Cohen Myron S. et al. (2011) Literature studies show Prevention of HIV-1 Infection with Early Antiretroviral Therapy. reported that the early initiation of antiretroviral therapy reduced rates of sexual transmission of HIV-1 and clinical events, indicating both personal and public health benefits from such therapy. total of 39 HIV-1 transmissions were observed; of these, 28 were virologically linked to the infected partner Of the 28 linked transmissions, only 1 occurred in the early therapy group. Subjects receiving early therapy had fewer treatment end point.

E Dejesus et al. (2009) reported that three hundred patients were evaluated The arms were well balanced at baseline with 88% males, 29% blacks, and a mean age of 43 years; 96% had HIV-1 and 88% were on their first ART regimen. Through 48 weeks, 89% vs. 88% in the EFV/FTC/TDF vs. SBR arms, respectively, maintained HIV-1 RNA <200 copies per milliliter by time to loss of virologic response algorithm with the difference (95% confidence interval) between arms of 1.1% (-6.7% to 8.8%), indicating noninferiority of EFV/FTC/TDF vs. SBR.

Devrukhakar Prashant S. et al. (2013) reported that RP-HPLC method for a combination of tenofovir disoproxil fumarate (TDF), emtricitabine (FTC), and efavirenz (EFV) was developed and validated with the help of a suitable statistical software as an application tool for the quality by design. The drugs individually, and in combination, were subjected to forced degradation (thermal, photolytic, hydrolytic, and oxidative stress conditions) and accelerated stability studies

Purnima Bommakanti Valli et al. (2015) reported that stability indicating reverse phase ultra performance liquid chromatography (RP-UPLC) method was developed and validated for the determination of Emtricitabine (EMT) and Tenofovir disoproxil fumarate (TDF) in pure and tablet dosage forms. The chromatographic separation was achieved by using Waters (Alliance) UPLC system equipped with autosampler and photo diode array detector.

Venkatesan S. et al. (2014) reported that a RP-HPLC method for a combination of tenofovir disoproxil fumarate, emtricitabine, and rilpivirine has been developed and subsequently validated in commercial tablets. The proposed HPLC method utilizes Phenomenex Gemini C18 column (150mm × 4.6mmi.d., 5 m) and mobile phase consisting of MeCN, potassium dihydrogen phosphate buffer (20mM, pH 3.3), and triethylamine 58.72 : 41.23 : 0.05 (v/v) at a flow rate of 1.7 mL/min. Quantitation was achieved with UV detection at 270 nm. The method was validated in terms of accuracy, precision, linearity, limits of detection, limits of quantitation, and robustness.
Dubey Som Shankar (2015) reported that HPLC method was developed and validated for the simultaneous determination of emtricitabine, tenofovir and efavirenz in commercial tablets. The method has shown adequate separation for emtricitabine, tenofovir and efavirenz. Separation was achieved on Inertsil C18 (250 mm × 4.6mm; 5 µm) column using isocratic method with 0.1% OPA: Methanol (55:45) system at room temperature and the detection was carried out at 260 nm using photodiode array (PDA) detector.

Varma PSRCHNP D et al. (2014) reported that HPLC method has been developed for the simultaneous determination of Efavirenz, Tenofovir and Emtricitabine in pharmaceutical dosage form. The method was carried out using Zorbax C8 column (150 mm x 4.6 mm, 5 µm) and mobile phase comprised of mixture of dilute orthophosphoric acid solution pH 2.4±0.02 as buffer and acetonitrile in the ratio of 70:30 v/v and degassed under ultrasonication. The flow rate was 1.0 mL/min and the effluent was monitored at 252 nm.

Mali Ajay D. et al. (2016) reported that a RP-HPLC gradient method developed for simultaneous determination of impurities and degradation products from Emtricitabine and Tenofovir Disoproxil Fumarate in pharmaceutical tablet dosage form. The chromatographic separation was achieved by using column ACE C18 (250 x 4.6, 5µ). The mobile phase-A consists of 0.01M potassium dihydrogen phosphate buffer with pH 4.0 adjusted using diluted ortho-phosphoric acid and mobile phase-B as methanol. The flow rate was 1mL min-1 throughout the gradient program with detection wavelength of 270 nm for both components with its related impurities. The column temperature was 30°C and injection volume of 20µl.

Ramaswamy Arun et al. (2014) reported that a HPLC method for the quantitation of Emtricitabine, Tenofovir, and Efavirenz in pure form and pharmaceutical formulations. The Zorbax SB CN, (250 · 4.6 mm, 5 lm) column was used. UV detection was performed at 260 nm. The mobile phase consisted of methanol (A) and buffer at pH 4.5(B) using the gradient: 0–10 min (90% B), 10–22 min (35% B), and 22–25 min (90% B). The flow rate was 1.5 ml/min in ambient temperature. The injection volume of sample was 20 ll.

Raju Appala N. et al. (2008) reported that HPLC method in isocratic mode has been developed for the estimation of Tenofovir disoproxil, Emtricitabine and Efavirenz in tablet dosage form. A Hypersil BDS C18, 250x4.6 mm, 5 µm partical size, with mobile phase consisting of acetonitrile and 0.03 M KH2PO4 water (pH adjusted to 3.2 with orthophosphoric acid) in the ratio of 60:40 v/v was used. The flow rate was 0.8 ml/min and the effluents were monitored at 260 nm. The
retention times were 3.105 min for Emtricitabine, 3.860 for Tenofovir disoproxil and 10.549 min for Efavirenz. The detector response was linear for Tenofovir disoproxil, Emtricitabine and Efavirenz are in the range of 6-72 mcg/ml, 4-48 mcg/ml and 12-144 mcg/ml respectively.

**Sharma Rajesh et al. (2009)** reported that a simple, rapid reversed-phase high performance liquid chromatographic method had been developed and validated for estimation of emtricitabine and tenofovir disoproxil fumarate in tablet dosage form. The estimation was carried out on Luna C18 (25cm x 4.60 mm, particle size 5µm) column with a mixture of acetonitrile: potassium dihydrogen phosphate buffer (pH 3.0 ± 0.05 adjusted with orthophosphoric acid): triethylamine in the ratio of 70:30:0.5(v/v) as mobile phase. UV detection was performed at 260 nm. The method was validated for linearity, accuracy, precision, specificity and sensitivity as per ICH norms. The developed and validated method was successfully used for the quantitative analysis of commercially available dosage form. The retention time was 1.78 and 2.27 min. for emtricitabine and tenofovir disoproxil fumarate respectively and total run time was 4 min. at a flow rate of 1.5 mL min\(^{-1}\).

**Bhirud Charushila H. (2012)** reported a simple, accurate, precise and rapid HPTLC methods for simultaneous determination of Tenofovir disoproxil fumarate (TDF) and emtricitabine (ETB) in combined dosage forms. The method is based on HPTLC separation of the two drugs followed by densitometric measurements of their spots at 276 nm. The separation was carried out on Merck TLC aluminium sheets of silica gel 60F254 using toluene: ethyl acetate: methanol: acetic acid (6: 4: 3:0.4, v/v/v) as a mobile phase. Stability of TDF and ETB was carried out by forced degradation study. TDF and ETB gave sharp and well defined peak at Rf 0.41 and 0.68, respectively. Calibration curves were linear in range 150-1500 ng/spot and 100-1000 ng/spot for TDF and ETB, respectively.

**Rao N. Srinivasa et al. (2008)** reported An accurate, precise, reproducible, gradient and stability indicating Reverse Phase High Performance Liquid Chromatographic (RP-HPLC) method was developed and validated for the estimation of Lamivudine, Tenofovir disoproxil fumarate and Efavirenz in pharmaceutical dosage forms. In this method Waters C18 (75x4.6mm, 5µ) column with gradient mobile phase containing methanol and water in different ratios were used. The flow rate was 1.0 ml/min. and the detection wavelength was 260nm.

**Chitlange S.S. et al. (2014)** reported accurate, HPTLC method for concurrent estimation of Rilpivirin, Emtricitabine and Tenofovir as the bulk drug and in combined tablet dosage form.
Chromatographic separation of the drugs was performed on aluminum plates precoated with silica gel 60 F254 as the stationary phase and the solvent system consisted of Methanol : Toluene : Ethylacetate : Ammonia (1.5: 5.5: 1.5: 0.1 v/v/v/v). Densitometric evaluation of the separated zones was performed at 272 nm. The three drugs were satisfactorily resolved with RF values $0.59 \pm 0.02$ and $0.29 \pm 0.02$, $0.41 \pm 0.02$ for Rilpivirin, Emtricitabine and Tenofovir respectively. The accuracy and reliability of the method was assessed by evaluation of linearity (40-140 ng/spot for Rilpivirin, 320-1120 for Emtricitabine and 480-1680 for Tenofovir).

Ramachandran Geetha et al. (2006) reported a high performance liquid chromatographic method for determination of efavirenz in human plasma was developed. The method involved extraction of sample with ethyl acetate and analysis using a reversed-phase C18 column (150 mm) with UV detection. The assay was linear from 0.0625 to 10.0 µg/ml. The method was specific for efavirenz estimation and the drug was stable in plasma up to one month at −20 °C. The average recovery of efavirenz from plasma was 101%.

Mogatle Seloi et al. (2009) reported a pharmacokinetic interaction study between efavirenz (EFV), a non-nucleoside reverse transcriptase inhibitor used in the treatment of HIV-1 infection, and an African traditional medicine, African potato in human subjects was undertaken. This necessitated the development and validation of a quantitative method for the analysis of EFV in plasma. A simple mobile phase consisting of 0.1 M formic acid, acetonitrile and methanol (43:52:5) was pumped at a low flow rate of 0.3 ml/min through a reverse phase Phenomenex® Luna C18 (2) (5 µm, 150 mm × 2.0 mm i.d.) column maintained at 40 °C. Diclofenac sodium was used as an internal standard (IS) and EFV and IS were monitored at 247 nm and 275 nm, respectively.

Sarasa-Nacenta María et al. (2001) reported a high-performance liquid chromatographic method has been developed and validated for the quantitative determination of efavirenz in human plasma. The method involved solid-phase extraction of the drug and the internal standard from 300 µl of human plasma. The analysis was via UV detection at 250 nm using a reversed-phase C8 analytical column and a isocratic mobile phase consisting of phosphate buffer (pH 5.75) acetonitrile that resolved the drug and internal standard from endogenous matrix components and potential co administered drugs. Within- and between-day precisions were less than 8.6% for all quality control samples.
Kappelhoff Bregt S et al. (2003) reported a rapid high-performance liquid chromatographic method for the simultaneous quantification of efavirenz and nevirapine in human plasma suitable for therapeutic drug monitoring is described. Sample pre-treatment consisted of protein precipitation with acetonitrile and subsequently dilution with distilled water. The drugs were separated from endogenous compounds by isocratic reversed-phase high-performance liquid chromatography with ultraviolet detection at 275 nm.

Yadav Manish et al. (2010) reported a liquid chromatography tandem mass spectrometry method is developed for the determination of one nucleotide tenofovir (TFV) and two nucleosides emtricitabine (FTC) and lamivudine (3TC) reverse transcriptase inhibitors in human plasma. Plasma samples were prepared by solid-phase extraction of the analytes and acyclovir (ACV) as internal standard using Waters Oasis MCX cartridges. The chromatographic separation is achieved in a run-time of 3.0 min on an ACE 5 CN column (150 mm × 4.6 mm, 5 µm) under isocratic conditions. The mobile phase consisted of 0.5% formic acid in water and acetonitrile (55:45, v/v).

Rao Janhavi R et al. (2011) reported a high performance thin-layer chromatographic (HPTLC) method has been developed for simultaneous analysis of tenofovir and emtricitabine in a tablet dosage form. Chromatographic separation was achieved on aluminum foil plates precoated with silica gel 60F254, with toluene : methanol : ethyl acetate: acetic acid (4:2:5:0.1v/v/v/v) as mobile phase. Detection was performed densitometrically at 270 nm. The RF of a tenofovir and emtricitabine were 0.52 ± 0.05 and 0.40 ± 0.02, respectively.

Joshi Maithilee et al. (2009) reported a high performance thin layer chromatographic method has been developed and validated for the estimation of emtricitabine and tenofovir simultaneously in combined dosage form. The stationary phase used was precoated silica gel 60F 254. The mobile phase used was a mixture of chloroform: methanol (9:1 v/v). The detection of spots was carried out at 265 nm. The method was validated in terms of linearity, accuracy, precision and specificity.

Pendela Murali et al. (2011) reported a liquid chromatographic method with UV detection was developed for the assay of a tablet for HIV (human immunodeficiency virus) treatment containing three active components, which are emtricitabine, tenofovir disoproxil fumarate and rilpivirine. A Hypersil BDS-C18 column was used as stationary phase and the assay was performed with gradient elution using mobile phases containing acetonitrile, 0.2 M potassium
dihydrogen phosphate and water. Dimethyl sulfoxide–distilled water (1:1) was used as solvent for the active components.

**Kumar Pradeep et al. (2011)** reported a high performance thin layer chromatographic method has been developed and validated for the estimation of Emtricitabine in capsule dosage forms. The method employed TLC aluminum plates pre-coated with silica gel 60 F 254 as the stationary phase. The mobile phase used was a mixture of (Chloroform: Methanol 8.5:1.5v/v). The detection of spot was carried out at 275nm. The calibration curve was found to be linear between 200 to 2200 ng mL-1 with regression coefficient of 0.9992.

**Prakash Anuj et al. (2015)** reported a genotoxic impurities in drug substances or drug products are increasing concern to safeguard public health. Presence of genotoxic impurity in drug substances and drug products may be DNA reactive and posed significant problems for drug regulators and industry over the last decade. The principal concern relates to drug safety is the prolong exposure to compounds that can alter DNA, may ultimately produce a carcinogenicity. Therefore, the practical issue is that the conventional procedures should be there to identify DNA-reactive impurities in the shelf life of drug product.

**Pratima Anna G et al. (2013)** reported a reversed-phase ultra performance liquid chromatographic method was developed and subsequently validated for quantitation of Emtricitabine (ECB) from drug substance matrix. The separation was achieved in less than 2.0 minutes on Waters ACQUITY UPLC BEH C18 (50 x 2.1) mm, 1.7µm column in isocratic mode with flow rate 0.25 mL/min. Mobile phase used was 0.015 M potassium dihydrogen phosphate buffer pH 2.2 and acetonitrile in ratio 75:25 v/v. Detection was carried out at the maximum wavelength of 284 nm using a photodiode array detector. **Jayapalu Kalpana et al. (2013)** reported a stability indicating liquid chromatography method was developed and validated for the simultaneous quantitation of related substances of antiretrovirals in combined oral dosage formulation. Separation was achieved using a Waters, Xterra RP-18 column (250 ◊ 4.6 mm) with a mobile phase containing a gradient mixture of sodium acetate trihydrate solution and acetonitrile with a flow rate of 1 mL/min, detection at 254 nm.

**Rathore Atul S. et al. (2012)** reported high-performance thin-layer chromatographic (HPTLC) method for the determination of emtricitabine both in bulk drug and pharmaceutical dosage form was developed and validated. The method employed aluminium plates precoated with silica gel G60 F254 as the stationary phase. The solvent system consisted of toluene : ethyl acetate :
methanol (2 : 8 : 1, v/v/v). This solvent system was found to give compact spots for emtricitabine with Rf value 0.26±0.01. Densitometric analysis of emtricitabine was carried out in the absorbance mode at 284 nm.

**Nagasarapu Mallikarjuna rao et al. (2016)** reported a reverse phase liquid chromatographic method was developed for the simultaneous estimation of Emtricitabine, Elvetigravir, Cobicistat and Tenofovir in bulk and tablet dosage form. A reverse phase gradient program has been developed to separate the all four active ingredients. The mobile phase consisting of 0.05M Phosphate buffer pH 3.0 (adjusted with dilute phosphoric acid) and Acetonitrile in the ratio 95:5 from 0 min to 4 minutes, further increased the Acetonitrile ratio from 5 to 50 from 4 min to 10 minutes, on a reverse phase C18 column (250x4.6mm, 5 µ) with a flow rate of 1.0 ml/min, monitored at 240nm.

**AbdelHay Mohammad H. et al. (2013)** reported two simple and selective methods were developed for the simultaneous determination of tenofovir fumarate (TEN) and emtricitabine (EMT) in combined tablets. The first method involves the application of first derivative spectrophotometry where the first derivative amplitudes were measured at 298.5nm for determination of EMT in presence of TEN. The second method involves first derivative of ratio spectra spectrophotometry where the amplitudes at 251.5nm have been used for quantitation of TEN in the presence of EMT.

**Patel Jitendra S et al. (2013)** reported that As per ICH guideline impurity may be defined as any component of drug product that is not the drug substance or an excipient. Now a day apart from purity profile there are an increasing essentiality of impurity profile by regulatory agency. Different regulatory agencies like ICH,USFDA, TGA, etc. work on control and identification of impurities in pharmaceutical dosage forms. To identify and characterize impurities are essential for establishing the biological safety of an pharmaceutical dosage forms.

**SAIRA MULLA et al. (2014)** reported synthesize and isolate in process impurity of Efavirenz in the presence of Tetrahydrofuran solvent.In the process related impurity ranging from 0.05% to 0.2% in Efavirenz were detected by a gradient reversed phase high performance liquid chromatography (RP-HPLC).This impurity was isolated from the crude sample of Efavirenz using gradient reversed-phase preparative high performance liquid chromatography. The unknown impurity of in process impurity of Efavirenz was synthesised and isolated by using the preparative chromatography of purity above 95%.
Gandhi B. Mohan et al. (2015) reported reversed-phase high performance liquid chromatographic method was developed and validated for the simultaneous estimation of Emtricitabine and Tenofovir disoproxil fumarate. Chromatography is carried out isocratically on C8 Phenomenex Luna (4.6X250 mm) column with a mobile phase composed of acetonitrile: phosphate buffer (60:40 v/v) at a flow rate of 1 ml/min. Detection was carried out using a UV detector at 260 nm. Parameters such as linearity, precision, accuracy, specificity and ruggedness are studied as per the ICH Q2(R1) guidelines.

Maniyar Umesh Ramnarayan et al. (2016) reported a simultaneous estimation by stability indicating RP-HPLC gradient method was developed for Assay test of Efavirenz, Emtricitabine and Tenofovir disoproxil tablet dosage form. The experiment was carried out on Hypersil BDS C18, (150mm x 4.6 mm), 5µ column using the gradient composition of phosphate buffer pH 3.5 as mobile phase A and mixture of methanol, acetonitrile and water 500:350:150 v/v. degas as mobile phase B at flow rate 1.5ml/min and detection wavelength 265 nm.

Gorja Ashok et al. (2013) reported a method, was developed and validated for the simultaneous estimation of Lamivudine and Tenofovir disoproxil fumarate in pharmaceutical dosage form. The method was based on RP-HPLC. Chromatographic separation was performed on Thermosil C18 (150mm x 4.6mm, 3.5µm particle size) column using a mobile phase consisting of a mixture of KH$_2$PO$_4$ buffer (pH 6.0 with dilute orthophosphoric acid): Methanol: Water (33:65:2%v/v/v) in an isocratic mode. The following system conditions were maintained throughout development and validation i.e., flow rate 0.8mL/min, column was maintained at room temperature and the detected by a UV-wave length at 260nm.

Reddy B. Venkateswara et al. (2014) reported a formulation of film coated tablets of Emtricitabine and Tenofovir disoproxil fumarate, drugs which are used in the treatment of HIV-1 infection. Tablets are prepared by wet granulation method using the different excipients, namely Sodium starch glycolate, Di calcium phosphate, starch 1500, ideal blue, Iso propyl alcohol. FTIR studies revealed that there are no incompatibilities between drugs and polymers used. The prepared tablets are evaluated for various properties.

Hussen Syed sajjad et al. (2013) reported a stability-indicating high performance liquid chromatographic (HPLC) method for Tenofovir Disproxil fumarate (TEN) with photodiode array (PDA) detection and validated as per International Conference on Harmonisation (ICH) guidelines. The developed method was successfully applied for assay of Tenofovir Disproxil
fumarate to nanoparticle formulation. A Lichrocart (C18) (250mm × 4.6mm, 5 µm particle size) column and a mobile phase composed of acetonitrile and 0.025M potassium di hydrogen phosphate buffer (pH 3.0 adjusted by using 10% v/v Orthophosphoric acid) in the ratio 35:65 (v/v) was used, and the detection wavelength of 260 nm.

Trinath MN et al. (2013) reported a reversed- phase high-performance liquid chromatographic method has been developed and validated for the simultaneous estimation of embtricitabine and tenofovir in pure and Pharmaceutical dosage form. In present work a simple, sensitive and specific method (RP-HPLC assay, stability indicating RP-HPLC) has been developed for the simultaneous estimation of embtricitabine and tenofovir in pure and Pharmaceutical dosage form. A phenomenex BDS C18, column having 5 µm particle size and 150 mm x 4.6 mm in length and gradient mode, with mobile phase containing potassium dihydrogen phosphate (pH3.0, adjusted with O-phosphoric acid) and acetonitrile in the ratio of 96:4.

Nandini K. et al. (2016) reported a reverse phase high performance liquidchromatography (RP-HPLC) method has been proposed for the estimation of Tenofovir Disoproxil Fumarate in pure form as well as in its pharmaceutical formulation. The chromatography was carried on Phenomenex Luna C18 (250 x 4.6 mm x 5 µm) column, with mobile phase Orthophosphoric Acid: Acetonitrile: Methanol in the ratio of (40:50:10% v/v) and pH adjusted to 3.0. The flow rate was 0.9 ml/min with detection at 254 nm. The retention time was found to be 2.21 min.

Gomes Noel A. et al. (2008) reported a liquid chromatography–tandem mass spectrometry (LC–MS/MS) method has been developed and validated for simultaneous quantification of Tenofovir (TEN) and Emtricitabine (EMT) in human plasma using Chromolith Speed Rod RP18. The mass transition ion-pair has been followed as m/z 288.10 → 176.10 for TEN, m/z 248.20 → 130.20 for EMT and m/z 230.10 → 112.10 for Lamivudine (LAM). The method involves solid phase extraction from plasma, simple isocratic chromatographic conditions and mass spectrometric detection using an API 5000 instrument that enables detection at nanogram levels.

CHANDRA P. et al. (2011) reported a high performance thin layer chromatographic method has been developed for the simultaneous determination of lamivudine (LAM) and tenofovir disoproxil fumarate (TDF) in pharmaceutical dosage form. The separation was carried out on Merck HPTLC aluminum plates of silica gel 60 F254, (20 × 10 cm) with 250 µm thickness using chloroform: methanol: toluene (8: 2: 2, v/v/v) as mobile phase. HPTLC separation of the two
drugs followed by densitometric measurement was carried out in the absorbance mode at 265 nm.