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ANALYTICAL METHODS OF EMTRICITABINE AND TENOFOVIR ALAFENAMIDE: A REVIEW

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ABSTRACT

The aim of this review is to estimate the anti-viral drugs like emtricitabine and tenofovir alfenamide in bulk and various dosage forms by using analytical methods. Emtricitabine belongs to the class of anti-retroviral tablets called nucleoside reverse transcriptase inhibitors which are used to treat HIV infection. tenofovir alafenamide is a prodrug of tenofovir that is used to treat HIV infections and hepatitis B. analytical techniques like High-performance liquid chromatography [HPLC], High-performance thin layer chromatography [HPTLC], UV spectroscopy, Hyphenated Techniques is used for the determination of antiviral drugs found in API in addition to the formulation.

Key words: Emtricitabine, Tenofovir alfenamide, Antiretroviral, HPLC

INTRODUCTION:

Emtricitabine is chemically known as 4-amino-5-fluoro-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2- one **[1]**. Emtricitabine is an antiviral agent used for the prevention of perinatal HIV-1 reverse transcriptase. It is also active against the hepatitis B virus **[2]**. The chemical name of TAF is L-alanine, [(S) [[(1R)-2-(6-amino-9H-purine-9yl)-1-(methyl ethoxy] methyl] phenoxyphosphinyl]-,1-methyl ethyl ester, (2E)-2-butenedioate **[3]**. Tenofovir alafenamide (TAF) is a prodrug of tenofovir as a potent nucleotide reverse transcriptase inhibitor. It is the active component for the treatment of chronic hepatitis B, first-line treatment of human immunodeficiency virus infection HIV **[4]**.

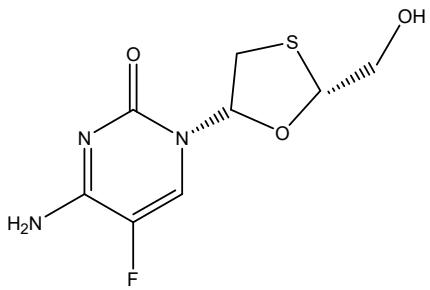

Figure 1: Emtricitabine

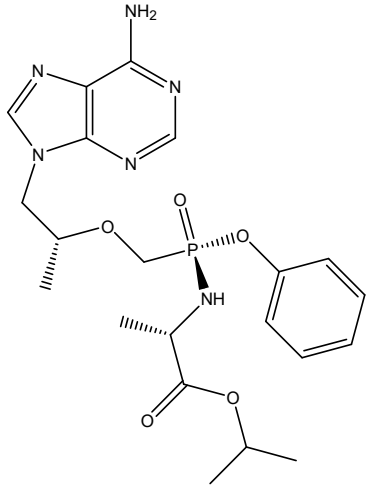

Figure 2: Tenofovir alafenamide

Table 1: UV Methods for determination of emtricitabine and tenofovir alafenamide

S. No.	Drug	Description	Reference
1.	Emtricitabine	Detection Wavelength: 258 nm Solvent: double distilled water Linearity: 2-12 µg/ml Correlation coefficient: 0.999	[5]
2.	Emtricitabine	Detection Wavelength: 225 nm Solvent: Methanol Linearity: 3-21 µg/ml Correlation coefficient: 0.999	[6]
3.	Tenofovir alafenamide	Detection Wavelength: 267 nm Solvent: methanol: distilled water (20: 80) Linearity: 10 -50 µg/ml Correlation coefficient: Less than 1 %	[7]
4.	Tenofovir alafenamide	Detection Wavelength: 260nm Solvent: distilled water Linearity: 2-10 µg/mL Correlation coefficient: 0.9986	[8]

Table 2: HPLC methods for determination of emtricitabine and Tenofovir alafenamide

S. No.	Drug	Description	Reference
5.	Emtricitabine, Tenofovir alafenamide	Detection Wavelength:260 nm Mobile phase: Methanol: Distil water in a proportion of 60:40 v/v Flow rate :1 ml/min Linearity range: Emtricitabine: 40-240µg/ml Tenofovir alfenamide: 5-30µg/ml, Column: C_{18}(250 x 4.6 mm, 5µ) Retention time: Emtricitabine:3.10 min Tenofovir alafenamide:7.38 min	[9]
6.	Emtricitabine, Tenofovir alafenamide	Detection Wavelength:259 nm Mobile phase: Acetonitrile: phosphate (80: 20) Flow rate :1 ml/min Linearity range: Emtricitabine: 20-100 µg/ml Tenofovir alfenamide: 0.25-12.5 µg/ml Column: ODS (4.6 × 250 mm, 5 mm) Retention time: Emtricitabine: 3.314 Tenofovir alafenamide: 5.068	[10]

7.	**Emtricitabine and its degradation substance**	**Detection wavelength:280nm Mobile phase: Ammonium formate: methanol Flow rate:1.0 ml/min Linearity range: Emtricitabine: 0.05 to 3.0 µg/mL. Column: C_{18}HIQSIL Retention time: Emtricitabine:1.00**	**[11]**
8.	**Emtricitabine and related substance in drug substance**	**Detection wavelength:280 nm Mobile phase: Acn, phosphate buffer, Water. Flow rate:1.0ml/min Linearity range: Emtricitabine: Column: RP C_{18} column (25 cm x 4.6 mm i.d.), 5 microns**	**[12]**
9.	**Tenofovir alafenamide**	**Detection wavelength:260nm Mobile phase: Methanol: Potassium dihydrogen orthophosphate buffer (30:70, v/v) Flow rate:1 ml/min Linearity range: Emtricitabine: 10-50 µg/ml Column: kromasil C_{18} (100mm × 4.6mm, 5 µm) Retention time: Emtricitabine:7.33**	**[13]**
10.	**Emtricitabine, Tenofovir, Isoniazid.**	**Detection wavelength:260nm Mobile phase: Acetonitrile: 0.02M Potassium dihydrogen Orthophosphate Buffer: HPLC grade Water Flow rate: 0.6ml/min Linearity range: Emtricitabine: 10-50µg/ml, Tenofovir Disopropoxil fumarate: 15-75µg/ml Isoniazid: 15-75µg/ml Column: Sunfire C_{18} column (4.6×150mm) 5µm Retention time: Emtricitabine: 2.334mins Tenofovir dispropoxil fumarate: 3.835mins Isoniazid: 5.209mins**	**[14]**
11.	**Emtricitabine, Tenofovir disoproxil fumarate, Efavirenz.**	**Detection wavelength:265 nm Mobile phase: 0.02M sodium dihydrogen orthophosphate: Methanol: water Flow rate: 1.5ml/min Linearity range: Emtricitabine: 8-120µg/ml, Tenofovir Disopropoxil fumarate: 12-180µg/ml Isoniazid: 20-360µg/ml Column: ODS 3V Column Retention time: Emtricitabine: 5.875 Tenofovir dispropoxil fumarate: 8.800 Isoniazid: 12.020 mins**	**[15]**
12.	**Emtricitabine, Tenofovir disoproxil fumarate, Rilpivirine.**	**Detection wavelength:262nm Mobile phase: Phosphate buffer: acetonitrile Flow rate: 1.2 ml/ min Linearity range: Emtricitabine: 24-56 µg /ml Tenofovir Disopropoxil fumarate: 30-70 µg /ml Rilpivirine: 3-7 µg /ml Column: Inertsil c18 Retention time: Emtricitabine: 2.523 Tenofovir dispropoxil fumarate:6.71 Rilpivirine: 3.28**	**[16]**
13.	**Emtricitabine**	**Detection wavelength:280nm Mobile phase: Buffer: methanol 90:10%(v/v) Flow rate: 1 ml/ min Linearity range: Emtricitabine :50-150 µg /ml Column: Peerless basic C_{18}**	**[17]**

14.	**Tenofovir alafenamide**	**Detection wavelength:260nm Mobile phase: n-hexane:2-propanol (60:40 v/v) Flow rate: 1ml/min Linearity range: 0.01–1 mg/ mL Emtricitabine: Column: CHIRALPAK AD-3 (250 x 4.6 mm; particle size 3 µm Retention time: Emtricitabine:7.340 min**	**[18]**
15.	**Emtricitabine and tenofovir alafenamide**	**Detection wavelength:252nm Mobile phase: Methanol: water (80:20%v/v) Flow rate: 0.8ml/min Column: Cosmosil C_{18} column (250mm×4.6ID, 5µm) Retention time: Emtricitabine:5.293 min Tenofovir alfenamide:4.277**	**[19]**

Table 3: HPTLC methods for determination Emtricitabine and Tenofovir alfenamide

S. No.	Drug	Description	Reference
16.	**Emtricitabine and tenofovir**	**Stationary phase: Precoated silica gel 60F 254 Mobile phase: Chloroform: methanol (9:1 v/v) Detection wavelength:265 nm Linearity: 200 to 1000 ng Rf value: Emtricitabine: 0.18 Tenofovir: 0.47**	**[20]**
17.	**Emtricitabine and tenofovir**	**Stationary phase: Aluminium foil plates precoated with silica gel 60F254, Mobile phase: Toluene: methanol: ethyl acetate: acetic acid (4:2:5:0.1v/v/v/v) Detection wavelength:270 nm Linearity: Emtricitabine: 80-560 ng spot Tenofovir: 120–600 ng spot Rf value: Emtricitabine: 0.40 ± 0.02 Tenofovir: 0.52 ± 0.05**	**[21]**
18.	**Emtricitabine and tenofovir alafenamide**	**Stationary phase: Silica gel 60 F254 aluminum plates Mobile phase: Ethyl acetate–n-hexane–methanol–ammonia solution (4:4:2:0.2, V/V). Detection wavelength: 260nm Linearity: Emtricitabine: 400–2000 ng/band Tenofovir alafenamide :50–250 ng/band Rf value: Emtricitabine: 0.56 Tenofovir alafenamide: 0.43**	**[22]**

Table: 4 Hyphenated techniques for determination of Emtricitabine and Tenofovir alfenamide

S. No.	Drug	Description	Reference
19.	**Emtricitabine, Cobicistat, Elvitegravir, Tenofovir dispropoxil fumarate. (UPLC)**	**Column: Endoversilo C18 (50 × 2.1 nm, 1.8 µm) Mobile phase: Acetonitrile and 0.1 % orthophosphoric acid (70:30%v/v) Detection wavelength: 252 nm Flow rate: 0.3 ml/min Correlation coefficient: 0.999 Run time: 4 min Retention time: Emtricitabine:1.48 min Cobicistat:2.51 min Elvitegravir:0.59 min Tenofovir disoproxil fumarate:0.73**	**[23]**
20.	**Emtricitabine, tenofovir disopropoxil fumarate (UPLC)**	**Column: BEH C18 (100 mm × 2.1, 1.8 mm) Mobile phase: 0.68% potassium dihydrogen orthophosphate buffer of pH = 6 and methanol in the ratio 45:55 v/v Detection wavelength: 261 nm Flow rate: 1.2 mL/min Correlation coefficient: 0.998 Retention time: Emtricitabine: 0.684 Tenofovir dispropoxil fumarate: 0.930**	**[24]**
21.	**Emtricitabine, Tenofovir alafenamide (LC-MS/MS)**	**Column: Gemini C18 column (4.6×100mm, 5µm) Mobile phase: 0.1 % formic acid: methanol at the ratio of 20:80 v/v Flow rate: 0.5ml/min Linearity range: 20-120 ng/ml**	**[25]**

CONCLUSION:

In order to estimate Emtricitabine and Tenofovir alafenamide in bulk and pharmaceutical dosage forms, a variety of techniques are available. According to the documented data, methanol and acetonitrile were the most regularly used solvents, and the column employed here is a c_{18} column with a flow rate of 1 ml/ min, and aluminium plates precoated with silica gel are commonly used in HPTLC since this approach is trustworthy. This review focused on a synopsis of the current state of the art of analytical methods for emtricitabine and tenofovir alafenamide determination.

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