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Doravirine: A Review on Analytical Method Development and Validation for Quantification of Bulk and Pharmaceutical Dosage Form by Liquid Chromatography

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ABSTRACT

Doravirine, a non-nucleoside reverse transcriptase inhibitor, has gained significant attention for its efficacy in treating HIV-1 infection due to its favourable pharmacokinetic profile and minimal drug-drug interactions. Accurate and reliable quantification of doravirine in bulk and pharmaceutical dosage forms is critical for ensuring quality control and regulatory compliance. This review focuses on the analytical method development and validation of liquid chromatography (LC) techniques for the determination of doravirine.

Various chromatographic methods, including high-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC), have been explored for doravirine quantification. These methods employ different stationary phases, mobile phases, and detection techniques to achieve optimal separation and sensitivity. The development process includes selecting suitable chromatographic conditions, optimizing parameters such as flow rate and wavelength, and ensuring robustness. Validation of the methods is performed in accordance with International Council for Harmonisation (ICH) guidelines, addressing key criteria such as specificity, linearity, accuracy, precision, limit of detection (LOD), and limit of quantification (LOQ).

This review provides a comprehensive overview of existing LC methods, highlighting their advantages, limitations, and suitability for routine quality control applications. Emphasis is placed on the role of method optimization and rigorous validation in ensuring reliability and reproducibility. The findings aim to serve as a reference for researchers and pharmaceutical analysts involved in doravirine quantification, contributing to improved analytical practices and regulatory compliance in pharmaceutical development.

KEYWORDS: Doravirine, HIV, NNRTI, Method development, Validation

INTRODUCTION:

Doravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) developed for the treatment of HIV-1 infection. Approved by the FDA in 2018, it is often used in combination with other antiretroviral agents. Doravirine inhibits the activity of reverse transcriptase, an enzyme crucial for the replication of HIV-1, thereby preventing viral replication. [1]

Known for its favourable safety profile, doravirine is associated with fewer central nervous system side effects compared to other NNRTIs. It demonstrates strong antiviral efficacy against wild-type HIV-1 and certain NNRTI-resistant strains, making it an important option in managing treatment-resistant cases. Its pharmacokinetic profile allows once-daily dosing, enhancing patient adherence. Doravirine is available as a standalone medication and in fixed-dose combinations, such as with lamivudine and tenofovir disoproxil fumarate.[2]

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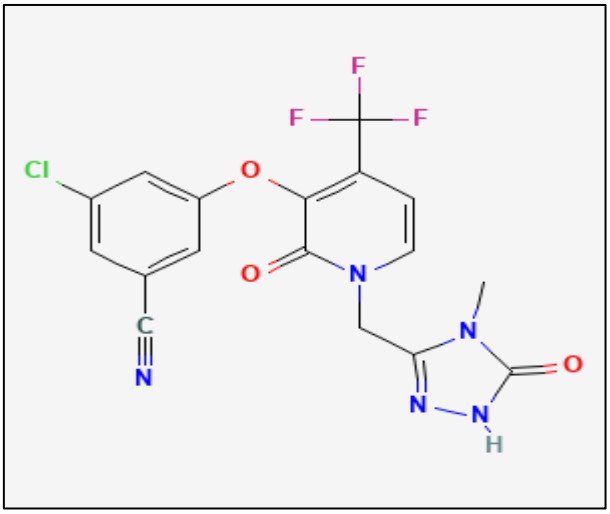

Figure No.1: Structure of Doravirine

PHARMACOLOGY:

Doravirine exhibits high selectivity and potency against HIV-1 reverse transcriptase (RT), the viral enzyme essential for converting viral RNA into DNA. It has a favourable pharmacokinetic profile, characterized by:

- Absorption: Rapid oral absorption, with peak plasma concentrations reached in 2 hours.
- Distribution: Moderate plasma protein binding (~76%).
- Metabolism: Primarily metabolized by the cytochrome P450 enzyme CYP3A4.
- Half-life: Approximately 15 hours, allowing once-daily dosing.
- Excretion: Eliminated mainly via feces (~50%) and urine (~7%) as metabolites.

Doravirine's pharmacological advantages include minimal interactions with other drugs and a reduced incidence of side effects, particularly central nervous system (CNS) adverse events commonly associated with earlier NNRTIs.

MECHANISM OF ACTION:

Doravirine targets the HIV-1 reverse transcriptase enzyme, which is critical for the viral replication process. Its mechanism of action involves:

1. Binding to a Non-Active Site: Doravirine binds to an allosteric site on the reverse transcriptase enzyme, distinct from the active site, inducing conformational changes.

2. Inhibition of Enzyme Function: This binding disrupts the enzyme's ability to synthesize viral DNA from RNA, halting the replication cycle of the virus.

3. Activity Against Resistant Strains: Unlike first-generation NNRTIs, doravirine retains activity against many NNRTI-resistant HIV-1 strains by overcoming mutations that confer resistance to other drugs in the class.

This unique binding profile enhances Doravirine's potency and helps reduce the development of resistance. Additionally, its selectivity minimizes off-target effects, contributing to its tolerability. [3]

ANALYTICAL METHOD VALIDATION:

A method-based technique called validation makes sure a method is appropriate for use as a quality control tool for analytical measurements. Accurate, reliable, and consistent results are the aim of each analytical measurement. To achieve this goal, it is essential to employ established analytical methods. Techniques, processes, protocols, and methods make up an analytical method. Validation of analytical methods involves determining linearity, range, robustness, detection limit, quantitation limit, accuracy, precision, and specificity. As a fundamental component of any effective analytical practice, the results of method validation can be utilised to moderate the quality, consistency, and reliability of analytical results. Validating analytical techniques is another requirement of most quality standards and laws governing laboratories.

REPORTED METHODS FOR DORAVIRINE:

Pandya Y et al

New, advanced chromatographic techniques have been used for quality control in the examination of pharmaceutical compounds. Given the circumstances, there are a lot of new medicines and more recent pharmaceutical formulations that are designed to treat illnesses. Hepatitis, HIV, AIDS, and other viral infections necessitate the use of novel medications and their combinations. This means that the medications must be analysed for quality control purposes. Here, the tablet dosage forms of the API-drugs Lamivudine LAM, Tenofovir TEN, and Doravirine DOR have been analysed using the RP-HPLC method. This technique is designed to analyse these three medications in combination for quick analysis using a minimal quantity of analyte medications. In contrast to Doravirine DOR, the concentration range for the linearity chosen was 7.5 to 45 µg/ml for Lamivudine LAM & Tenofovir TEN. 2.5–15 µg/ml. 269 nm was the wavelength chosen for estimation, and the Acclaim 120 C-18 chromatographic column (250 mm x 4.6 mm, 5 µm id) was employed. The retention times for LAM, TEN, and DOR were 2.16, 2.65, and 3.25 minutes, respectively. The correlation coefficient, which was determined to be 0.9999, is used in formulation and chemical analysis of pharmaceuticals in synthetic combinations. The stability and forced degradation investigations are conducted under various stress settings, and the devised HPLC method effectively detects both pure medication components and contaminants. In a single HLPC run time, the technique efficiently studies the in vitro dissolution profile of the medications in solid oral tablet dosage forms, which is advantageous and time-saving for the examination of the medications in various dosage forms and combinations. [4]

Ramya Kuber B et al

According to the current regulatory environment, the Analytical Quality by Design (AQbD) approach was used to optimise the Doravirine (DRN) Quality Control technique. Full factorial design in Design Expert software is used to obtain experimental data, and three crucial process parameters are flow rate, aqueous mobile phase ratio, and wavelength. For the aforementioned process parameters, theoretical plates, retention time, and capacity factor were the dependent important quality attributes. The ideal chromatographic conditions included a BDS (150×4.6 mm, 5µm) Kromasil column, a mobile phase consisting of a 65:35 v/v mixture of buffer, potassium hydrogen phosphate, and acetonitrile, and a flow rate of 1.0 ml/min. The ICH guidelines were taken into account when validating the approach. With a concentration range of 5–30 µg/ml, the technique was linear between concentration and peak area. They determined that the quantification and detection limits were 0.07 µg/ml and 0.02 µg/ml, respectively. The DRN remained at its maximal absorbance wavelength of 272.0 nm for 2.2 minutes. A number of stressors, such as hydrolytic (base, neutral, and acid). To examine the pattern of deterioration, the medication was exposed to oxidative, thermal, and photolytic processes. The state of degradation was more fundamental. Thus, it was possible to apply the created approach for routine analysis because it was stable, accurate, sensitive, and robust. The technique was expanded to include drug analysis when degradants were present. [5]

Suneetha A et al

For determining the amount of doravirine in tablets, an isocratic reversed phase high-performance liquid chromatographic method that is easy to use, accurate, quick, and precise has been developed and validated. Using a mobile phase consisting of a methanol: 0.05M potassium dihydrogen phosphate (40:60% v/v) mixture with a flow rate of 1.5 mL/min, the chromatographic separation was performed using a Dionex C18 (250 x 4.6mm, 5µ). The wavelength of UV detection was 306 nm. Doravirine had a retention time of 5.24 minutes. Throughout the 200–600 µg/mL concentration range, the calibration curve was linear (r2=0.999). The accuracy, precision, specificity, linearity, robustness, LOD, and LOQ of the method were all validated. Tablet quantitative analysis was accomplished with success using the suggested approach. There was no evidence of influence from any pharmacological dosage form component. The approach is reproducible, dependable, fast, and specific, according to validation studies. The method's usefulness for routinely determining the dosage of doravirine in bulk and tablet form is confirmed by the high recovery and low relative standard deviation.[6]

Balan P et al

The amount of Doravirine in bulk and solid dose forms can now be accurately and consistently measured using a new and affordable reverse phase high performance liquid chromatography (RP-HPLC) technique. A 250 x 4.6 mm Dionex C18 column with a 5µ particle size was used for the separation process. Ortho phosphoric acid pH-6.0 buffer and methanol in a 60:40 (v/v) ratio made up the mobile phase of the isocratic technique experiment. With a flow rate of 1.0 mL min-1, the mobile phase was pumped into the column. A UV detector set up to work at 316 nm was used to identify the eluent from the column. In total, the experiment lasted six minutes, during which the column was kept at room temperature. 2.20 minutes was the measured retention time for Doravirine. With a good coefficient of determination (R2 = 0.9997), the standard curves showed linearity within the concentration range of 10–50 µg/ml. There was a range of percentage recoveries from 102% to 98% in the experiment. Moreover, 0.3693% was determined to be the RSD. It was determined that the measured percentage content of a commercially available formulation of Doravirine was 100.30%. The method was verified in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) criteria. Through research, the suggested RP-HPLC technology has been validated, proving its simplicity, specificity, speed, reliability, and consistency. Therefore, the approach suggested in this study could be applied to the regular analysis of doravirine in both its solid and condensed forms, especially in order to guarantee quality control. [7]

Gollu G et al

In order to measure doravirine and its impurities (IMP-A, IMP-B), the current study aims to create a robust, sensitive, and dependable stability-indicating RP-HPLC method. Using 0.1% orthophosphoric acid and acetonitrile at a flow rate of 1 mL/min, the separation was carried out on an Inertsil ODS C18 (250 × 4.6 mm, 5 µm) column at 216 nm. For IMP-A, IMP-B, and doravirine, the retention times were 2.52 minutes, 3.96 minutes, and 8.74 minutes, respectively. According to the International Council for Harmonization's criteria, the optimised technique was validated for accuracy, precision, linearity, specificity, system appropriateness, and robustness. The optimised method demonstrated linearity for doravirine, IMP-A, and IMP-B within the concentration ranges of 10–200 µg/mL, 0.7–14 µg/mL, and 0.5–10 µg/mL, respectively. %RSD < 2 and percentage recovery of 100.46%, 100.2%, and 99.2% for doravirine, IMP-A, and IMP-B, respectively, were found to be accurate and precise. The refined approach turned out to be sturdy, specific, and sensitive. For the routine measurement of doravirine and its contaminants, quality control labs can use this optimised technique. [8]

T K Kokkirala et al

Doravirine, lamivudine, and tenofovir disoproxil fumarate were all simultaneously estimated in the pharmaceutical dose form using a new technique. A 50:50 (v/v) phosphate buffer and acetonitrile mobile phase was used to run the chromatogram through an Ascentis C18 column (150 × 4.6 mm, 2.7 µm). At a flow rate of 1 mL/min, the mobile phase was pushed through the column. A constant temperature of 30°C was maintained in the column. For doravirine, lamivudine, and tenofovir disoproxil fumarate, 230.0 nm was the ideal wavelength. The retention durations for tenofovir disoproxil, lamivudine, and doravirine were 3.403, 2.222, and 2.764 minutes, respectively; the relative standard deviation (%) values of method precision for these three drugs were 0.1, 0.6, and 0.6, respectively. Tenofovir disoproxil fumarate, lamivudine, and doravirine had recovery rates of 100.20%, 100.15%, and 100.36%, respectively. Using regression models for doravirine, lamivudine, and tenofovir disoproxil fumarate, the limits of detection and quantification were determined to be 0.24 and 0.73 ppm, 0.53 and 1.60 ppm, and 0.47 and 1.43 ppm, respectively. Tenofovir disoproxil fumarate, lamivudine, and doravirine have the following regression equations: y = 15,250x + 31,663, y = 15,555x + 10,791, and y = 17,541x + 117,303, respectively. The developed method was inexpensive, sensitive, accurate, straightforward, and exact. To estimate doravirine, lamivudine, and tenofovir disoproxil fumarate, it might therefore be used for routine quality control in the pharmaceutical industry. [9]

Gollu G et al

For the simultaneous measurement of lamivudine, tenofovir disoproxil fumarate (TDF), and doravirine in bulk and pharmaceutical dosage form, a novel isocratic reverse-phase high performance liquid chromatography (RP-HPLC) approach that is straightforward, accurate, and reliable was created and validated. LOD and LOQ features, precision, robustness, specificity, linearity, and system adaptability were all included in the validation. Acetonitrile and hexane-1-sulfonic acid (pH 2.5; 50:50, v/v) were eluted with a flow rate of 0.8 mL/min on a C18X bridge phenyl column (150 × 4.6 mm, 3 µm particle size) to produce the chromatographic separation. The column was monitored at 243 nm for 12 minutes. TDF, doravirine, and lamivudine were shown to have retention durations of 7.3, 8.79, and 2.45 minutes, respectively. Lamivudine and TDF showed linearity in the range of 5 to 100 µg/mL (r2 = 0.999), whereas doravirine showed linearity in the range of 1.75 to 35 µg/mL (r2 = 0.999). Three medications had recoveries that fell between the permissible range of 98 and 102%. As indicated by % RSD < 0.6, the approach was determined to be accurate. In forced degradation research carried out in accordance with ICH recommendations, the three medications demonstrated deterioration in the range of 21.4 to 33.8% under circumstances of hydrolysis, photolysis, oxidation, acidity, and basicity. Without any interference

from excipients, the suggested RP-HPLC method can be utilised to quantify lamivudine, TDF, and doravirine in API and tablets. [10]

Godela R et al

In order to determine Tenofovir disoproxil fumarate, Doravirine, and Lamivudine in blended bulk form and their combination tablet form simultaneously, the study's primary goal was to create a cost-effective, perceptive, accurate, and straightforward RP-HPLC-DAD method with high precision and good sensitivity.

All three medicines were successfully separated using a method that used an Ascentis C18 (150 × 4.6 mm, 5 m) column, a mobile phase ratio of 0.1% ortho phosphoric acid and acetonitrile in 70:30 (v/v), a flow rate of 1 mL/min, and a detection wavelength of 260 nm. In compliance with ICH guidelines, the devised approach was validated. Tenofovir disoproxil fumarate, Doravirine, and Lamivudine were shown to have retention durations of 2.4, 2.9, and 3.6 minutes, respectively. Tenofovir disoproxil fumarate, Doravirine, and Lamivudine all showed linear responses in the range of 12.5–75 g/mL, 75–225 g/mL, and 75–225 g/mL, respectively. 0.36 g/mL and 0.11 g/mL for Lamivudine, 0.55 g/mL and 1.66 g/mL for Tenofovir disoproxil fumarate, and 0.03 g/mL and 0.09 g/mL for Doravirine were determined to be the limit of detection and quantification values. Within the range of 0.134 to 1.749, the percentage RSD values of the intra-day and inter-day precision were determined. For all three analytes, the average recovery percentage fell between 98.85 and 100.18%. The validation parameters' statistical outcomes guaranteed the method's accuracy, specificity, precision, and excellent sensitivity. Analytes that are investigated under various stressful situations are guaranteed to be stable and to reflect the method's stability indication. In terms of separating Lamivudine, Doravirine, and Tenofovir disoproxil fumarate, the created approach is highly proficient. Additionally, the degradation products produced by stressful situations separated with good resolution. With suitable specificity, accuracy, precision, and sensitivity, the current approach is a stability-indicating assay. There is a good chance that the pharmaceutical industry will adopt the developed method. [11]

Desai R et al

To support human clinical trials aimed at assessing the compound's safety, pharmacokinetics, and effectiveness, a technique for quantifying doravirine (MK-1439) in human plasma has been created. In order to quantify the analyte, it was extracted using liquid-liquid extraction, separated on a reverse phase HPLC column, and detected on an API-4000 mass spectrometer utilising a Turbo-Ion spray source in positive ionisation mode in conjunction with multiple reaction monitoring mode. With 100 µl of human plasma, the assay's dynamic range was 0.02–10 ng/ml. The assay was used to assist the doravirine clinical development program when it was determined to be sensitive, selective, and repeatable. [12]

Marakatham S et al

A method for measuring doravirine (MK-1439) in human plasma has been developed to aid in human clinical trials intended to evaluate the compound's safety, pharmacokinetics, and use. The analyte was separated on a reverse phase HPLC column, identified on an API-4000 mass spectrometer using a Turbo-Ion spray source in positive ionisation mode in combination with multiple reaction monitoring mode, and extracted using liquid-liquid extraction in order to quantify it. This assay's dynamic range was 0.02–10 ng/ml with 100 µl of human plasma. Following its determination to be sensitive, selective, and reproducible, the test was employed to support the doravirine clinical development program. [13]

Balaji Gupta Tiruveedhi V L N et al

An assay method based on RP-HPLC (stability-indicating) was described in this study for the simultaneous quantification of doravirine (DRV), tenofovir disoproxil fumarate (TFF), and lamivudine (LMV) in the tablets.

DRV, TFF, and LMV were all analysed simultaneously using an Agilent 1100 series HPLC system and a Luna Phenomenex C18 (250 mm × 4.6 mm × 5 µ) column with an isocratic mobile phase (35% volume ratio of methanol and 65% volume ratio of 20 mmol ammonium formate, pH 5). Sensitivity, linearity, accuracy, selectivity, precision, robustness, and specificity were all evaluated in order to validate the assay technique. For DRV, the calibration curves were linear across the 25–200 µg/ml range, but for TFF and LMV, they ranged from 75–600 µg/ml. The intraday variation/precision, robustness, intermediate precision/ruggedness, and intraday variation/precision percent relative standard deviations were all less than 2%. Good accuracy was confirmed by the recovery of LMV (99.09-99.76%), TFF (99.10-99.41%), and DRV (98.65-99.28%). In 0.1N NaOH, 3% peroxide, 0.1N HCl, UV radiation, and dry heat of 60 °C, the stability of LMV, TFF, and DRV was assessed. Because of the results, the technique for measuring DRV, TFF, and LMV can now be used in tablets. [14]

A P. Schauer et al

First-line treatment options for HIV include doravirine (DOR), a non-nucleoside reverse transcriptase inhibitor, and bictegravir (BIC), an integrase inhibitor that was recently approved by the US FDA. We created a completely validated LC-MS/MS technique for the simultaneous assessment of BIC and DOR alongside a legacy integrase inhibitor, raltegravir (RAL), in human plasma throughout a clinically relevant 1000-fold range for each analyte because some clinical circumstances demand for their usage in tandem. Protein precipitation using their stable, isotopically labelled internal standards (BIC-d5, 13C6-DOR, and RAL-d6) was used to extract these analytes from the plasma. After being extracted, the samples were subjected to reverse phase chromatography on a Waters Atlantis T3 C18 (50 × 2.1 mm, 3 µm particle size) column. They were then detected using electrospray ionisation in positive ion mode on an AB Sciex API-5000 triple quadrupole mass spectrometer. Throughout the chosen calibration ranges (20.0–20,000 ng/mL (BIC), 3.00–3000 ng/mL (DOR), and 10.0–10,000 (RAL), the assay was linear (R2 >0.994). The assay demonstrated accuracy (inter-assay %Bias < ± 8.5) and precision (inter-assay %CV ≤11.4). This approach can be used to evaluate the pharmacokinetics of two recently licensed antiretrovirals or to enable therapeutic drug monitoring for contemporary antiretroviral therapy. It was verified in accordance with FDA instructions for industry. [15]

Hanuman T et al

Doravirine was estimated using the RP-HPLC methodology, and a straightforward, precise, and accurate approach was created. Using Agilent C18 (250 x 4.6 mm5) as the stationary phase, 0.01N KH2PO4: Methanol in a 50:50 ratio, with a flow rate of 1.0 ml/min, a detection wave length of 210 nm, a column temperature of 30 °C, and diluent as the mobile phase, the chromatographic conditions were optimised. Six injections of the standard were used to study the system suitability characteristics, and the findings fell well within the acceptable range. A linearity analysis was conducted at 25% to 150% levels, and the R2 value was 0.999. The LOQ is 0.61µg/ml, and the LOD is 0.20µg/ml. [16]

P Courlet et al

For persons living with HIV (PLWH), the prognosis has significantly changed due to the widespread use of highly active antiretroviral therapy. However, because these medications must be taken for the rest of one's life, there are concerns about maintaining their therapeutic efficacy and long-term tolerability. Newly approved or experimental antiretroviral medications offer significant benefits, including the ability to be taken orally once daily and action against resistant forms (e.g., bictegravir and doravirine) as well as parenteral intramuscular delivery that promotes treatment compliance (e.g., long-acting injectable formulations like cabotegravir and rilpivirine). Because to problems with absorption, aberrant elimination, drug-drug interactions, and other factors, there is still a chance of inadequate or inflated circulation exposure. The plasma levels of bictegravir, cabotegravir, doravirine, and rilpivirine in PLWH can be tracked using a multiplex ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) bioassay. The supernatant was directly injected into the UHPLC-MS/MS apparatus after a quick and easy protein precipitation.

In less than three minutes, the four analytes were eluted utilising a reversed-phase chromatography technique in conjunction with triple quadrupole mass spectrometry detection. Over the clinically relevant concentration ranges (from 10 to 1800 ng/mL for rilpivirine and from 30 to 9000 ng/mL for bictegravir, cabotegravir, and doravirine) and with good trueness (94.7%-107.5%), repeatability (2.6%-11%), and intermediate precision (3.0%-11.2%), this bioassay was fully validated in accordance with international guidelines. Our lab currently uses this sensitive, accurate, and quick UHPLC-MS/MS assay for routine therapeutic drug monitoring of the oral medications doravirine and bupregravir. It is also designed to be used for monitoring the levels of cabotegravir/rilpivirine in plasma from PLWH who receive intramuscular injections of these long-acting antiretroviral medications once a month or every two months. [17]

S Addanki et al

The goal is to develop a straightforward, sensitive, accurate, precise, affordable, and efficient RP-UPLC method for the simultaneous measurement of Doravirine, Lamivudine, and Tenofovir disoproxil fumarate in bulk and in combination with their pharmaceutical forms. Chromatographic separation was optimised using analytical column HSS C18 (100×2.1 mm, 1.8 µ) kept at 30 °C with a mobile phase made up of 0.01 N potassium dihydrogen orthophosphate buffer (pH-4.8) and acetonitrile in a 60:40 v/v ratio and flow rate of 0.3 mL/min in isocratic mode.

With a detection wavelength of 260 nm, the injection volume was fixed at 1 µl. Validation of the suggested approach was completed in accordance with Q2 (R1) recommendations from the International Council on Harmonisation. Tenofovir disoproxil fumarate, doradirine, and lamivudine were eluted at retention durations of 1.2, 1.5, and 1.8 minutes, respectively. For Doravirine, the suggested approach demonstrated outstanding linearity throughout a concentration range of 12.5–75.0 µg/mL, Lamivudine, 37.5–225.0

µg/mL, and Tenofovir disoproxil fumarate, 37.5–225.0 µg/mL. The current method's intra-day and inter-day precision percentage relative standard deviation for Doravirine, Lamivudine, and Tenofovir disoproxil fumarate was less than 2%. Recovery tests were used to assess the accuracy of the current approach, and the results ranged from 99.62 to 99.88% for Doravirine, 98.78 to 99.44% for Lamivudine, and 99.67 to 100.52% for Tenofovir disoproxil fumarate. For Doravirine and Lamivudine, the limits of detection and quantification were 0.249 µg/mL and 0.756 µg/mL, respectively, and 0.24 µg/mL and 0.727 µg/mL and 0.797 µg/mL and 2.966 µg/mL, respectively. Studies on forced deterioration were conducted in a variety of stressors, including neutral, acidic, basic, peroxide, thermal, and UV environments.

Because the current method ensures that there is no interference from deteriorated impurity peaks at the retention period of the analyte peak, it can be used for quality control investigations of Doravirine, Lamivudine, and Tenofovir disoproxil fumarate in pharmaceutical formulations and bulk. [18]

P Chengalva et al

For the simultaneous measurement of lamivudine, tenofovir disoproxil fumarate, doravirine, and efavirenz in bulk and pharmaceutical formulations, a straightforward and quick stability indicating reverse phase ultra-performance liquid chromatographic approach has been developed and validated. Acquity Ethylene Bridged Hybrid Phenyl (50 mm × 2.1 mm, 1.7 µm) was used for the chromatographic separation. Using a 50:50 v/v water and acetonitrile ratio, the isocratic elution system is pumped at a rate of 0.4 millilitres per minute. The wavelength for detection was 238 nm, and the injection volume was set at 1 µl.
A temperature of 30 degrees Celsius was established for the column. With a total run time of three minutes, the retention times for lamivudine, tenofovir disoproxil fumarate, doravirine, and efavirenz were determined to be 1.012, 1.233, 1.428, and 1.666 minutes, respectively. The International Council on Harmonization's Q2 (R1) guidelines were followed in the validation of the suggested approach. It was discovered that the percentage recoveries fell between 99.56 and 100.40 percent. Precision studies revealed that the relative standard deviation values were less than 2. Within the designated concentration range, there was linearity between concentration and reaction, and the correlation coefficient for all medications was 0.999. Degradation tests were conducted in a variety of stressors, including acid, base, oxidation, heat, and light. The retention time of analyte peaks was not affected by deteriorated impurity peaks. Consequently, the suggested ultra-performance liquid chromatographic technique can be applied to the routine quality assessment of efavirenz, doravirine, tenofovir disoproxil fumarate, and lamivudine, either separately or in combination in bulk and co-formulated dosage forms. [19]

V Dadi et al

Using reverse phase ultra-performance liquid chromatography (RP-UPLC), the proposed method's primary goal is to develop, validate, and carry out forced degradation studies for the simultaneous quantification of lamivudine, doravirine, and tenofovir in active pharmaceutical ingredients (API) and formulation. Using an HSS C18 (100 mm x 2.1 mm, 1.8µ) column, the estimate was carried out in isocratic mode with a flow rate of 0.3 mL/minute. The mobile phase consisted of acetonitrile and 0.1% ortho phosphoric acid (OPA) (35:65). 260 nm was the detecting wavelength, and the column temperature was kept at 30°C. The developed approach was validated in accordance with ICH guidelines. For lamivudine, tenofovir, and doravirine, the method complied with Beer's law within the concentration range of 37.5 µg/mL–225 µg/mL, 37.5 µg/mL–225 µg/mL, and 12.5 µg/mL–75 µg/mL, respectively. When subjected to various stressful situations, the technique remains steady and degrades less. This UPLC method can be used for routine examination of the estimated levels of doravirine, tenofovir, and lamivudine in tablet formulation. [20]

B Bhadru et al

A non-nucleoside reverse transcriptase inhibitor called doravirine is used to treat HIV/AIDS. Doravirine in human plasma samples can be determined utilising a straightforward, quick, and sensitive liquid chromatography with tandem mass spectrometry (LC-MS/MS) test technique that uses Delavirdine as the internal standard (IS). Using solid phase extraction (SPE), the analyte and IS were separated from 100 µL of K2 EDTA human plasma. Using a mobile phase consisting of a methanol and 0.1% formic acid buffer mixture (85:15, v/v) at a flow rate of 1.0 mL/min, the chromatographic separation was accomplished on a Zodiac C18 column. The resultant calibration curve was linear (r2 -0.99) across the 0.15–40.4 ng/mL concentration range. In the positive ion mode, the internal standard for the mass detection of delavirdine is m/z-457.2 (parent) and 362.1 (product), while that of doravirine is m/z-426.5 (parent) and 112.5 (product). The results satisfied the acceptance requirements, and the method validation was carried out in accordance with FDA recommendations. Three validation batches covering six concentration levels showed accuracy and intra- and inter-day precision (%CV) values that were substantially within acceptable bounds. Productivity increased because more samples could be analysed quickly with a run time of two minutes per sample. It was discovered that the assay was repeatable, sensitive, and selective. [21]

T Majumder et al

The purpose of this work is to develop a straightforward, precise, and accurate stability indicating method for UPLC-based doravirine (DRVN) quantification in tablet dosage form. Chromatography was performed on an HSSC18 (100 mm x 2.1 mm, 1.8 mm) reverse phase column using an isocratic elution of buffer acetonitrile, methanol, and 0.01 N potassium dihydrogen orthophosphate (pH-4.5) in a 40:25:35% V/V composition at a flow rate of 0.30 ml/min. Both the wavelength detection and the column oven temperature were maintained at 30.0°C and 238 nm, respectively. It was determined that the DRVN's retention time was 0.91 minutes. The method's repeatability was assessed using the percentage RSD, and the result was 0.33. It was discovered that the method's mean recovery percentage was 99.57%. The regression equation of DRVN yielded LOD and LOQ values of 0.71 and 2.31 mg/ml, respectively. The values of the regression equation and correlation coefficient for DRVN were 0.9997 and y = 17003x + 7203.1. According to the results of the drug's acid, peroxide, photolytic, alkali, neutral, and thermal degradation studies, the percentage of degradation ranged from 6.12% to 8.96%. The devised procedure was straightforward and cost-effective, and it reduced the drug's retention time and overall run duration. Therefore, industries can use the suggested approach as a routine quality control test for DRVN measurement. [22]

B N Thakare et al

Doravirine (DOV), lamivudine (LVD), and tenofovir disoproxil fumarate (TDF) were all determined simultaneously using an effective, reliable, and specific stability-indicating UHPLC assay technique. The UPLC system was utilised to determine the agents that were cited. A solvent system consisting of 60:40% v/v acetonitrile: potassium dihydrogen orthophosphate buffer was used with a UPLC BEH C18 (150 mm × 2.1 mm) column with a 1.7 µm particle size column at room temperature; 0.1% OPA was used to adjust the pH to 4.5 ± 0.2. The PDA detector was exposed to a 235 nm wavelength. In accordance with the ICH's recommendation, DOV, LVD, and TDF were put through a variety of stress processes in forced deterioration experiments to evaluate the stability and practicability of the established approach. By employing the optimal process, the chosen agents were effectively separated from the peaks of the corresponding degradation products. In addition, the calibration curves for DOV, LVD, and TDF include broad concentration ranges of 2–12 µg/mL, 5–30 µg/mL, and 5–30µg/mL, in that order, with r2 measurements of 0.997, 0.9994, and 0.9994. Less than 2% of the relative standard deviations for accuracy, precision, repeatability, and robustness were found in the method validation assays. [23]

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CONFLICTS OF INTEREST:

The author declares there is no conflict of interest.

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