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ESTIMATION OF LAMIVUDINE BY DIFFERENT ANALYTICAL METHODS - A REVIEW

K. LATHA SRI*, G. GAYATHRI, P. PRACHET, M. SIVA PRASAD AND RAMA RAO

Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Chalapathi Nagar, Lam, Guntur-522034

***Corresponding Author: K. Latha Sri: E Mail: lathasrikondaveeti@gmail.com**

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ABSTRACT

The current review paper focuses on using several analytical approaches to estimate Lamivudine and their combination of drugs. Lamivudine is used to treat HIV and Hepatitis B infection. It acts as a competitive inhibitor of the HBV DNA polymerase and blocks viral replication by inhibiting the viral polymerase by chain termination. Lamivudine and its combinations are estimated by using various analytical techniques like UV-Visible spectrophotometer, High Performance Liquid Chromatography (HPLC), Liquid chromatography –Tandem mass spectrophotometry (LC-TMS), High Performance Thin Layer Chromatography (HPTLC). This review makes clear about the usage of precise solvents for the estimation of lamivudine and its combinations.

Keywords: Lamivudine, UV, HPLC, HPTLC, LC-TMS

INTRODUCTION:

HIV is a retrovirus that attacks the immune system. It damages or destroys CD4 cells, which are white blood cells. Antiretroviral therapy inhibits the virus from replicating, lowering the body's HIV levels **[1]**. Antiretroviral drug classifications- Nucleoside reverse transcriptase inhibitors (NRTIs), Non-nucleoside reverse transcriptase inhibitors (NNRTIs), Protease inhibitors (PIs), Integrase inhibitors **[2]**.

Lamivudine **(Figure 1)** is a nucleoside reverse transcriptase inhibitor. U.S. Food and Drug Administration (FDA) has approved lamivudine (brand name: Epivir) for the treatment of HIV infection in adults and children **[3]**. The chemical name of lamivudine is 4-amino-1- [(2R, 5S)-2-(hydroxymethyl)-1, 3-oxathiolan-5-yl]-1, 2-dihydropyrimidin-2-one **[3]**.

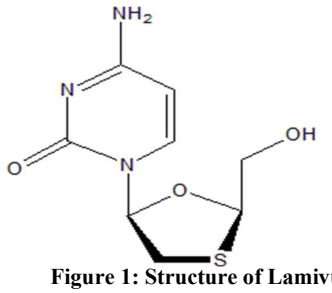

Figure 1: Structure of Lamivudine

METHODS FOR LAMIVUDINE

Spectroscopic methods:

Various methods for the estimation of Lamivudine in single and in combination with other drugs by UV spectroscopic methods are enlisted in the **Table 1**.

Chromatographic methods:

Chromatographic methods like HPLC, HPTLC, UPLC, LC-TMS was developed for the estimation of Lamivudine in single and combination with other drugs. Methods for estimation of HPLC ana HPTLC are listed in **Table No: 2-5**.

Table 1: Methods for estimation of Lamivudine single and combined with other drugs by UV-Visible Spectrophotometry

S. No	Drugs	Description	Reference
1.	Tenofovir Disoproxil Fumarate, Lamivudine and efavirenz	Detection wavelength: Tenofovir disoproxil fumarate: 247 nm, Lamivudine: 259 nm, Efavirenz: 272 nm. Solvent: Methanol: Water (50:50). Linearity range: Tenofovir disoproxil fumarate: 5-30 µg/ml, Lamivudine: 5-30 µg/ml, Efavirenz: 10-60 µg/ml.	[4]
2.	stavudine, lamivudine and nevirapine	Detection wavelength: Stavudine: 266 nm, Lamivudine: 271 nm, Nevirapine: 315 nm Solvent: phosphate buffer pH – 6.8 Linearity range: 5-80 µg/ml.	[5]

3.	Lamivudine, Zidovudine and Nevirapine	Detection wavelength: Lamivudine: 271 nm, Zidovudine: 270 nm, Nevirapine: 310 nm Solvent: Methanol: water (60:40) v/v Linearity range: 4-24 µg/ml	[6]
4.	Stavudine, Lamivudine and Nevirapine	Detection wavelength: Stavudine: 265nm, Lamivudine: 272nm, Nevirapine: 282nm Solvent: Methanol Linearity range: Stavudine:2.0 - 8.0 µg/ml, Lamivudine: 12.0 - 18.0 µg/ml, Nevirapine:14.0 - 26.0 µg/ml	[7]
5.	Lamivudine, Nevirapine and zidovudine	Detection wavelength: Lamivudine- 280.2 nm, Nevirapine 312 nm and Zidovudine-266.8nm Solvent: Distilled water. Linearity range: 5-25 mg/ ml, 5-50mg/ ml and 5-40mg/ml	[8]
6.	Lamivudine	Detection wavelength:272 nm Solvent: Methanol Linearity range: 2.5-20 µg/ml	[9]
7.	Abacavir and Lamivudine	Detection wavelength: 224, 241, 257, 280 and 296 nm Solvent: acetonitrile and methanol Linearity range: 20 µg/ml and 10 µg/ml	[10]
8.	Dolutegravir, Lamivudine, abacavir	Detection wavelength:210-330nm Solvent: distilled water Linearity range: 2 µg/ml,12 µg/ml,24 µg/ml.	[11]

Table 2: Methods for estimation of Lamivudine single and combination with other drugs by UPLC

9.	Zidovudine, Lamivudine and Nevirapine	Detection wavelength: 266nm Mobile phase: 0.1%, v/v trifluoroacetic acid in water and acetonitrile. Column: C18 column consisting high strength silica (ACQUITY UPLC HSS-T3), 100 × 2.1 mm, 1.8 mm Flow rate: 0.4 ml/min. Range: Zidovudine, Lamivudine and Nevirapine 100-500, 50-250 and 100-180 mg/ml Retention time: 3TC, AZT and NVP were 1.888, 3.497 and 4.786 min	[12]
10.	Lamivudine, abacavir and zidovudine	Detection wavelength: 280nm Mobile phase: phosphate Buffer (60%) [pH3.0] & Methanol (40%) Column: Symmetry C18 (2.1 x 100mm, 1.7µm Flow rate: 0.25ml/min Range: 20 to 60ppm for the drug Abacavir & 10 to30ppm for the drug Lamivudine & 20 to60ppm for the drug Zidovudine Retention time: Lamivudine, Abacavir and Zidovudine were 1.019 min., 1.271 min. & 1.617 min	[13]

Table 3: Methods for estimation of Lamivudine and single and combination with other drugs by LC-TMS

11.	Lamivudine and zidovudine	Mobile phase: acetonitrile–water (15: 85 v/v) Column: Aquasil (C 5 18 mm, 15032.1 mm) Flow rate: 0.3 ml/min Linearity range: 500, 1000, 2500 and 5000 ng/ml	[14]
12.	Zidovudine, lamivudine and nevirapine	Mobile phase: water: methanol (15:85, v/v) Column: Peerless Basic C18 column Flow rate: 0.8ml/min Linearity range: Zidovudine and Nevirapine:5–1500 ng/ml, Nevirapine:10–3000 ng/ml	[15]

Table 4: Methods for estimation of Lamivudine and single and combination with other drugs by HPTLC

13.	Lamivudine, Tenofovir Disoproxil Fumarate, and Efavirenz	Detection of spot: 375–900 ng spot–1 for lamivudine, tenofovir disoproxil fumarate and 750–1800 ng spot–1 for efavirenz Stationary phase: pre coated plate with silica gel 60F2 Mobile phase: toluene–methanol (27:6 v/v). Linearity range: 0.5, 0.7, 0.8, 1, and 1.2 mL Retardation Factor: 0.18 ± 0.02 for lamivudine, 0.33 ± 0.05 for tenofovir disoproxil fumarate, and 0.48 ± 0.02 for efavirenz	[16]
14.	Dolutegravir, Lamivudine, and Tenofovir	Stationary phase: Premium purity silica gel 60 F254 plates (20 cm × 10 cm) Mobile phase: ethyl acetate– methanol–acetone: concentrated ammonium hydroxide (30:7:3:1)	[17]

	Disproxil Fumarate	Linearity range: Retardation factor: L (RF = 0.22) and TDF (RF = 0.46) D (RF = 0.56)	
15.	Lamivudine, Tenofovir Disoproxil Fumarate and Efavirenz	Detection of spot: 260 nm Stationary phase: aluminium plates precoated with silica gel G60 F254 (20 × 10 cm) Mobile phase: chloroform–methanol–toluene (9:1.2:0.3, v/v) Linearity range: 400–800 ng spot–1 for LAM and TDF and 800–1600 ng spot–1 for EFV Retardation factor: 0.20 ± 0.02, 0.61 ± 0.01 and 0.73 ± 0.02 for Lamivudine, Tenofovir Disoproxil Fumarate and Efavirenz	[18]
16.	Abacavir Sulfate, Lamivudine Hydrochloride, and Dolutegravir Sodium	Detection of spot: 267 nm Stationary phase: pre-coated silica gel aluminium HPTLC plate 60 F254 Mobile phase: ethyl acetate–ethanol–acetone–ammonia (4.478:0.740:0.50:0.15, v/v) Linearity range: 4.8, 7.2, 9.6, 12.0, and 14.4 µg per band for ABC, 2.4, 3.6, 4.8, 6.0, and 7.2 µg per band for LAM, and 0.4, 0.6, 0.8, 1.0, and 1.2 µg per band for DTG Retardation factor: Abacavir Sulfate, Lamivudine Hydrochloride, and Dolutegravir Sodium were found to be 0.65, 0.34, and 0.26	[19]
17	zidovudine and lamivudine	Detection of spot: 276nm Stationary phase: silica gel 60F254 T Mobile phase: toluene: ethyl acetate: methanol: formic acid 6.5:2.5:1.5:1.5 (v/v) Linearity range: zidovudine and lamivudine were prepared at concentration levels of 50 to 400 µg/ml and 25 to 200 µg/ml respectively. Retardation factor: zidovudine and lamivudine 0.27 ± 0.03 and 0.78 ± 0.03	[20]

Table 5: Methods for estimation of Lamivudine and single and combination with other drugs by HPLC

S. No	Drugs	Description	Reference
18.	Lamivudine	Detection wavelength: 256 nm Mobile phase: 0.25% Triethylamine buffer (pH 3.0): acetonitrile (70:30, v/v) Column: Hypersil BDS C-18 column (250 mm 4.6 mm, 5 mm) Flow rate: 1.0 ml/ min Linearity range: 25–2000 ng/mL Retention time: 8.78 min	[21]
19.	Zidovudine, Lamivudine Nevirapine	Detection wavelength: 265 nm Mobile phase: 20 mM sodium phosphate buffer acetonitrile (86:14, v/v) Column: octysilane Flow rate: 1.0 ml/ min Linearity range: 57.6–2880 ng/ml for Zidovudine, 59.0–17 650 ng/ml for Lamivudine and 53.2–13 300 ng/ml for nevirapine Retention time: Zidovudine 3.1 min Lamivudine 6.1 min nevirapine 15.0 min	[22]
20.	lamivudine and zidovudine	Detection wavelength: Mobile phase: methanol: water: acetonitrile (70:20:10 (v/v/v)). Column: C 18 reversed-phase column Flow rate: 0.9 ml/min Linearity range: 0.025–50 µg/mL for lamivudine and 0.15–50 µg/mL for zidovudine. Retention time: 2.06 min for lamivudine, 3.36 min for zidovudine	[23]
21.	lamivudine and stavudine	Detection wavelength: 270 nm Mobile phase: methanol: water (20:80) Column: C18 Symmetry® (4.6 mm i.d., 250 mm length, 5m Flow rate: 0.6 ml/min Linearity range: 2–14g/ml of stavudine and 2–20 g/ml for lamivudine a Retention time: 8 min for lamivudine and 10 min for stavudine	[24]
22.	lamivudine	Detection wavelength: Mobile phase: phosphate buffer (0.05 M) containing triethylamine (1 mL/L, v/v; pH 3.5) and methanol (91:9v/v) Column: (150 mm × 6 mm i.d.) which was packed with 5m particles of ODS packing material. Flow rate: 2.2 mL/mi Linearity range: 5–2500 ng/mL Retention time: 3.1 min	[25]
23.	Lamivudine And Zidovudine	Detection wavelength: 271 nm Mobile phase: Methanol: Phosphate buffer mixed in the ratio of 55:45 % v/ v	[26]

		Column: XTerra C18 (150 mm x 4.6 mm i.d., 5 µm particle size) Flow rate: 0.5ml/min Linearity range: 10-50 µg Retention time: Lamivudine 3.556 Zidovudine 5.364	
24.	Lamivudine, Tenofovir, and Dolutegravir	Detection wavelength: 260 nm. Mobile phase: water and methanol 30:70 used Column: C18 column (250 ×4.6 mm, 5 micron) Flow rate: 1 mL/min, Linearity range: Lamivudine, Tenofovir, and Dolutegravir was found to be 27 e162 mg/mL, 27e162 mg/mL and 4.5e28 mg/mL Retention time: Lamivudine, Tenofovir, and Dolutegravir were found to be 2.8, 5.2 and 11.5 min	[27]
25.	lamivudine, stavudine and nevirapine	Detection wavelength: 270 nm Mobile phase: mobile phase (A) comprising of 80% of 10 mM acetate buffer adjusted to pH 3.5 with glacial acetic acid and 20% methanol and mobile phase (B) comprising of 50% acetonitrile with 50% isopropyl alcohol Column:C-18 column (5 µm, 250 mm × 4.6 mm i.d.) Flow rate: 0.6 ml min Linearity range: 5–100 µg ml Retention time: lamivudine, stavudine and nevirapine were 5.9, 8.8 and 14.2 min	[28]
26.	Lamivudine and Stavudine	Detection wavelength: 266nm Mobile phase: methanol and water (80:20 v/v) Column: C-18 Symmetry Flow rate: 1.5 ml/min Retention time: Lamivudine and Stavudine was 4.288and 7.488.min	[39]
27.	Lamivudine and Stavudine	Detection wavelength: 254 nm. Mobile phase: methanol, acetonitrile and 0.05 M phosphate buffer at a ratio of 60:20:20 v/v/v Column: C 18column grace smart RP18 (250×4.6 mm, 5 µm) Flow rate: 1.0 mL/min Linearity range: 10-602 2 µg/mL (r =0.9992) for lamivudine 10-60 µg/mL (r =0.999) for stavudine Retention time: Lam2.50 min and Stavudine 4.25 min	[30]
28.	lamivudine	Detection wavelength: 278 nm Mobile phase: 50 mM sodium dihydrogen phosphate–triethylamine (96:4, v/v), Column: Chromolith RP-18e (100 mm × 4.6 mm) Flow rate: 1.5 ml/min Linearity range: 40–2560 ng/ml Retention time: 2.7 min	[31]
29.	Abacavir, lamivudine, dolutegravir	Detection wavelength: 257 nm Mobile phase: pH 3.0 Phosphate buffer: Acetonitrile: Methanol (50:20:30 %v/v) Column: Inertsil ODS 250×4.6 mm Flow rate: 1.0ml/min Linearity range: 15 -90 µg/ml for Lamivudine, 30-180 µg/ml for Abacavir and 2.5-15 µg/ml for Dolutegravir. Retention time: Lamivudine, Abacavir and Dolutegravir were found to be 2.169, 2.676 and 6.367	[32]

CONCLUSION

This study reviewed the reported spectroscopic approaches such as UV Spectroscopy and chromatographic techniques such as HPLC, HPTLC, and LC-MS/MS methodologies for the estimation of Lamivudine in single and mixed formulations that have been developed and validated. HPLC with UV detection was employed frequently among these methods, with the best solvents for better resolution being acetonitrile, methanol, and phosphate buffer. The highest effective flow rate for identifying

compounds was found to be 1.0ml/min. As a result, as compared to modern technology, all of these techniques were precise, and accurate, and they provided repeatability and reliability at a reasonable cost.

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