Research Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2014, Volume 2, Issue 2
ISSN : 2321–3647(online)

In-vitro Evaluation of Lamivudine Extended Release Matrix Tablets Formulated By Eudragit S-100 And Eudragit L-100

Thumma Praveen Kumar Reddy[1*], Ponnada Nutan. Deepthi[2], B. Sudheer[3], Swathi Kandukuri[1], Poreddy Praveen Reddy[1], Madatha Praveen Kumar[1]
1.Nalanda College of Pharmac ,Department of Clinical Trials, Nalgonda, India
2. Global Data Pharmaceutics, Department of Clinical Trials, Hyderabad
3. ASN Pharmacy, Tenali, India

ABSTRACT

The aim of present research work was in-vitro evaluation of lamivudine extended release matrix tablets formulated by Eudragit S-100 and Eudragit L-100. FTIR studies shows that no chemical interactions were found. Physical mixture was evaluated for bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose before being punched as tablets. Various formulations of extended release matrix tablets of Lamivudine were prepared by different ratios of Eudragit S-100 and Eudragit L-100 by direct compression method with the rato of 16.66, 25.3 and 33. 3 % weight of both eudragit S-100 and eudragit L-100 were according to the total weight of tablet such formulations F1 to F6 and F7 to F9 both the polymers were taken as a combination F7 contains 8.33 % of eudragit s-100 and 8.33 % of eudragit L-100 similarly F8 and F9 also.. The tablets were evaluated for physical characterization. From *in-vitro* dissolution studies all the formulations were analyzed and for the optimized formulation (F6) drug release was found to be 98% in 24hr with first order kinetics. The *n* values for the optimized F6 formulation was 0.620 which follows case II non-Fickian (anomalous) release ($0.5 \leq n \leq 0.89$). In the non-Fickian (anomalous) case II release, the rate of drug release is due to the combined effect of drug diffusion and polymer relaxation. Super Case II release generally refers to the polymer relaxation.

Keywords: Lamivudine, Extended release tablet, Eudragit S-100 and Eudragit L-100

*Corresponding Author Email: thummapraveen.mph@gmail.com
Received 05 February 2014, Accepted 14 February 2014

Please cite this article in press as: Reddy PT *et al.*, In-vitro Evaluation of Lamivudine Extended Release Matrix Tablets Formulated By Eudragit S-100 And Eudragit L-100. American Journal of Pharmacy & Health Research 2014.

INTRODUCTION

Lamivudine is (-)- 4- amino-1-[(2R, 5S)-2-(hydroxylmethyl0, 3-oxidation-5-yl} pyrimidine-2(1-H)-one. Lamivudine is a potent nucleoside analog reverse transcriptase inhibitor (NRTI) and it is the (-) enantiomer of a dideoxy analogue of cytidine. It is a potent antiviral agent used in the treatment of AIDS administered in dose of 150 mg twice a day. Lamivudine is rapidly absorbed with a bioavailability of over 80% following oral ingestion. It is bound to plasma proteins less than 36%. It can inhibit both types (1 and 2) of HIV reverse transcriptase and also the reverse transcriptase of hepatitis. Conventional oral formulations of Lamivudine are administered multiple times a day because of its moderate half-life of 5 to 7 hours[1, 2and3]. Treatment of AIDS using conventional formulations of Lamivudine is found to have many drawbacks, such as adverse side effects resulting from accumulation of drug in multi dose therapy, poor patient compliance and high cost. Controlled release formulations of Lamuvidine can overcome some of these problems. Hence our aim was to design oral controlled release matrix tablets of Lamivudine using different proportion of Eudragit S-100[4] and Eudragit L-100[4] as the retardant polymer.

MATERIALS AND METHOD

Lamivudine is the gift sample obtained from Emcure Pvt Ltd, Eudragit L- 100 obtained from Colorcon Limited, India , Tabletose PH 101 obtained from Cornilieus Pharmaceutical Pvt Ltd India and all other excipients such as l, pvp k-30, talc and magnesium stearate were obtained from S.D fine chemicals Ltd Mumbai.

Method of preparation of matrix tablets:

Matrix tablets containing lamivudine were prepared by direct compression method using varying ratios of different grades of polymers. Eudragit S-100 and Eudragit L-100 by direct compression method with the ratio of 16.66, 25.3 and 33. 3 % weight of both eudragit S-100 and eudragit L-100 were according to the total weight of tablet such formulations F1 to F6 and F7 to F9 both the polymers were taken as a combination in the ratio of 1:1 i.e F7 contains 8.33 % of eudragit s-100 and 8.33 % of eudragit L-100 similarly F8 and F9 also. The composition of Lamivudine matrix tablets were tabulated in table 1.

All the ingredients were weighed accurately & mixing was done by spatulation & tumbling in glass mortar and pestle. Lamivudine was first mixed with the polymer and directly compressible Tabletose pH 101 for 10 min to obtain uniform mixture. Then the mixture is passed through 60# sieve. Finally the mixture is blended with talc and magnesium stearate, and the obtained granules

were evaluated for pre compression parameters were evaluated such as bulk density, angle of repose, Hausner ratio the results were tabulated in table no 2 and Flat 300 mg tablets were compressed using 12.5 mm flat punches in Cadmach Press - I tablet compression machine. These compressed tablets were evaluated for hardness, friability, drug content, weight variation and dissolution and the results were shown in table 3.

Table: 1 Composition of Lamivudine Matrix tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lamivudine	150	150	150	150	150	150	150	150	150
Eudragit S 100	-	-	-	50	75	100	25	36.2	50
Eudragit L 100	50	75	100	-	-	-	25	36.2	50
Tabletose PH 101	90	65	40	90	65	40	90	65	40
MG Stearate	6	6	6	6	6	6	6	6	6
Talc	4	4	4	4	4	4	4	4	4
Total WT	300	300	300	300	300	300	300	300	300

Units for all the ingredients were milligrams

RESULTS AND DISCUSSION:

To determine the any possible chemical interaction FTIR study was carried out and figure1 shows compatibility spectra's of Lamivudine, Lamivudine +eudragit s-100 and Lamivudine + Eudragit L-100. In the lamivudine spectrum two peaks at1286.52cm,1559.52cm-1-1 for symmetric and asymmetric–C-C- stretching,1651.1cm-1forcarbonylgroup,3326.8cm for–NH stretch,3194.12-12cm –OH stretch, 1452.4 cm for aromatic C=Cstretchare-1-1seen. Other important peaks are 918.12cm and 850.65cm.$^{-1}$. Similarly the same peaks were observed in Lamivudine containing eudragit s-100 and Lamivudine containing eudragit L-100 this indicates that in three spectrums the stable nature of lamivudine in the solid admixtures of the drug with various excipients[5, 6] can be observed.

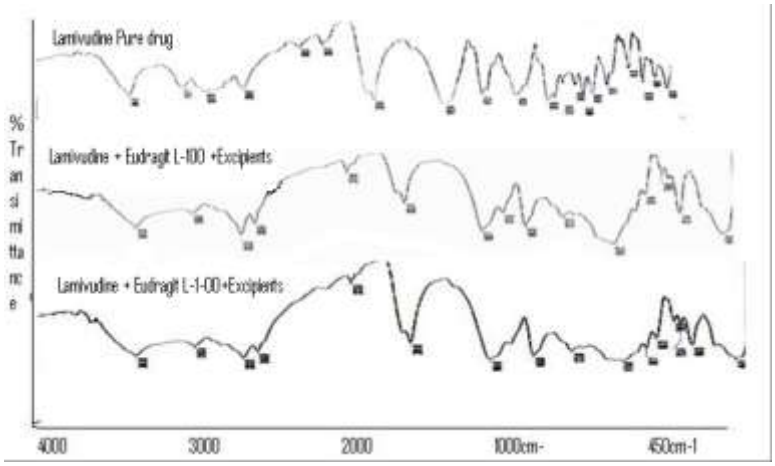

Figure 1: FTIR spectra's of Lamivudine, Lamivudine+EudragitS-100 and Eudragit L-100

The physicochemical characteristics of the tablets were summarized in the table 2 and 3. All the tablet formulations showed acceptable physicochemical properties of both pre compression parameters and post compression parameters such as angle of repose(< 30), bulk density(<0.41), tapped density(<0.5), compressibility index(<17) and finally the Hausner's ratio(<1.15) indicates that all the parameters were within limit and complied with the pharmacopoeial specifications (IP) such as granules having good flow property, good compressibility where as post compressional parameters such as hardness, friability, weight variation, and drug content[7,8].

Hardness of the tablets were observed in the range of 5.8 to 6.8 Kg/Cm^2 and friability was observed less than 1% indicates that the compressed tablets were having good mechanical strength and having good mechanical resistance.

Table .2 Evaluation results of pre-compressive parameters.

Formulation Code	Bulk density(g/ml)	Tapped density(g/ml)	Carr`s index(%)	Hausner`s ratio	Angle of repose
F1	0.34	0.40	14.16	1.14	25.32
F2	0.36	0.42	12.53	1.12	28.71
F3	0.34	0.46	13.25	1.13	25.24
F4	0.36	0.39	16.50	1.12	27.07
F5	0.41	0.44	11.42	1.1.5	29.41
F6	0.39	0.40	16.72	1.10	27.64
F7	0.34	0.49	12.53	1.15	28.71
F8	0.36	0.45	14.16	1.12	25.32
F9	0.36	0.42	13.25	1.14	27.07

Table 3 Evaluation Results of Pre-compression Evaluation parameters

Formulation code	Thickness (mm)	Weight variation(mg)	Hardness test (kp)	Friability test (%)	Content uniformity
F1	3.75±0.01	300.2±2.42	6.22±0.27	0.29	98.55
F2	3.83±0.01	298.2±2.28	6.20±0.22	0.31	97.88
F3	3.75±0.01	300.2±2.22	6.00±0.25	0.33	98.39
F4	3.92±0.02	297.2±2.48	5.98±0.25	0.33	99.89
F5	3.78±0.01	300.6±2.10	5.88±0.33	0.32	99.10
F6	3.78±0.01	302.2±2.10	6.30±0.22	0.33	99.89
F7	3.75±0.02	300.2±2.22	6.5±0.55	0.29	97.64
F8	3.76±0.02	300.6±2.40	6.8±0.33	0.31	99.20
F9	3.82±0.01	300.2±1.1	6.6±0.22	0.30	99.40

The weight of the tablets were ranged from 295 to 310 mg indicates that all tablets were with in limits. The percentage of drug content was found to be in the range of 98.4%-100.9%, the results were observed in table 3.

For in-vitro release of Lamivudine from matrix tablet, Electro lab Dissolution apparatus was used at 50 rpm in 900 ml dissolution medium at 37^0C. Buffer solution of pH 6.8 for 24 h was employed as the dissolution media. Samples were withdrawn at appropriate time intervals,

filtered and assayed for Lamivudine using aUV-1800shimadzu spectrophotometer at 271 nm respectively[9, 10].

Up to 98% of drug was released in 14 hr for the formulations of F1 to F3 which is having eudragit L 100 polymer and for the eudragit s-100 containing formulations the drug release was found to be for F4 (100% in 22 hr), F5 (99%in 22 hr) and F6 (98% in 24 hr) the drug release was found to be showing good release rate and for the F7 to F9 formulations which contain both the eudragit L-100 and eudragit S-100 the drug release rate was found to be better than the F1 to F3 formulations that is 90 % was released in 20 hrs and the results were summarized in figure 2.

In order to determine the mechanism of drug release the kinetics values were tabulated in table 2. The *n* values for all the formulations ranged from 0.530 to 0.690 indicating that the release patterns follows that case II non-Fickian (anomalous) release ($0.5 \leq n \leq 0.89$.

Table 4: Mathematical modeling of drug release kinetics

Formulation Code	Zero order	First order	Higuchi	Peppas	n
F1	0.381	0.853	0.987	0.922	0.551
F2	0.135	0.911	0.958	0.908	0.532
F3	0.041	0.888	0.986	0.933	0.531
F4	0.811	0.916	0.996	0.934	0.636
F5	0.664	0.954	0.980	0.948	0.622
F6	0.569	0.966	0.990	0.943	0.670
F7	0.725	0.910	0.968	0.996	0.676
F8	0.678	0.915	0.959	0.987	0.688
F9	0.761	0.956	0.970	0.984	0.656

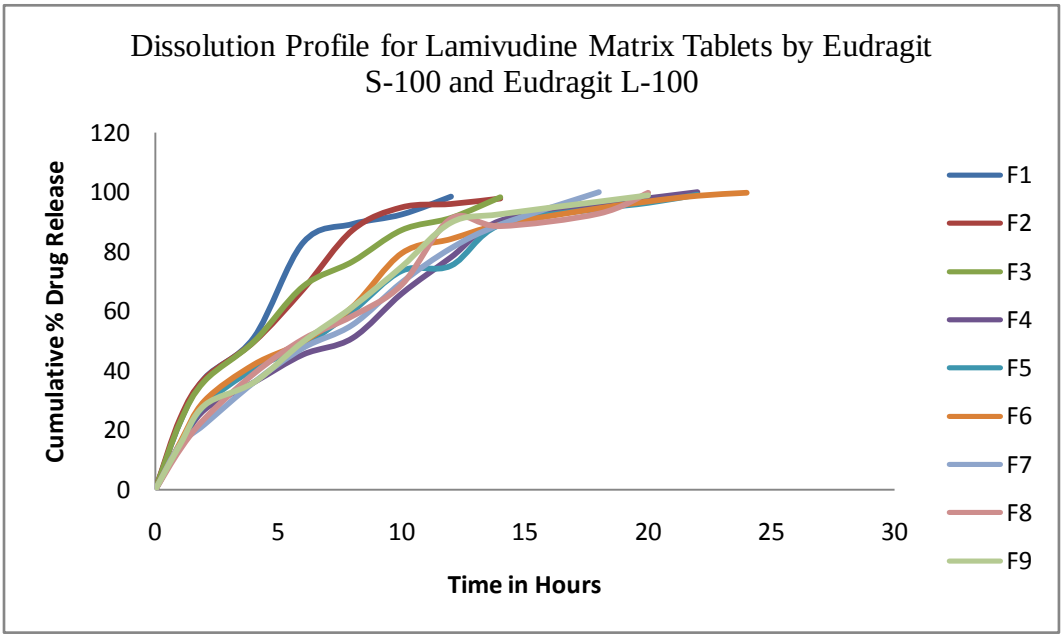

Figure 2: Comparisons of dissolution profile for formulations F1 to F9

Based on the dissolution studies, it was observed that the optimized formulation F6 follows first-order release (0.966) with higuchi model following endured super case II release mechanism (n= 0.670), which may be due to that polymer relaxation had a significant role in the drug release mechanism and the results were observed in table 4.

CONCLUSION:

From results and discussions, it can be concluded that the formulated sustained release matrix tablets of lamivudine, using widely accepted and physiologically safe polymers and other excipients was capable of exhibiting sustained release properties equivalent to that of the marketed product . Thus the optimized formulation F6 prepared using Eudragit S-100 as binding agent was found to produce extended release with a single dosage tablets and serves to be economical for patient as well as the manufacturer due to low cost of polymers but provides equal therapeutic efficiency with that of marketed product.

REFERENCES:

1. YeluriP, AshokKumar P, Someshwara Rao B, KulkarniSV, RanjitkumarP.Formulation and invitro evaluation of controlled release matrix able to flamivudine. J.G.Pharm.Tech., 2010; 2(7): 52-59.
2. JohnM.Beale, Jr, Antiviralagents, InWilson and Gisvold. Textbook of organic medicinal and pharmaceutical chemistry, John.H.Block, JohnM.Beale, Jr, elevent edition ,Lippincott Wilkins, 2004:p367-380.
3. Jr Grangeiro S, Strattmann R.R, Alburquerque M.M, Araujo A.A.S, Matos J.R. In vitro Evaluation of Dissolution Profiles and Thermal Properties of Some Commercial Formulations of Nevirapine Tablets. Acta Farm. Bonaerense.2006; 25 (1):76 -82.
4. WHO Drug information, 19(2), Proposed Inn list 93. International Nonproprietary names for Pharmaceutical Substances. WHO, Geneva; 2005: 156 – 160.d
5. AzarmiS, Farid J, Nokhodchi A, Bahari-Saravi SA, Valizadeh H, Thermal treating as a tool for sustained release of indomethacin from Eudragit RS and RL matrices, Int.J.Pharm.2002;246:171-77.
6. Punna Rao RaviL, Ganga S, Saha RN, Design and study of Lamivudine Oral controlled release tablets, AAPS Pharm SciTech.2007;8(4):167–75
7. Subramanyam CVS, Thimmasetty J. Laboratory manual of physical pharmaceutics. Delhi: Vallabh Prakashan; 2005.

8. The United State of Pharmacopoeia and National Formulary-19: The official compendia of standards, United State Pharmacopeia convention, Inc. US, Asian edn. (2005) 1763.
9. ArkhelNA, BhumarkarL, RamtekeS, Formulation development and evaluation of sustained release matrix tablet of lamivudine using tamarind seed polysaccharide, DerPharmaciaLettre,2011;3(3):250-58.4.
10. Abbaspour MR, Sadeghi F, Garekani HA, Thermal treating as a tool to produce plastic pellets based on Eudragit RS PO and RL PO aimed for tableting, E. J. Pharm. Bio. 2007; 67:260-267.5.