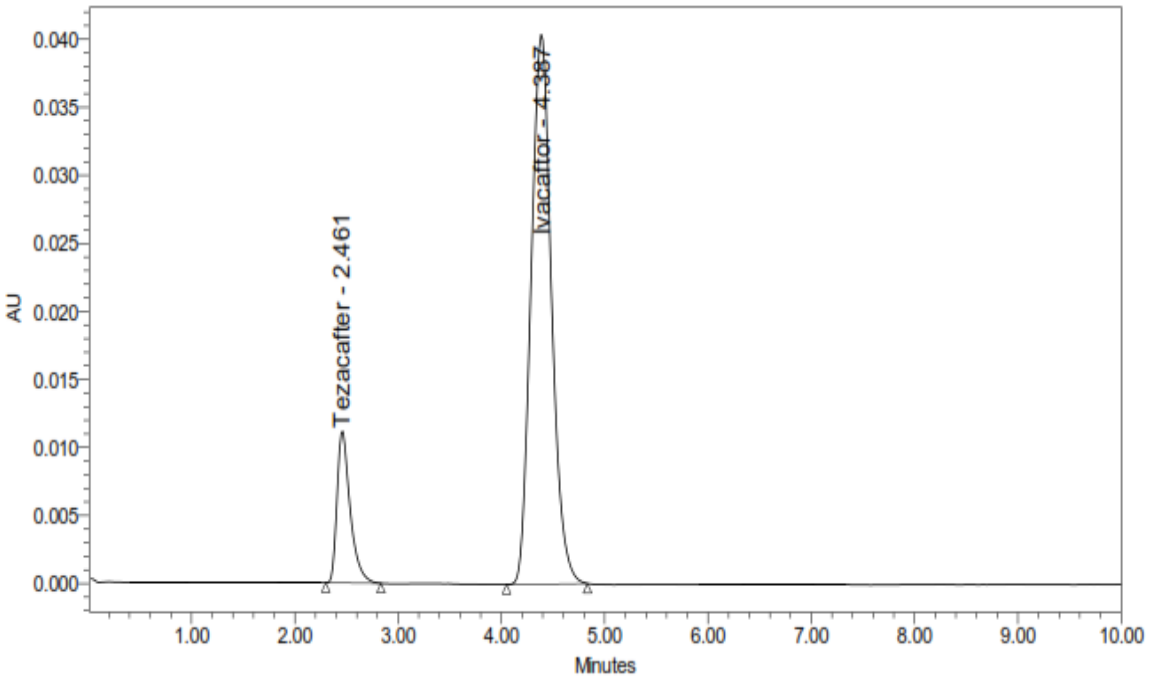


**Fig 3: Optimized chromatograms of tezacaftor and ivacaftor**

### 3.2. System suitability parameters

The resolution between two drugs must be at least 2. Theoretical plates must be at least 2000. The tailing factor must not exceed 2. The above data indicate that all system suitability parameters for the developed method were within limits, and the results are shown in Table 1.

**Table 1: Results of system suitability parameters**

| S. No | Name | RT (min) | Area (µV sec) | Height (µV) | USP resolution | USP tailing | USP plate count |
|---|---|---|---|---|---|---|---|
| 1 | Tezacaftor | 2.461 | 86152 | 10411 | | 1.63 | 4171.14 |
| 2 | Ivacaftor | 4.387 | 487733 | 40550 | 7.55 | 1.31 | 5625.95 |

### 3.3. Linearity studies of tezacaftor and ivacaftor

The linearity of tezacaftor and ivacaftor was assessed, with correlation coefficients of 0.999 and 0.999, respectively, indicating that the method has good sensitivity. The results are given in Table 2 and Figs. 4 & 5.

**Table 2: Linearity results for tezacaftor and ivacaftor**

| S. No | Linearity level | Concentration | Tezacaftor | Ivacaftor |
|---|---|---|---|---|
| | | | Area | Area |
| 1 | I | 0 | 0 | 0 |
| 2 | II | 10 | 28773 | 162697 |
| 3 | III | 20 | 57656 | 325417 |
| 4 | IV | 30 | 86579 | 482354 |
| 5 | V | 40 | 115411 | 646520 |
| 6 | VI | 50 | 146452 | 813562 |
| Correlation Coefficient ($R^2$) | | | 0.999 | 0.999 |

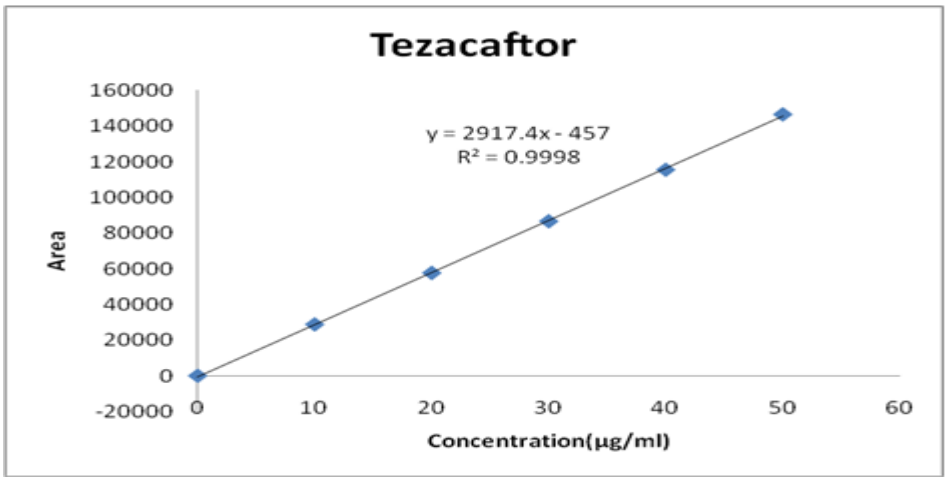


**Fig 4: Calibration graph for Tezacaftor**

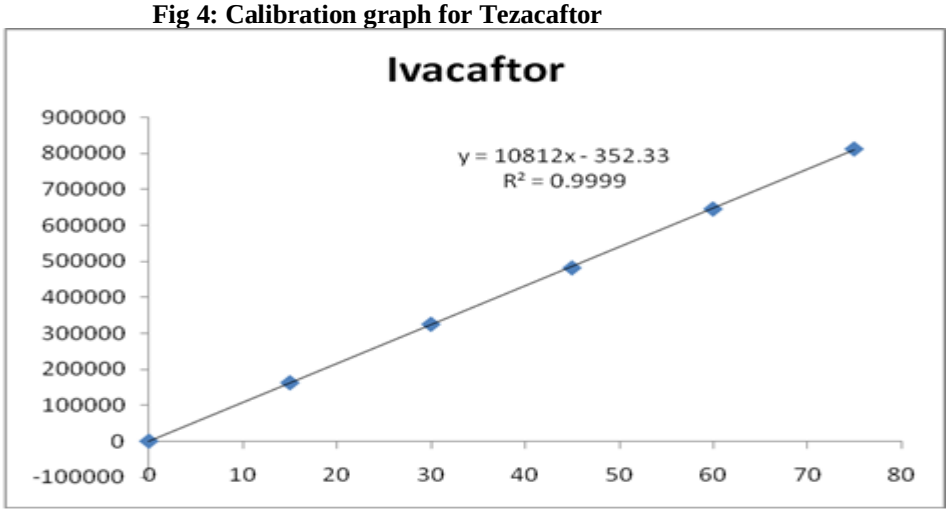


**Fig 5: Calibration graph for**

### 3.3. Precession

The acceptance criterion for precision is that RSD should not exceed 2.0%. The method shows precision of 0.2 and 0.6 for tezacaftor and ivacaftor, indicating that the method is precise [17]. The results are shown in Table 3.

**Table 3: Results showing values of tezacaftor and ivacaftor**

| Injection | Area for tezacaftor | Area for ivacaftor |
|---|---|---|
| Injection-1 | 86515 | 485692 |
| Injection-2 | 86737 | 487526 |
| Injection-3 | 86642 | 489964 |
| Injection-4 | 86433 | 490536 |
| Injection-5 | 86271 | 483951 |
| Injection-6 | 86622 | 484285 |
| **Average** | 86536.7 | 486992.3 |
| **Standard deviation** | 167.5 | 2826.4 |
| **% RSD** | 0.2 | 0.6 |

The %RSD for the standard solution is below 1, which is within the limits, hence the method is precise. %RSD for the sample should be NMT 2.

### 3.4. Intermediate precision

There was no significant change in assay content and system suitability parameters across different ruggedness conditions, including day-to-day and system-to-system variations; the results are presented in Table 4.

**Table 4: Results showing values of tezacaftor and ivacaftor**

| Injection | Area for tezacaftor | Area for ivacaftor |
|---|---|---|
| Injection-1 | 86920 | 484166 |
| Injection-2 | 86661 | 489355 |
| Injection-3 | 86367 | 484046 |
| Injection-4 | 86918 | 486215 |
| Injection-5 | 86842 | 488012 |
| Injection-6 | 86851 | 486148 |
| **Average** | 86759.8 | 486323.7 |
| **Standard Deviation** | 214.4 | 2094.1 |
| **%RSD** | 0.2 | 0.4 |

The acceptance criteria for intermediate pre-decision are that RSD should not exceed 2.0%. The method shows pre-decision values of 0.2 and 0.4 for tezacaftor and ivacaftor, indicating that the method is repeatable when performed on different days [18].

**3.5. Accuracy**

Sample solutions at different concentrations (50%, 100%, and 150%) were prepared, and the % recovery was calculated. The results are shown in Table 5.

**Table 5: The accuracy results for tezacaftor and ivacaftor**

| Conc level (%) | Area | Amount added (mg) | Amount found (mg) | % Recovery | Mean recovery |
|---|---|---|---|---|---|
| **Tezacaftor** | | | | | |
| 50% | 43621.3 | 10 | 10.08 | 100.83 | 100.29 |
| 100% | 86196.3 | 20 | 19.92 | 99.62 | |
| 150% | 130315.3 | 30 | 30.12 | 100.41 | |
| **Ivacaftor** | | | | | |
| 50% | 245026.7 | 15 | 15.06 | 100.41 | |
| 100% | 485769.3 | 30 | 29.86 | 99.53 | 100.11 |
| 150% | 734871.3 | 45 | 45.17 | 100.38 | |

The % recovery was within the limit (98-102%). The results obtained for Recovery at 50%, 100%, and 150% are within limits. Hence, the method is accurate. The total recovery was 100.29% for tezacaftor and 100.11% for ivacaftor, respectively. The validation of the developed method shows that its accuracy is well within acceptable limits, indicating good accuracy and reproducibility [19].

**3.6. Limit of detection and limit of quantification**

The lowest concentration of the sample was prepared relative to the baseline noise, and the signal-to-noise ratio and the data are shown in Table 6.

**Table 6: Results of LOD and LOQ**

| Drug name | Baseline noise (µV) | Signal obtained (µV) | S/N ratio |
|---|---|---|---|
| **Limit of detection** | | | |
| Tezacaftor | 43 | 129 | 3.00 |
| Ivacaftor | 43 | 130 | 3.02 |
| **Limit of quantification** | | | |
| Tezacaftor | 43 | 431 | 10.02 |
| Ivacaftor | 43 | 433 | 10.07 |

The acceptance criteria for LOD and LOQ are 3 and 10, respectively. The LOD and LOQ for tezacaftor were 3.00 and 10.02, and for ivacaftor, 3.02 and 10.07 [20].

**3.7. Robustness**

The standard and samples of tezacaftor and ivacaftor were injected by varying the chromatographic conditions. There was no significant change in parameters such as tailing factor and plate count; the results are presented in Tables 7 and 8.

**Table 7: Results for variation in flow for tezacaftor and ivacaftor**

| S. No | Flow Rate (ml/min) | System suitability results | |
|---|---|---|---|
| | | USP tailing | USP plate count |
| **Tezacaftor** | | | |
| 1 | 0.9 | 1.49 | 4685.99 |
| 2 | 1.0 | 1.63 | 4171.14 |
| 3 | 1.1 | 1.49 | 4253.39 |
| **Ivacaftor** | | | |
| 1 | 0.9 | 6.22 | 1.10 |
| 2 | 1.0 | 7.55 | 1.31 |
| 3 | 1.1 | 6.22 | 1.10 |

**Table 8: Results for changes in mobile phase for tezacaftor and ivacaftor**

| S. No | Change in organic composition in the mobile phase | System suitability results | |
|---|---|---|---|
| | | USP plate count | USP tailing |
| **Tezacaftor** | | | |
| 1 | 10% less | 1.49 | 4253.39 |
| 2 | *Actual | 1.63 | 4171.14 |
| 3 | 10% more | 1.49 | 4936.98 |
| **Ivacaftor** | | | |
| 1 | 10% less | 6.83 | 1.10 |
| 2 | *Actual | 7.55 | 1.31 |
| 3 | 10% more | 5.79 | 1.10 |

The USP plate count and USP tailing factor obtained for the change of flow rate. Variations in the mobile phase were found to be within the acceptance criteria. Hence, the method is robust [21].

**3.8. Degradation studies**

The stress degradation studies performed on tezacaftor and ivacaftor demonstrated selectivity and stability, indicating the capability of the proposed RP-HPLC method. Accordingly, degradation stress studies were conducted by exposing tezacaftor and ivacaftor to acidic, basic, peroxide, thermal, and photo-induced conditions. The results are presented in Table 9. The degradation study revealed that tezacaftor and ivacaftor were degraded only under thermal and photolytic conditions [22].

**Table 9: Degradation results for Tezacaftor and Ivacaftor**

| Degradation studies | Tezacaftor | | Ivacaftor | |
|---|---|---|---|---|
| | Area | % Degraded | Area | % Degraded |
| **Standard** | 86350 | 0 | 487070.3 | 0 |
| **Acid** | 81637 | 5.46 | 448922 | 7.83 |
| **Base** | 83562 | 3.23 | 452928 | 7.01 |
| **Peroxide** | 82081 | 4.94 | 459177 | 5.73 |
| **Thermal** | 84017 | 2.70 | 462638 | 5.02 |
| **Photo** | 84261 | 2.42 | 465877 | 4.35 |

## 4. CONCLUSION:

In the present study, a sensitive, precise, and accurate RP-HPLC method was developed and used to estimate tezacaftor and ivacaftor in bulk drugs quantitatively. All the parameters met the criteria of the ICH guidelines for method validation. Stress degradation studies on tezacaftor and ivacaftor were performed, and the results revealed that the drugs were liable under thermal and photo conditions, whereas stable under acidic, peroxide, and basic degradation conditions. The method could therefore be recommended for routine quality-control analysis of raw materials and various dosage formulations by assaying for potency and accuracy.

## REFERENCES:


1. Kasture AV, Mahadik KR, Wadodkar SG, More HN. Pharmaceutical Analysis: Vol-II. 8th Ed. Pune: Nirali Prakashan; 2002: 48-57.
2. Shethi PD. HPLC- Quantitative analysis of pharmaceutical formulations. 1st Ed. New Delhi: CBS Publishers & Distributors; 2001: 8-10, 101-103.
3. Sharma BK. Instrumental Method of Chemical Analysis. 20th Ed. Meerut: Goel Publishing House; 2001: 54-83.
4. Skoog DA, West DM. Principles of Instrumental Analysis. 2nd Ed. Saunders Golden Sunburst Series. Philadelphia; 1980: 674-675, 690-696.
5. Drug Bank Open Data Drug and Drug Target Database. Version 4.1. http://www.drugbank.ca/drugs/DB01183.
6. Sonawane M. D., Gade S. T., and B. M. Narwate, Application of UV Spectrophotometer in Method Development and Validation for Simultaneous Estimation of Tezacafor and Ivacaftor In Pharmaceutical Dosage Form, World Journal of Pharmaceutical Research, Vol 7, Issue 14, 2018.
7. Narendra Singh, Parveen Bansal, Mukesh Maithani, Yashpal Chauhan, Development and Validation of a Novel Stability-Indicating RP-HPLC Method for Simultaneous Determination of Tezacaftor and Ivacaftor in Fixed Dose Combination, Journal of Chromatographic Science, Volume 58, Issue 4, April 2020, Pages 346–354.
8. Ramanjaneyulu K. V, Venkata Ramana K, M. Prasada Rao. Stability-Indicating LC Method Development and Validation for the Simultaneous Analysis of Cystic Fibrosis Drugs Ivacaftor and Tezacaftor in Pharmaceutical Formulations. Research J. Pharm. And Tech 2020; 13(5): 2076-2080.
9. Dharmamoorthy G, G. Sarath Kumar, Poornima B, P. Jayachandra Reddy, and K. Chandan Kumar. Stability Indicating RP-HPLC Method Development and Validation for the Simultaneous Estimation of Ivacaftor and Tezacaftor in Bulk and Pharmaceutical Dosage Form, European Journal of Pharmaceutical and Medical Research, 2020,7(1), 342-346.
10. Pawanjeet J. Chhabda, M. Balaji, Srinivasarao V, Development and Validation Of A New And Stability Indicating RP-HPLC Method For The Determination Of Ivacaftor in the Presence Of Degradant Products, International Journal of Pharmacy and Pharmaceutical Sciences, Vol 5, Suppl 4, 2013.
11. N. Md. Akram and Dr. M. Umamahesh, A New Validated RP-HPLC Method For The Determination Of Lumacaftor And Ivacaftor In Its Bulk And Pharmaceutical Dosage Forms, Oriental Journal of Chemistry, 2017, Vol. 33, No. (3): Pg. 1492-1501.
12. B. Sravanthi, M. Divya, Analytical Method Development and Validation Of Ivacaftor And Lumacaftor by RP-HPLC Method, Indo American Journal Of Pharmaceutical Sciences, 2016, 3 (8), 900-904.
13. Gadeela Srimounika, Shyamala, J V C. Sharma, A. Swarupa. A New Stability Indicating Method for Simultaneous Estimation of Ivacaftor and Tezacaftor by RP-HPLC in Bulk and Its Dosage Form, International Journal of Research and Analytical Reviews (IJRAR), 2018 IJRAR December 2018, Volume 5, Issue 4, Pages: 774-785.
14. Heinisch S, Rocca JL. Effect of mobile-phase composition, pH, and buffer type on the retention of ionizable compounds in reversed-phase liquid chromatography: application to method development. J. Chromatogr. A. 2004; 183–193.
15. Gritti F, Guiochon G. Role of the buffer in retention and adsorption mechanism of ionic species in reversed phase liquid chromatography. J. Chromatogr A. 2004; 1038(1-2):53–66.
16. Bosch E, Espinosa S, Roses M. Retention of ionizable compounds on high-performance liquid chromatography: III. Variation of pKa values of acids and pH values of buffers in acetonitrile–water mobile phases. J. Chromatogr. A. 1998; 824(2):137–146.
17. Kupiec T. Quality control analytical methods: high-performance liquid chromatography. Int. J. Pharma. Compound. 2004; 8(3): 223-227.
18. Wuelfing WP, Kosuda K, Templeton AC, et al. Polysorbate 80 UV/ vis spectral and chromatographic characteristics – defining boundary conditions for use of the surfactant in dissolution analysis. J Pharm Biomed Anal, 2006; 41: 774-82.
19. Sweetman SC. 2009. Martindale's Complete Drug Reference. London: Pharmaceutical Press.

20. Valko K, Snyder LR, Glajch J. Retention in Reversed-Phase Liquid Chromatography as a function of mobile phase composition. J. Chromatogr. A. 1993; 656(2): 501-520.
21. S. Lakshmi Maneka, R. T. Saravanakumar, C.N. Anjana. Development and validation of a stability-indicating RP-UPLC method for the simultaneous estimation of Tezacaftor and Ivacaftor in formulations. International Journal of Pharmacy and Pharmaceutical Sciences. Vol 12, Issue 9, 2020.
22. Ayyappa, M. Rama; Babu, G. Raveendra; Sushama, C.; Sowjanya, M.; Murthy, G. Lakshmana. A Novel Stability-Indicating RP-HPLC method for the simultaneous analysis of Ivacaftor and Tezacaftor in Pure and Its Pharmaceutical Formulations. International Journal of Pharmaceutical, Chemical & Biological Sciences. Oct-Dec 2019, Vol. 9 Issue 4, p172- 179.