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A COMPREHENSIVE REVIEW OF METHOD DEVELOPMENT AND VALIDATION STUDIES FOR SIMULTANEOUS ESTIMATION OF DORAVIRINE, LAMIVUDINE AND TENOFOVIR DISOPROXIL FUMARATE IN DIFFERENT SAMPLE MATRIX

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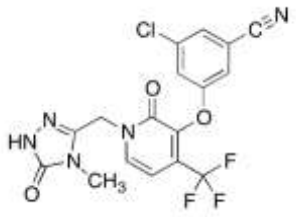
ABSTRACT

This comprehensive review aims to summarize and evaluate the existing literature on the method development and validation studies conducted for the simultaneous estimation of Doravirine (DOR), Lamivudine (LAM), and Tenofovir Disoproxil Fumarate (TDF) in different sample matrices. The review focuses on the various analytical techniques used for the determination of these drugs, including High-Performance Liquid Chromatography (HPLC), Ultra-High-Performance Liquid Chromatography (UHPLC) and Liquid Chromatography-Mass Spectrometry (LC-MS), and other relevant methods. The article also highlights the importance of method validation and degradation studies in ensuring the accuracy and reliability of the developed analytical methods. The review concludes that the choice of analytical technique for the determination of these drugs depends on several factors, including the nature of the sample matrix, the sensitivity required and the availability of the required instrumentation. Overall, this comprehensive review consolidates the available knowledge on the method development and validation studies for the simultaneous estimation of DOR, LAM, and TDF in different sample matrices. It serves as a valuable resource for researchers and analysts working in the pharmaceutical industry and academia, aiding in the selection of suitable analytical methods for drug quantification in clinical, bioanalytical, and quality control laboratories.

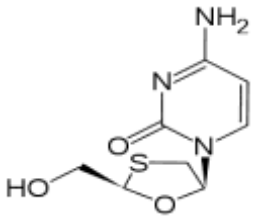
INTRODUCTION

Doravirine, Lamivudine and Tenofovir Disoproxil Fumarate (DOR/3TC/TDF) is a fixed-dose combination medication used to treat Human Immunodeficiency Virus (HIV) infection in adults. The medication is taken orally once daily and is effective at reducing the amount of HIV in the blood and preventing the progression of acquired immune deficiency syndrome (AIDS). Doravirine[1] is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that prevents the HIV virus from replicating by inhibiting reverse transcriptase, an enzyme needed by the virus to replicate. Lamivudine[3] and Tenofovir Disoproxil Fumarate[5] are nucleoside reverse transcriptase inhibitors (NRTIs) that also inhibit the replication of the virus by blocking reverse transcriptase. The combination of these three medications has been shown to be effective at reducing the viral load and increasing the number of CD4 cells in the blood, which are important cells for a healthy immune system. Common side effects of DOR/3TC/TDF include headache, nausea, diarrhoea, and fatigue. It is important to note that DOR/3TC/TDF should only be taken under the supervision of a healthcare professional and as part of a comprehensive treatment plan for HIV infection. The medication

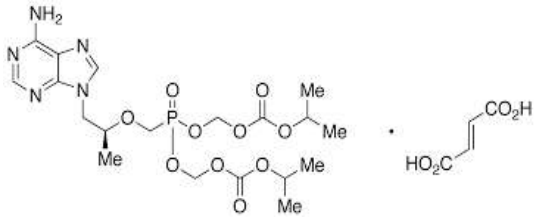
should not be used alone or as a substitute for other antiretroviral medications.



Chemical structure of Doravirine



Chemical structure of Lamivudine



Chemical structure of Tenofovir Disoproxil Fumarate

Delstrigo Tablets[7] (Doravirine, Lamivudine, and Tenofovir disoproxil fumarate) 100mg/300mg/300mg manufactured by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. received US FDA approval on August 30, 2018, for the treatment of HIV-1 infection in adults who have no prior antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed on a stable antiretroviral regimen for at least six months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Delstrigo. The approval was based on the results of clinical trials showing that the combination of Doravirine, Lamivudine, and Tenofovir disoproxil fumarate is effective in reducing HIV-1 viral load and increasing CD4+ cell counts.

Delstrigo is a fixed-dose combination tablet containing Doravirine (100mg), Lamivudine (300mg) and Tenofovir disoproxil fumarate (300mg) that should be taken orally once a day with or without food. It works by preventing the replication of the HIV virus, reducing the amount of the virus in the body, and slowing down the progression of the disease. It is important to note that Delstrigo is not a cure for HIV infection and should not be used in combination with other HIV medicines.

Chromatographic Methods: Chromatography is a set of laboratory techniques used to separate, identify, and quantify components of a mixture. Chromatographic methods rely on the differential distribution of components between two phases, a stationary phase, and a mobile phase.In general, chromatographic methods can be divided into two types: preparative and analytical. Preparative chromatography is used to isolate and purify a particular component of a mixture, while analytical chromatography is used to identify and quantify the individual components of a mixture. Following are the different simultaneous estimation methods in different matrix published by researchers,

- Gollu Gowri and Sowjanya Gummadi[8] reported "Simultaneous quantification of Lamivudine, Tenofovir disoproxil fumarate and Doravirine in pharmaceutical dosage form by liquid chromatography with diode array detection." The method involved the use of a reverse-phase C18 column and a mobile phase consisting of solvents. The validation of the method included assessing parameters such as linearity, accuracy, precision, specificity, limit of detection (LOD), and limit of quantification (LOQ). The method was successfully applied to the analysis of a pharmaceutical dosage form containing Lamivudine, Tenofovir disoproxil fumarate, and Doravirine.
- Tiruveedhi VLN Balaji Gupta, Venkateswara Rao Battula and Kishore Babu Bonige[9] reported "RP-HPLC (stability-indicating) based assay method for the simultaneous estimation of Doravirine, Tenofovir disoproxil fumarate and Lamivudine. This study developed a RP-HPLC (stability-indicating) based assay method for the estimation of doravirine (DRV), tenofovir disoproxil fumarate (TFF) and lamivudine (LMV) simultaneously in tablets. Validation of the assay method was done on sensitivity, linearity, accuracy, selectivity, precision, robustness and specificity. Results showed

that the calibration curves were linear through the range of 25-200 g/ml for DRV and 75-600 g/ml for TFF and LMV, and the percent relative standard deviation for intraday variation/precision, interday variation/precision, intermediate precision/ruggedness and robustness was lower than 2%. The stability of LMV, TFF and DRV was determined in 0.1N NaOH, 3% peroxide, 0.1 N HCl, UV light and dry heat of 60°C.

- Kokkirala, Tej Kumar et al[10]. reported "A simple alternative and improved HPLC method for the estimation of doravirine, lamivudine, and tenofovir disoproxil fumarate in solid oral dosage form". A novel method was developed to estimate the doravirine, lamivudine, and tenofovir disoproxil fumarate in the pharmaceutical dosage form. The chromatogram was run through an Ascentis C18 column. The relative standard deviation (%) values of method precision for doravirine, lamivudine, and tenofovir disoproxil were 0.6, 0.6, and 0.1, respectively. The limit of detection and limit of quantification values were obtained from regression equations of doravirine, lamivudine, and tenofovir disoproxil fumarate.
- Godela R and S Gummadi[11] reported "A simple stability indicating RP-HPLC-DAD method for concurrent analysis of Tenofovir Disoproxil Fumarate, Doravirine and Lamivudine in pure blend and their combined film coated tablets." The main aim of this study was to develop an economical, insightful, accurate and simple RP-HPLC-DAD method with high precision and good sensitivity for concurrent determination of Tenofovir disoproxil fumarate, Doravirine and Lamivudine in blended bulk form and their combined tablet form. A method with Ascentis C18 column. The limit of detection and quantification values were calculated to be 0.36g/mL and 0.11g/mL for Lamivudine, 0.55g/mL and 1.66g/mL for Tenofovir disoproxil fumarate and 0.03g/mL and 0.09g/m
- Addanki, Swetha, and B Ramya Kuber[12] reported "A new stability indicating RP-UPLC method for simultaneous estimation of Doravirine, Lamivudine and Tenofovir disoproxil fumarate in bulk and their combined pharmaceutical formulation." It is a simple, sensitive, accurate, precise, efficient, economical RP-UPLC method for simultaneous estimation of Doravirine, Lamivudine and Tenofovir disoproxil fumarate. Optimization of Chromatographic separation was achieved on analytical column HSS C18 (100 2.1 mm, 1.8). The proposed method was evaluated by recovery studies which were in the range of 99.62 – 99.88% for Doravirine, 98.78 – 99.44% for Lamivudine and 99.67 – 100.52% for Tenofovir disoproxil fumarate. The limit of detection and limit of quantification were found to be 0.249 g/mL and 0.756 g/mL.
- Marakatham S and P Shanmugapandiyan[13] reported "Bioanalytical method development and validation of doravirine, lamavudine and tenofovir disoproxil fumarate using HPLC in human plasma." A novel, simple and sensitive bioanalytical method was developed to estimate Doravirine, Lamavudine and Tenofovir disoproxil fumarate in human plasma with daclatasvir as internal standard. The linearity range was 50-2000ng/ml, 125-5000ng/ml and 20-800ng/ml. Correlation coefficient was 0.999. Validation and stability study were carried out as per FDA guidelines and all the validation results were found to be well within the acceptance criteria.
- Pandya Yogi and Samixa Patel[14] reported "A novel rapid combined RP-HPLC stability method development and validation for antiviral HIV combinations Lamivudine, Tenofovir, Doravirine in dosage form and its application to in vitro dissolution". The RP-HPLC method was used to analyse three pharmaceutical agents, Lamivudine LAM, Tenofovir TEN, and Doravirine DOR, in tablet dosage-forms. The concentration range for the linearity was 7.5 to 45 g/ml for Lamivudine LAM and Tenofovir TEN, and 2.5 to 15 g/ml for Doravirine DOR. The wavelength selected for estimation was 269nm and the chromatographic column used was Acclaim 120 C-18 column. The method was proved to be accurate, precise and efficient for regular analysis.

- Sowmya P S, G Somsekhar and H A Ahad[15] reported "Stability Indicating Rp-Hplc Method for Estimation of Doravirine in Tablet Dosage Form". The estimation of Doravirine was done by RP-HPLC and the assay was found to be 100.50. The acceptance criteria for precision were not more than 2.0% and the accuracy limit was in the range of 98.0% - 102.0%. The LOD and LOQ for Doravirine were 2.98 and 9.97, the robustness limit for mobile phase variation and flow rate variation were well within the limit, and the acceptance criteria for degradation studies were less than 15%. This method was found to be accurate, precise, reproducible and specific and can be used for estimation of Doravirine in tablet dosage form.
- Pavani Challamalla and V Jayashree[16] reported "Development of a Novel Stability quoting RP-Ultra Performance Liquid Chromatography approach for Synchronous Assessment of Doravirine, Lamivudine, and Tenofovir Disproxil fumarate in Pure API Form and Tablet Dosage Based on ICH Guidelines". This study studied the concomitant measurement of Tenofovir DF, Lamivudine, and Doravirine in bulk and tablet dose form with UPLC. The separation was performed using acetonitrile and 0.1% TEA buffer at pH-3. The eluents were identified at 260.0 nm using a PDA detector. The Lamivudine had a detection limit of 0.09 g/mL, Tenofovir DF had a detection limit of 0.04 g/mL, and Doravirine had a percentage mean recovery of 99.68 percent, Tenofovir DF had a detection limit of 99.55 percent, and Doravirine had a percentage mean recovery of 100.17%. Optimized conditions were discovered to be exceptionally suitable for determining all of them concurrently in both marketed dose form and bulk form.
- Thakare Balaji N[17] reported "Validated Stability-Indicating Assay UHPLC Method for Simultaneous Estimation of Doravirine, Lamivudine and Tenofovir Disoproxil Fumarate in Pure Material and Pharmaceutical Matrix". It is an efficient, robust, and specific stability-indicating UHPLC assay method was developed for simultaneous determination of antiretroviral agents doravirine (DOV), lamivudine (LVD), and tenofovir disoproxil fumarate (TDF). The determination was performed on UPLC system using UPLC BEH C18 with 1.7 m particle size column at ambient temperature. The calibration curves for DOV, LVD, and TDF had determination coefficients (r2) of 0.997, 0.9994, and 0.9994. The method validation assays had less than 2 % relative standard deviations for accuracy, precision, repeatability, and robustness.
- Chengalva Prasanthi and Madhavi Kuchana[18] reported "Development and Validation of Ultra Performance Liquid Chromatographic Method for the Simultaneous Estimation of Lamivudine, Tenofovir Disoproxil Fumarate, Doravirine and Efavirenz in Bulk and Pharmaceutical Formulations". It is a simple and rapid stability indicating reverse phase ultra-performance liquid chromatographic method, established and validated for the simultaneous quantification of lamivudine, tenofovir disoproxil fumarate, Doravirine and efavirenz in bulk and pharmaceutical formulations. The chromatographic separation was performed on Acquity Ethylene Bridged Hybrid Phenyl (50 mm2.1 mm, 1.7 m) column and found highly efficient. The method was found to be precise, accurate and robust thereby can be employed for regular analysis.

CONCLUSION:

The present review highlights the recent developments in the analytical methods for the determination of Doravirine, Lamivudine, and Tenofovir Disoproxil Fumarate in combination. The review covers various analytical methods such as HPLC, UPLC, and LC-MS/MS methods, which have been developed and validated for the simultaneous estimation of these three drugs. The review also emphasizes the importance of stability-indicating methods in the development of these analytical methods, as they provide a reliable indication of the drug's degradation under various conditions. The stability-indicating methods are also useful in assessing the drug's shelf-life, which is crucial for ensuring the quality of the drug product. The validation of the analytical methods is essential to ensure that the methods are suitable for their intended use.

Chromatographic system	Column	Mobile Phase	Flow rate	Detector	Detection Wavelength	Injection volume	Temperature	Retention Time	Run Time	Sample matrix	Reference
HPLC	Phenomenex C18 column (250 mm x 4.6 mm, 5 µm)	A mixture of 0.1% trifluoroacetic acid (TFA) in water (pH adjusted to 3.0 with orthophosphoric acid) and acetonitrile in a ratio of 70:30 (v/v)	1mL/min	Diode Array	260nm	20 µL	30°C	LAM – 2.47 TDF – 7.23 DOR – 8.63	12min	Tablets (Stability Indicating)	8
HPLC	BDS Hypersil C18 column (250 mm x 4.6 mm, 5 µm)	A mixture of 0.1% trifluoroacetic acid (TFA) in water (pH adjusted to 3.0 with orthophosphoric acid) and acetonitrile in a gradient elution mode	1mL/min	UV	240nm	20 µL	30°C	LAM – 3.35 TDF – 4.95 DOR – 8.15	14min	Pure API's (Stability Indicating)	9
HPLC	XBridge C18 Column (250 mm x 4.6 mm, 5 µm)	A mixture of acetonitrile and 0.1% trifluoroacetic acid (TFA) in water (pH adjusted to 3.0 with orthophosphoric acid) in a ratio of 55:45 (v/v) was used as the mobile phase.	1mL/min	UV	260nm	20 µL	30°C	DOR – 2.21 LAM – 2.76 TDF – 3.40	7min	Pure API's (Stability Indicating)	10
RP-HPLC-DAD	Phenomenex Gemini	mixture of 0.1% v/v trifluoroacetic acid (TFA) in water (pH	1mL/min	UV	260nm	20 µL	30°C	DOR – 2.4 LAM – 2.9 TDF – 3.6	6min	Tablets (Stability Indicating)	11

	C18 column (250 mm x 4.6 mm, 5 µm)	adjusted to 2.5 with orthophosphoric acid) and acetonitrile in a gradient elution mode									
HPLC	Inertsil ODS-3V column (250 mm x 4.6 mm, 5 µm)	A mixture of acetonitrile and 0.1% phosphoric acid (pH adjusted to 3.0 with triethylamine) in a gradient elution mode	1mL/min	UV	260nm	20 µL	30°C	LAM – 2.16 TDF – 2.65 DOR – 3.25	5min	Tablets (Assay & Dissolution) (Stability Indicating)	14
HPLC	Symmetry C18 column (250 mm x 4.6 mm, 5 µm)	A mixture of acetonitrile and 0.1% trifluoroacetic acid (pH adjusted to 3.0 with triethylamine) in a gradient elution mode	1mL/min	UV	260nm	20 µL	30°C	DOR – 2.43 LAM – 3.18 TDF – 4.33	7min	Tablet (Stability Indicating)	15
HPLC	XSelect CSH C18 column (100 mm x 4.6 mm, 3.5 µm)	A mixture of acetonitrile and 0.1% formic acid in water (pH adjusted to 3.0 with triethylamine) in a gradient elution mode	1mL/min	UV	260nm	10 µL	25°C	DOR – 2.53 LAM – 4.21 TDF – 5.38	8min	Human Plasma	13

UPLC	Acquity UPLC BEH C18 column (100 mm × 2.1 mm, 1.7 µm)	A mixture of 0.1% formic acid in water (pH adjusted to 3.0 with triethylamine) and acetonitrile in a gradient elution mode	0.4mL/ min	UV	260nm	2 µL	30°C	DOR – 1.2 LAM – 1.5 TDF – 1.8	4min	Tablets (Stability Indicating)	12
UPLC	Acquity UPLC HSS T3 column (100 mm x 2.1 mm, 1.8 µm)	A mixture of 0.1% formic acid and acetonitrile in a gradient elution mode	0.3mL/ min	UV	260nm	2 µL	30°C	LAM – 0.326 TDF – 0.481 DOR – 0.805	3min	Tablets (Stability Indicating)	16
UPLC	UPLC BEH C18 column (150 mm × 2.1 mm, 1.7 µm)	proportion of (60:40 % v/v) acetonitrile: potassium dihydrogen orthophosphate buffer; pH 4.5 ± 0.2 was adjusted with 0.1 % OPA	0.3mL/ min	PDA	235nm	10 µL	30°C	LAM – 1.037 TDF – 1.923 DOR – 2.786	4min	Tablets (Stability Indicating)	17
UPLC	Acquity UPLC BEH C18 column (1.7 µm, 2.1 mm x 100 mm)	10 mM ammonium formate buffer (pH adjusted to 3.0 with formic acid) and Acetonitrile in a gradient elution mode	0.3mL/ min	UV	255nm	2 µL	30°C	LAM – 1.013 TDF – 1.236 DOR – 1.430 EFA – 1.671	3min	Tablets (Stability Indicating)	18

Parameter	Doravirine	Lamivudine	Tenofovir DF
FDA Approval	Doravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) used in the treatment of HIV-1 infection. It was approved by the FDA in August 2018 for use in combination with other antiretroviral agents.	Lamivudine is a nucleoside reverse transcriptase inhibitor (NRTI) used in the treatment of HIV-1 infection and chronic hepatitis B virus (HBV) infection. It was approved by the FDA in 1995 for the treatment of HIV-1 infection.	Tenofovir disoproxil fumarate (TDF) is a nucleotide reverse transcriptase inhibitor (NtRTI) used in the treatment of HIV-1 infection and chronic hepatitis B virus (HBV) infection. It was approved by the FDA in 2001 for the treatment of HIV-1 infection.
Chemical name	3-Chloro-5-[[1-[(4,5-dihydro-4-methyl-5-oxo-1H-1,2,4-triazol-3-yl) methyl] -1,2-dihydro-2-oxo-4-(trifluoromethyl)-3-pyridinyl] oxy] benzonitrile	(-)-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl] cytosine	9-[(R)-2-[[bis[[(isopropoxycarbonyl) oxy] methoxy] phosphinyl]- methoxy] propyl] adenine fumarate (1:1).
Molecular Formula	$C_{17}H_{11}ClF_3N_5O_3$	$C_8H_{11}N_3O_3S$	$C_{19}H_{30}N_5O_{10}P.C_4H_4O$
Molecular Weight	425.75 g/mol	229.26 g/mol	635.52 g/mol
Appearance	White to off-white crystalline powder	White to off-white crystalline powder	WHITE to off-white crystalline powder
BCS Class	II	III	III
Solubility	Practically insoluble in water	Soluble in water	Slightly soluble in water
Melting point	>278°C	172 – 178°C	114 – 118°C
Hygroscopicity	Slightly hygroscopic	Non-hygroscopic	Slightly hygroscopic
pH	5.1	7.0	3.13
pKa	9.56	4.1	3.2
Log P	1.1	0.89	1.3
Mechanism of action	Doravirine is a pyridinone non-nucleoside reverse transcriptase inhibitor of HIV-1 and inhibits HIV-1 replication by non-competitive inhibition of HIV-1 reverse transcriptase (RT). Doravirine does not inhibit the human cellular DNA polymerases α, ß, and mitochondrial DNA polymerase γ.	Lamivudine is a synthetic nucleoside analogue. Intracellularly, lamivudine is phosphorylated to its active 5´-triphosphate metabolite, lamivudine triphosphate (3TC-TP). The principal mode of action of 3TC-TP is inhibition of RT via DNA chain termination after incorporation of the nucleotide analogue. Lamivudine triphosphate (3TC-TP) is a weak inhibitor of mammalian DNA polymerases α, β, and mitochondrial DNA polymerase γ.	TDF is an acyclic nucleoside phosphonate diester analog of adenosine monophosphate. TDF requires initial diester hydrolysis for conversion to tenofovir and subsequent phosphorylations by cellular enzymes to form tenofovir diphosphate. Tenofovir diphosphate inhibits the activity of HIV-1 RT by competing with the natural substrate deoxyadenosine 5′-triphosphate and, after incorporation into DNA, by DNA chain termination. Tenofovir diphosphate is a weak inhibitor of mammalian DNA polymerases α, β, and mitochondrial DNA polymerase γ.
Absolute Bioavailability	64%	86%	25%

T_{max}	2h	NA	1h
V_{dss}	60.5L	1.3L/kg	1.3L/kg
Plasma Protein Binding	76%	<36%	<0.7%
Metabolism Primary pathway	Cytochrome P450 3A	Minor	No CYP Metabolism
Major route of elimination	Metabolism	Glomerular filtration and active tubular secretion	Glomerular filtration and active tubular secretion
Urine (unchanged)	6%	71%	70 – 80%
Half-life ($t_{1/2}$)	15h	5 to 7h	17h

The validation parameters include specificity, linearity, accuracy, precision, robustness, and system suitability, which have been thoroughly discussed in the review. Overall, the analytical methods reviewed in this paper are suitable for the routine analysis of Doravirine, Lamivudine, and Tenofovir Disoproxil Fumarate in their combined dosage form. The review also highlights the need for the development of more efficient and accurate analytical methods to meet the growing demand for these drugs in the pharmaceutical industry.

REFERENCES:

1. Doravirine Drug Profile. Available at https://go.drugbank.com/drugs/DB12301
2. Colombier MA, Molina JM. Doravirine: a review. Current Opinion in HIV and AIDS. 2018 Jul 1;13(4):308-14.
3. Lamivudine Drug Profile. Available at https://go.drugbank.com/drugs/DB00709
4. Johnson MA, Moore KH, Yuen GJ, Bye A, Pakes GE. Clinical pharmacokinetics of lamivudine. Clinical pharmacokinetics. 1999 Jan;36:41-66.
5. Tenofovir DF Drug Profile. Available at https://go.drugbank.com/salts/DBSALT000172
6. Gallant JE, Deresinski S. Tenofovir disoproxil fumarate. Clinical Infectious Diseases. 2003 Oct 1; 37(7):944-50.
7. Full Prescribing Information (PIL) of Delstrigo Tablets, US FDA
8. Gollu, Simultaneous quantification of lamivudine, tenofovir disoproxil fumarate and doravirine in pharmaceutical dosage form by liquid chromatography with diode array detection. Pharmaceutical Chemistry Journal. 2020 Aug;54:526-35.
9. Tiruveedhi, RP-HPLC (stability-indicating) based assay method for the simultaneous estimation of doravirine, tenofovir disoproxil fumarate and lamivudine. International Journal of Applied Pharmaceutics. 2021 Jan 7:153-9.
10. Kokkirala, A simple alternative and improved HPLC method for the estimation of doravirine, lamivudine, and tenofovir disoproxil fumarate in solid oral dosage form. Biomedical Chromatography. 2021 Aug; 35(8):e5121.
11. Godela R, Gummadi S. A simple stability indicating RP-HPLC-DAD method for concurrent analysis of Tenofovir Disoproxil Fumarate, Doravirine and Lamivudine in pure blend and their combined film coated tablets. InAnnales Pharmaceutiques Françaises 2021 Nov 1 (Vol. 79, No. 6, pp. 640-651). Elsevier Masson.
12. Addanki S, Kuber BR. A new stability indicating RP-UPLC method for simultaneous estimation of Doravirine, Lamivudine and Tenofovir disoproxil fumarate in bulk and their combined pharmaceutical formulation. Future Journal of Pharmaceutical Sciences. 2021 Dec;7:1-4.
13. Marakatham, Bioanalytical method development and validation of doravirine, lamavudine and tenofovir disoproxil fumarate using HPLC in human plasma. Research Journal of Pharmacy and Technology. 2021;14(8):4087-91.
14. Pandya Y, Patel S. A novel rapid combined RP-HPLC stability method development and validation for antiviral HIV combinations lamivudine, tenofovir, doravirine in dosage form and its application to in vitro dissolution.
15. Sowmya, Stability Indicating Rp-Hplc Method for Estimation of Doravirine in Tablet Dosage Form. Pharm Anal Acta. 2021; 12:616.
16. Pavani C, Development of a Novel Stability quoting RP-Ultra Performance Liquid Chromatography approach for Synchronous Assessment of Doravirine, Lamivudine, and Tenofovir Disproxil fumarate in Pure API Form and Tablet Dosage Based on ICH Guidelines. Journal of Drug and Alcohol Research. 2022 Aug 1; 11(7).
17. Thakare BN. Validated Stability-Indicating Assay UHPLC Method for Simultaneous Estimation of Doravirine, Lamivudine and Tenofovir Disoproxil Fumarate in Pure Material and Pharmaceutical Matrix.
18. Chengalva P, Kuchana M. Development and Validation of Ultra Performance Liquid Chromatographic Method for the Simultaneous Estimation of Lamivudine, Tenofovir Disoproxil Fumarate, Doravirine and Efavirenz in Bulk and Pharmaceutical Formulations. Indian Journal of Pharmaceutical Sciences. 2020 Dec 31; 82(6):1006-14.