Available online at www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Pharmacia Sinica, 2010, 1 (2): 61-76

Der Pharmacia Sinica

ISSN: 0976-8688
CODEN (USA): PSHIBD

Design and Study of Lamivudine Oral Sustained Release Tablets

Abdul S.Althaf [*1], Seshadri.T [1], Sivakranth .M [1],Umal S. Khair[1]

[1]*Sri Venkateswara University, Division of Pharmacy, Department of Biochemistry, Tirupati, Andhra Pradesh, India.*

ABSTRACT

The objective of this study was to design oral sustained release matrix tablets of lamivudine using hydroxyl propyl methyl cellulose and ethyl cellulose as retardant polymers and to study the effect of various mixtures of drug and polymers on the release profile of the formulation. In vitro release studies were performed using ELECTROLAB TDT 08L 8 basket dissolution apparatus in 900(ml) of pH 6.8 phosphate buffer at 100rpm. The release kinetics were analyzed using zero-order, Higuchi's equation and Korsmeyer-Peppas equation. The in-vitro kinetic data is subjected to log time-log drug release transformation plot (Korsmeyer-Peppas plot),all the slope values ranges from 1.020803 to 1.116491(n>1) revealed the fact that the drug release follows super case II transport diffusion , possibly owing to chain distanglement and swelling of hydrophilic polymer. The formulations were also subjected to FT-IR compatibility study by mixing the physical mixtures of lamivudine and polymers in various ratios. The obtained FT-IR spectra revealed that there is no major compatibility issues with the physical mixtures. The in vitro studies revealed that the formulation F7 can be taken as an ideal or optimized formulation of sustained release tablets for 16 hours release as it fulfills all the requirements for sustained release tablet.

Key words: Lamivudine, HPMC, Ethyl cellulose, Direct compression, FT-IR.

INTRODUCTION

The development of sustained release (SR) dosage form has become the subject of interest to many pharmaceutical scientists in recent years[1-4]. Among numerous approaches to oral SR formulation, matrix system of dosage form proves to be potential because of its simplicity, ease of manufacturing, low cost, high level of reproducibility, stability, ease of scale up, and process validation [4,5]. Development of dosage form depends on chemical nature of the drug/polymers,

matrix structure, swelling, diffusion, erosion, release mechanism and the in vivo environment [6].

Now-a-days, various hydrogels (matrix builders) with various degree of substitution are applied according to the characteristics of drug and its pharmacological action to control release of both hydrophilic and hydrophobic medicinal agents from matrix granules [9– 16]. Hydroxypropyl methyl cellulose (HPMC) and cellulose ether are widely used to control release of drug, usually, by two mechanisms: drug diffusion through swelling and erosion of swollen polymer [17–19].Use of single hydrophilic polymer is not justified in case of highly water-soluble drugs because it diffuses out rapidly through the water-filled pores of matrix. Hydrophobic polymers (glycerides, ethyl cellulose (EC)) are used for such drugs [20–25].

Developing oral-sustained release formulations for highly water-soluble drugs with constant rate of release has become a challenge to the pharmaceutical technologists. Fast release drug generally causes toxicity if not formulated as extended release dosage form. Among various formulation approaches, in controlling the release of water-soluble drugs, the development of sustained release coated granules has a unique advantage of lessening the chance of dose dumping which is a major problem when highly water-soluble drug is formulated as matrix tablets. Most of the researchers have worked on matrix tablets and multilayered matrix tablets. In the present study, a sustained release dosage form of Lamivudine has been developed that enables less frequent administering of drug [26].The objectives of this work are: (1) to evaluate the physical characters of prepared sustained release tablets, (2) to elucidate the effect of polymer composition, on the release kinetics and (3) to determine the chemical compatibility of formulation containing various ratios of polymer and drug. Lamivudine (β-L-2',3'-dideoxy-3'-thiacytidine)(LAM),one of the dideoxycytidine analogue NRTIs, is the first nucleoside analogue approved to treat chronic HBV infection and AIDS. Conventional oral formulations of LAM are administered multiple times a day (150 mg twice daily) because of its moderate half-life ($t_{1/2}$ = 5-7 hours)[28,29].Treatment of AIDS using conventional formulations of LAM is found to have many drawbacks, such as adverse side effects resulting from accumulation of drug in multi-dose therapy,[30] poor patient compliance, and high cost. Sustained release once-daily formulations of LAM can overcome some of these problems.

Aim of the work

Lamivudine is approved for clinical use and used widely in treatment of Hepatitis B and AIDS either alone or in combination with another antiviral drugs because of its water solubility and shorter half -life (5-7 hours) drug requires frequent dosing by oral route, of various recent techniques for controlling drug release, matrix system offer various advantages of ease of formulation better control on release profile of drug and better patient compliance.

The pronounced fluctuation resulting from the conventional drug administration are likely to yield period of therapeutic effects when the concentration falls below the minimum therapeutic drug concentration and can be controlled within the narrow therapeutic range by use of sustained release system. Which will minimize the severity of side effects. Hydrophilic and hydrophobic polymer matrix system are widely used for designing oral controlled drug delivery dosage form because of their flexibility to provide a desirable drug release profile, cost effectiveness and broad regulatory acceptance.

Large scale production needs more simplicity in the formulation with economic and cheapest dosage form. The matrix tablets formulation by direct compression method is most acceptable in large scale production.

MATERIALS AND METHODS

The following materials were used in the present study. Lamivudine USP was a gift sample from Hetero Drugs Ltd., Medak, Andhra Pradesh ,India. Lactose monohydrate BP, Cepam Specialties Ltd., Punjab. Hydroxypropyl Methylcellulose E-15 USPNF, Huzhou Zhanwang Pharmaceuticals Co. Ltd., China. Ethyl cellulose BP, Zhongbao Chemicals, China. Magnesium Stearate BP, Arian Enterprises, Delhi. Colloidal Silicon dioxide (Aerosil-200) USPNF, Nippon Aerosol Co. Ltd., Tokyo, Japan. Acetone BP, V.S. Interchem P. Ltd., Jhajjar. Sodium hydroxide BP, Clarian Sauti Chem, China. Glacial acetic acid, BP, Shree Scientific System, New Delhi. Potassium dihydrogen Phosphate BP, Shree Scientific System, New Delhi. Demineralized water IP, Ajanta Pharma Ltd. Mumbai (Maharastra). Methanol BP, V.S. Interchem P. Ltd., New Delhi. Ammonium acetate BP, Shree Scientific System, New Delhi.

Experimental

4.1 formulation development of lamivudine sustained-release matrix tablets dose calculation (theoretical release profile)

Total dose of Lamivudine for once daily sustained release formulation was calculated by the following equation using available pharmacokinetic data.

$$\mathbf{D_t = Dose\ (1 + 0.639 \times t / t_{½})}$$

Where D_t is total dose of drug; Dose of immediate release part (100);

't' is time in hours during which the sustained release is desired;

$t_{½}$ is half- life of the drug (5-7 hours)

$D_t = 30\ (1 + 0.639 \times 24 / 6)$

$= 106.68$ (mg)

Hence, the formulation should release 30 (mg) in first couple of hour like conventional tablets, and remaining amount completely in 24 hours. The polymers , excipients and lamivudine were mixed accordingly as shown in Table 1. The individual trail formulations were coded from F1-F8.

4.2 formulations (direct compression method):

All ingredients were collected and weighed accurately. Sift Lamivudine USP with lactose and polymers through sieve no. 60# and then rinse with remaining excipients. Sift colloidal silicon dioxide (Aerosil-200) and magnesium stearate separately, through sieve no. 60#. Pre-blend all ingredients (except lubricant- magnesium stearate) in blender for 15 minutes. Add magnesium stearate and then again blend for 5-6 minutes. Lubricated powder was compressed by using 9 station single rotary machine having 9.5 (mm) diameter and circular standard concave shaped punch, with pressure of 7-8 tons. Compressed tablets were examined as per official standards and unofficial tests (discussed below). Tablets were packaged in well closed light resistance and moisture proof containers.

Table 1: Quantity of raw materials per tablet (in mg)

S.NO.	INGREDIENT	F1	F2	F3	F4	F5	F6	F7 Best	F8
1.	Lamivudine USP	100	100	100	100	100	100	100	100
2.	Lactose monohydrate	132	132	132	132	132	132	132	132
3.	Hydroxypropyl Methylcellulose E-15	30	35	40	50	60	70	80	90
4.	Ethylcellulose	130	125	120	110	100	90	80	70
5.	Colloidal Silicon Dioxide (Aerosil®)	4	4	4	4	4	4	4	4
6.	Magnesium Stearate	4	4	4	4	4	4	4	4

*Total weight of per unit tablet is 400 (mg).

4.3 Evaluation:

A) Identification of drug and compatibility study of drug-excipients by FT-IR(fourier transform) spectroscopy

The identification of drug and drug-excipients compatibility was performed using FT-IR spectroscopy. The compatibility of the drug and formulation is an important pre-requisite for formulation. Therefore, in preformulation study, compatibility evaluation was carried out using infra-red spectra. Infrared spectrum of formulated powder and drug in various ratios were obtained between 4000cm^{-1} - 400 cm^{-1}. Infra-red spectrum of pure drug was also obtained individually.

Characterization of drug, polymer and their physical mixture: IR has been the method of choice to prove the nature and extent of interaction in polymer blends. The premise of using an IR to study polymer blends is that the mixing of the two compounds at molecular level will cause changes in oscillating dipole of the molecule. This will manifest itself as changes in frequency and bandwidth of interaction group, in the spectrum. if the drug and polymer interact then functional groups in FTIR spectra will show band shift and broadening compared to the spectra of pure drug.

Method: The FT-IR spectrum of pure drug and Physical mixture of pure drug and polymers were analyzed to check the compatibility between the pure drug and polymers using Shimadzu Fourier Transform Spectrophotometer by KBr disc method. The procedure consisted of dispersing a sample (drug alone or mixture of drug and polymers) in KBr and compressing into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained.

B) Assay:
The amount of drug was determined using High Performance Liquid Chromatography.

Test solution: Dissolve 25 mg of the substance under examination in 100 ml of mobile phase.
Reference solution: A 0.025 per cent w/v solution of *lamivudine RS* in mobile phase.

Chromatographic system:

- A stainless column 15 cm × 4.6 mm, packed with octa-decylsilane chemically bonded to porous silica (5 µm),
- Temperature column 35°C,
- Mobile phase: a degassed mixture of 5 volumes of methanol and 95 volumes of buffer prepared by dissolving 1.9 (g) of ammonium acetate in 1000(ml) of water and adjusting the pH to 3.8 ± 0.2 with glacial acetic acid,
- Flow rate -1 (ml) per minute,
- Spectrophotometer set at 270 (nm),
- A 20 (µl) loop injector.

Inject the reference solution. The test is not valid unless the column efficiency determined from the lamivudine peak is not less than 5000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 percent. Inject alternatively the test solution and the reference solution. Calculated the content of $C_8H_{11}N_3O_3S$. The percent labeled amount was calculated by,

$$\% \text{ Labeled amount} = \frac{A_t}{A_s} \times \frac{W_s}{100} \times \frac{5}{25} \times \frac{100}{W_t} \times \frac{100\ P}{4} \times \frac{T}{100\ L} \times 100$$

Where A_t is mean area of standard, A_s is mean area of Sample, P is % purity of standard, T is theoretical average weight, and L is label claim.

C) in-vitro dissolution study

In-vitro dissolution study was performed using USP basket type apparatus(ELECTROLAB TDT 08L - 8 basket dissolution apparatus). Place 900 (ml) of pH 6.8 phosphate buffer in the vessel of apparatus and assembled, equilibrate the dissolution medium to 37 ±0.5 °C. The speed was maintained at 100rpm. Place 1 tablet in basket and immediately operate the apparatus at 100 rpm. Then withdraw 5 (ml) samples at 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, and 16 hours, from midway between the surface of dissolution medium and the top of the rotating basket, not less than 1 (cm) from the vessel wall and replace fresh buffer solution. After appropriate dilution the samples were analyzed. Cumulative percentage of the drug released was calculated, and the mean of 6 tablets from formulations was used in data analysis.

D) Preparation of standard curve

a) Preparation of 6.8 pH phosphate buffer:

Placed 50 (ml) of the monobasic potassium phosphate solution in a 200 (ml) volumetric flask, added 22.4 (ml) of 0.2 M sodium hydroxide, then added water to volume.

b) Preparation of standard curve of Lamivudine in 6.8 pH phosphate buffer:

Accurately weighed 100 (mg) of Lamivudine was dissolved in 100 (ml) of phosphate buffer (6.8 pH) which gives the concentration of 1000(µg/ml). 1(ml) of this solution was taken and made up to 100(ml) with buffer solution which contains the concentration of 10 (µg/ml), 1 to 10(ml) were taken from this solution and made up to 10(ml) to get the concentration ranges of 1 to 10(µg/ml). The absorbance of the resulting solutions was then measured at 265(nm) using U.V. spectrophotometer, against respective parent solvent as a blank. The standard curve was obtained by plotting absorbance vs. concentration in (mcg/ml) and data was subjected to weighed linear regression analysis in Microsoft excel.

E) kinetic modeling

The *in vitro* and *in vivo* data were analyzed by the zero order kinetics equation as well as Higuchi's and Korsmeyer-Peppa's equation to understand the release profile and release mechanism. When a graph of the cumulative percentage of the drug released from the matrix against time is plotted, zero order release is linear in such a plot, indicating that the release rate is independent of concentration. The rate of release of the drug can be described mathematically as follows:

$$\textbf{Rate of release} = (dC_s/dt) = k$$

Where C_s = concentration of the drug present in the matrix, k = rate constant and t = time. Since C_s is a constant, and x = amount of drug released described as dx/dt = k integration of the equation yields x = kt + constant.

A plot of x versus t results is a straight line with the slope = k. The value of k indicates the amount of the drug released per unit time and the intercept of the line at time zero is equal to the constant in the equation. The curves plotted may have different slopes, and hence it becomes difficult to exactly pin-point which curve follows perfect zero order release kinetics. Therefore, to confirm the kinetics of drug release, data were also analyzed using Korsemeyer's equation. Korsemeyer used a simple empirical equation to describe general solute release behavior from controlled release polymer matrices:

$$M_t/M_o = a.t^n$$

Where M_t/M_o = fraction of drug released, a = kinetic constant, t = release time and n = the diffusional exponent for drug release.

The slope of the linear curve gives the 'n' value. Peppas stated that the above equation could adequately describe the release of solutes from slabs, spheres, cylinders and discs, regardless of the release mechanism. The value of 'n' gives an indication of the release mechanism. When n = 1, the release rate is independent of time (zero order) (case II transport); n = 0.5 for Fickian diffusion; and when $0.5 < n < 1$, diffusion and non-Fickian transport are implicated. Lastly, when $n > 1.0$ super case II transport is apparent. 'n' is the slope value of log M_t/ M_o versus log time curve.

The different models, viz.-zero-order, Higuchi's equation and Korsmeyer-Peppa's equation were used to study the *in vitro* release of the sustained release matrix tablets. The zero order plots of formulations were found to be fairly linear as indicated by their high regression values. The zero

order curves alone are not sufficient to predict zero order since each curve, albeit straight, has a different slope. Hence to confirm the exact mechanism of drug release from the tablets, the data was computed and graphed according to Higuchi's equation and Korsemeyer's-Peppa's equation.

RESULT AND DISCUSSION

1) identification of drug and compatibility study of drug-excipient by Ft-Ir spectroscopy

The procured sample of Lamivudine was tested for its identification. The FT-IR spectra of the physical mixture exhibited absorption peaks similar to those of the pure drug sample. The results of FT-IR analysis indicated that there was no chemical interaction between the drug and the excipients in the Matrix tablets formulation.

The characteristics peak of the carbonyl group(C=O stretching) present in the cystedine nucleus at 1650.95 cm^{-1}, a band peak at 1456.16 cm^{-1} owing C=C stretching(aromatic) confirm the presence of lamivudine . Peaks at 1286.43 and 1160.07 cm^{-1} owing to asymmetrical and symmetrical stretching of C-O-C system present in the oxathiolane ring conforms the stable nature of the drug in the polymer mixture

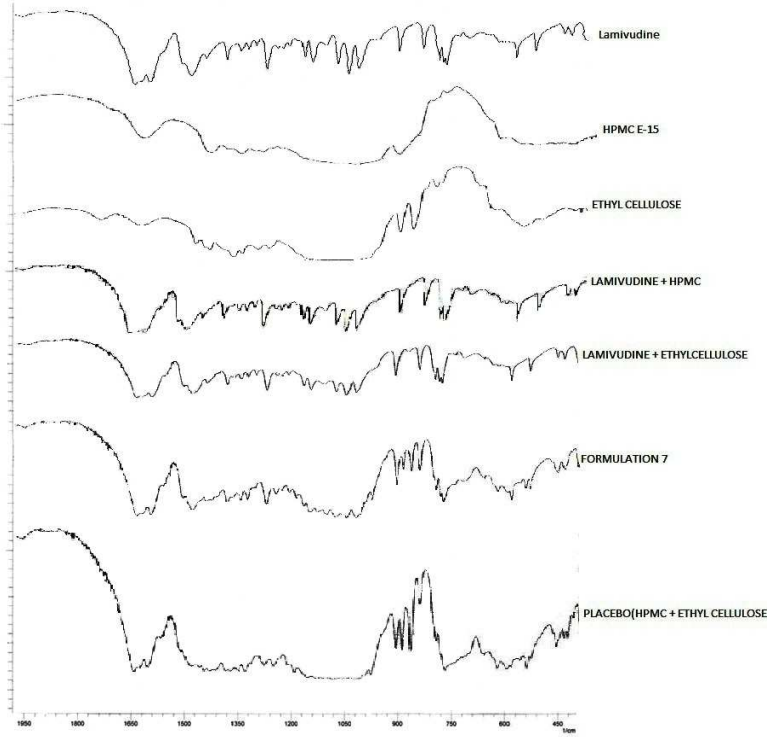


Figure 1: Comparative Fourier transform infrared spectroscopy of Lamivudine, HPMC, Ethyl Cellulose , Mixture of Lamivudine+ HPMC, Mixture of Lamivudine + Ethyl Cellulose, Formulation F-7 and Placebo(Mixture of HPMC+ Ethyl Cellulose).

2) Evaluation of tablets:

A. Tablet Description:

The tablets descriptions found to be White, round flat, with smooth surface in both side, uncoated tablets.

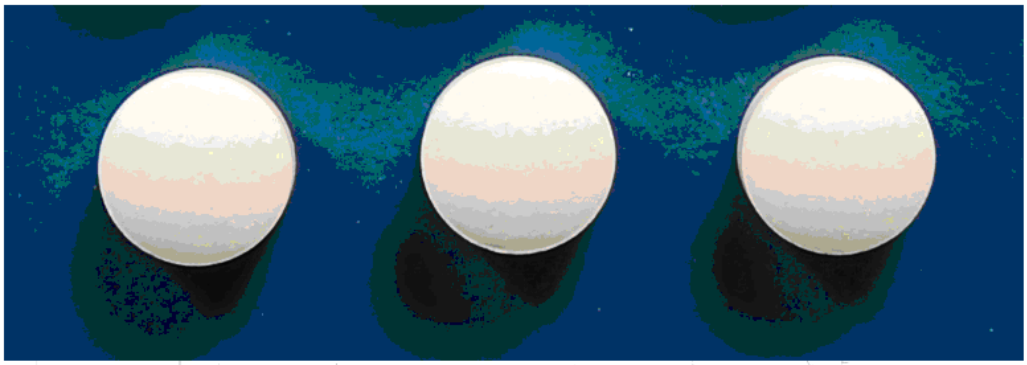


Figure 2: Photographs of Tablets

B. Tablet Diameter and Thickness:

The tablet dimension includes diameter and thickness of tablets. The diameter was found to be 9.51 to 9.53 mm.

Thickness of all formulations was found to be between 4.917 to 4.943. No significant difference was observed in the thickness of individual tablet from the average value.

C. Weight variation:

No significant difference was observed in the weight of individual tablets form the average weight. Tablet weights of all bathes were found with in recommended USP limits, between 400 ± 8 mg.

Table 2: Observations of all tablets evaluation parameters

PARAMETERS	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8
Uniformity of weight (mg)*	400 ± 6	400 ± 8	400 ± 7	400 ± 5	400 ± 7	400 ± 6	400 ± 6	400 ± 5
Thickness (mm)*	4.9 ± 0.26	4.9 ± 0.17	4.9 ± 0.33	4.9 ± 0.20	4.9 ± 0.43	4.9 ± 0.39	4.9 ± 0.26	4.9 ± 0.30
Diameter (mm)*	9.5 ± 0.02	9.5 ± 0.03	9.5 ± 0.02	9.5 ± 0.01	9.5 ± 0.03	9.5 ± 0.01	9.5 ± 0.01	9.5 ± 0.02
Friability (%)*	0.06	0.11	0.19	0.14	0.16	0.11	0.09	0.07
Tablet Hardness (K_p)*	11 ± 0.08	11 ± 0.05	11 ± 0.06	11 ± 0.09	11 ± 0.10	11 ± 0.14	11 ± 0.74	12 ± 0.09
Assay (%)	97.88	98.63	98.12	97.34	97.68	97.24	98.76	98.44

*Average of three times measure

D. Mechanical strength:

Crushing strength *(Hardness)* of tablets of all batches are in between 11 ± 0.05 to 12 ± 0.09 (K_p) which is acceptable limits, which shows in the literature.

Abrasion *(Friability)* of all the formulation showed % friability less than 1% that indicates ability of tablets to withstand shocks, which may encountered.

E. Assay

The data of uniformity of content which was performed by HPLC, indicated that tablets of all batches had drug content within USP limits. i.e. between 97.34 to 98.76 %.

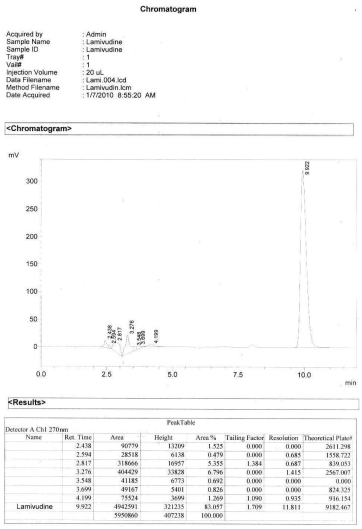
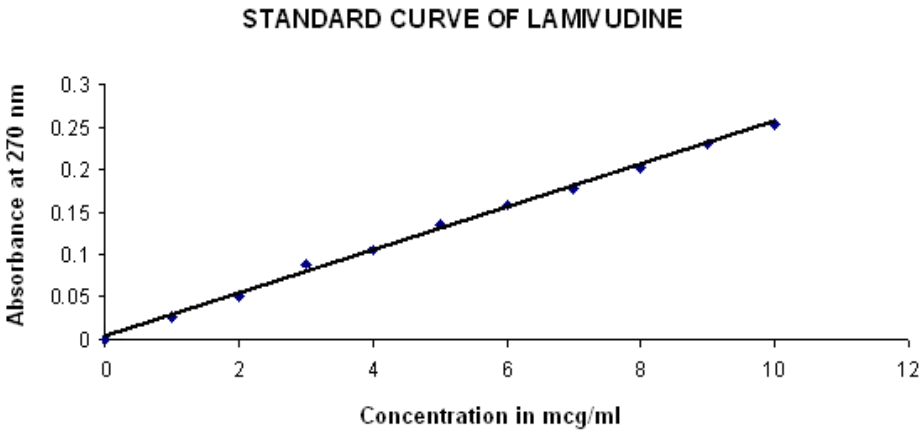


Figure 3: HPLC Graph of formulation -7.

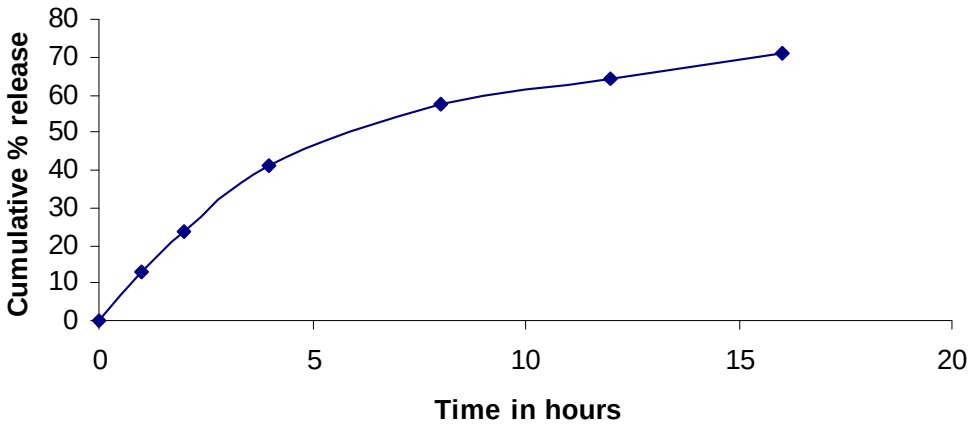
F. in vitro dissolution study

Standard Curve of Lamivudine in pH 6.8 phosphate buffer:

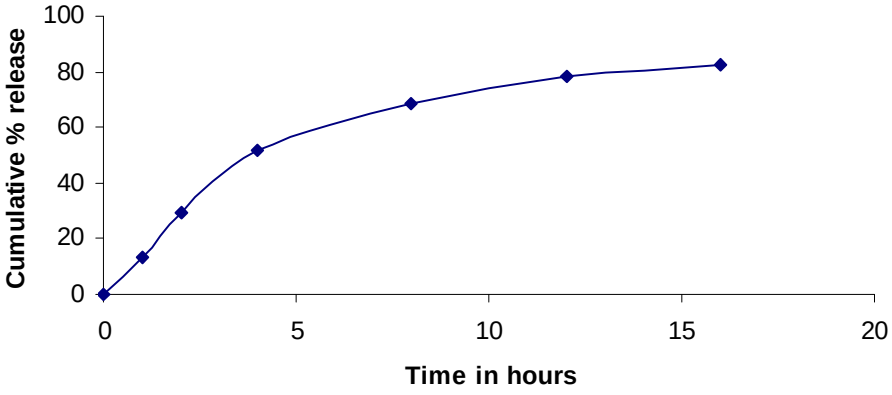
Standard calibration curve of Lamivudine were prepared in phosphate buffer of 6.8 pH. Correlation coefficient value (0.998648) indicates that there is a linear correlation between concentration and absorbance.



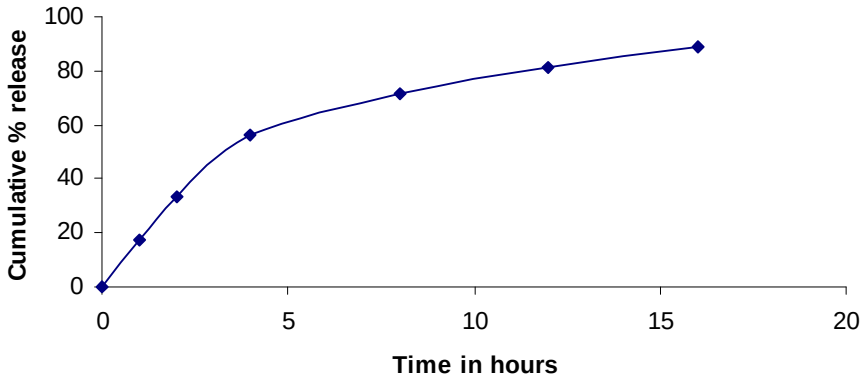
***IN VITRO* DRUG RELEASE OF F1**

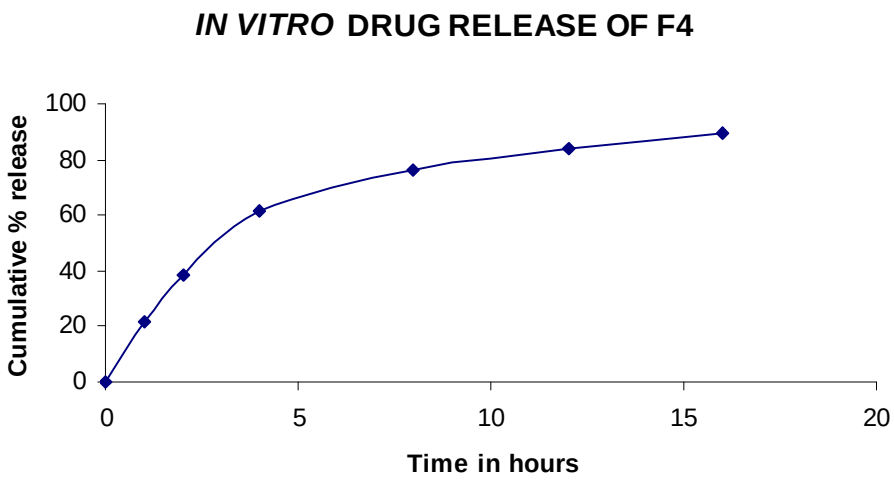


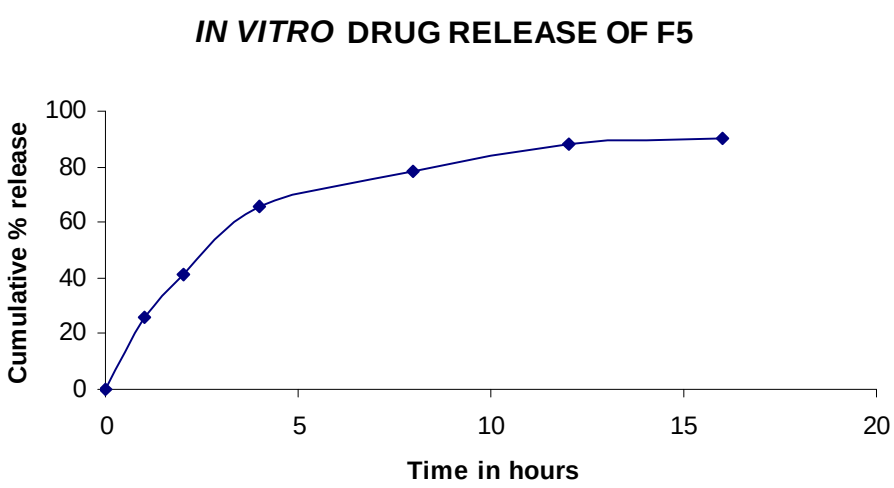
***IN VITRO* DRUG RELEASE OF F2**

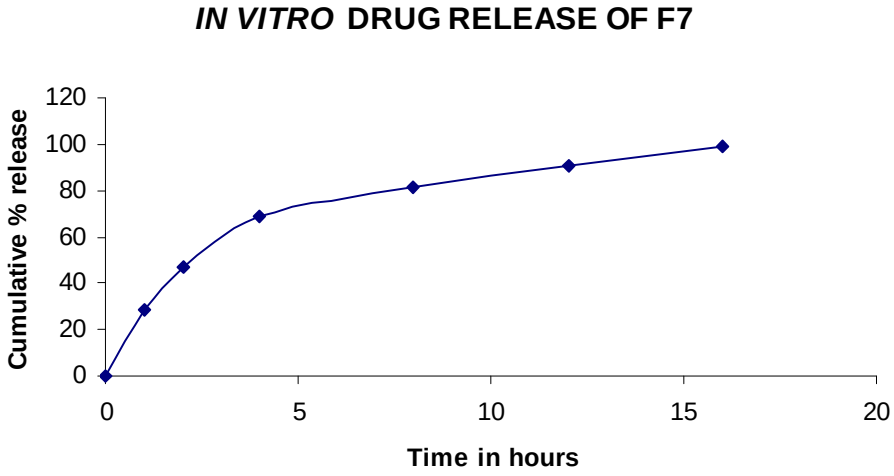


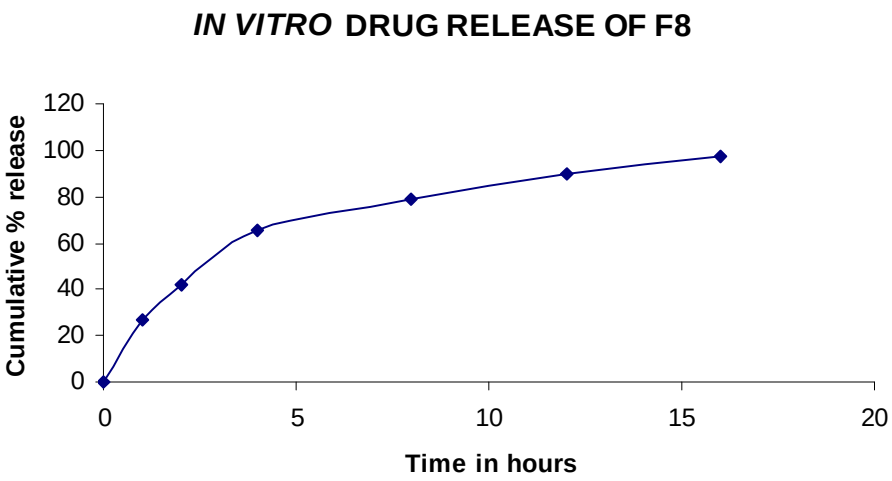
***IN VITRO* DRUG RELEASE OF F3**




IN VITRO DRUG RELEASE OF F4
Cumulative % release
100
80
60
40
20
0
0
5
10
15
20
Time in hours


IN VITRO DRUG RELEASE OF F5
Cumulative % release
100
80
60
40
20
0
0
5
10
15
20
Time in hours


IN VITRO DRUG RELEASE OF F7
Cumulative % release
120
100
80
60
40
20
0
0
5
10
15
20
Time in hours



The amount released in fixed duration is importance and was performed with precision and accuracy, the amount of drug release was largely dependent on the hydrophobic and hydrophilic nature of polymers used in the dissolution study. As the amount of ethyl cellulose was decreased and amount of HPMC was increased there is increase in release rate in the order F1 to F7, probably the reason for this was hydrophilic nature of HPMC and hydrophobic nature of ethyl cellulose. The formulation F7 was found to give best release rate with 98.901 (Cumulative % drug release).

G. Kinetic modeling:

The different models, viz.-zero-order, Higuchi's equation and Korsmeyer-Peppas equation were used to study the *in vitro* release of matrix tablets. The zero order plots of formulations were found to be fairly linear as indicated by their high regression values. Therefore, it was ascertained that the drug release from matrix tablets followed either near zero or zero order kinetics. The zero order curves alone are not sufficient to predict zero order since each curve, albeit straight, has a different slope. Hence to confirm the exact mechanism of drug release from the films, the data were computed and graphed according to Higuchi's equation and Korsemeyer's Peppa's equation. Regression values of Higuchi's plot revealed that the mechanism of drug release was diffusion. The *in-vitro* kinetic data is subjected to log time-log drug release transformation plot (Korsmeyer-Peppas plot), all the slope values ranges from 1.020803 to 1.116491(n>1) revealed the fact that the drug release follows super case II transport diffusion , possibly owing to chain distanglement and swelling of hydrophilic polymer.

Regression values of Higuchi's plot revealed that the mechanism of drug release was dissolution and diffusion. The *in-vitro* kinetic data is subjected to log time-log drug release transformation plot (Korsmeyer-Peppas plot), all the slope values ranges from 1.020803 to 1.116491

(n>1) revealed the fact that the drug release follows super case II transport diffusion, possibly owing to chain distanglement and swelling of hydrophilic and hydrophobic polymer.

***In-vitro* drug release kinetic data**

Formulation Code	Zero order		Higuchi's		Peppa's	
	Slope	Regression	Slope	Regression	Slope	Regression
F1	4.21780	0.93927	18.99421	0.99014	1.06699	0.81223
F2	4.98077	0.92686	22.59234	0.98413	1.11649	0.81076
F3	5.13193	0.92506	23.39370	0.98709	1.08484	0.78347
F4	5.04823	0.90158	23.45237	0.98045	1.04857	0.75297
F5	5.01458	0.88668	23.56630	0.97542	1.02466	0.73177
F6	5.16955	0.89104	24.24039	0.97804	1.02635	0.72778
F7	5.29398	0.89397	24.79492	0.98011	1.02080	0.72015
F8	5.35343	0.90911	24.81010	0.98625	1.03096	0.73149

Comparison of formulation-7 and marketed tablets

The formulations obtained in evaluation studies were compared with marketed product (Epivir HBV Tablets). The evaluation parameters tested and compared were physical and analytical parameters. The Physical parameter values obtained are recorded in results and discussion part.

The Analytical parameters formulation F-7 and marketed product (Epivir HBV Tablets) are given in the following tables and is constructed graphically.

The above study has shown that the contents of drug, *In-Vitro* drug release profile and physical parameters of F-7 formulations were found to be equivalent compared with that of marketed product of Lamivudine (Epivir HBV Tablets).

Table 3: content uniformity of active ingredients

Parameters	F-7*	Epivir HBV Tablets *
Contents uniformity of Drug (%)	100.05% ± 0.66	101.09% ± 0.78

***** Average of three determinations

Table 4: Physical Characteristics.

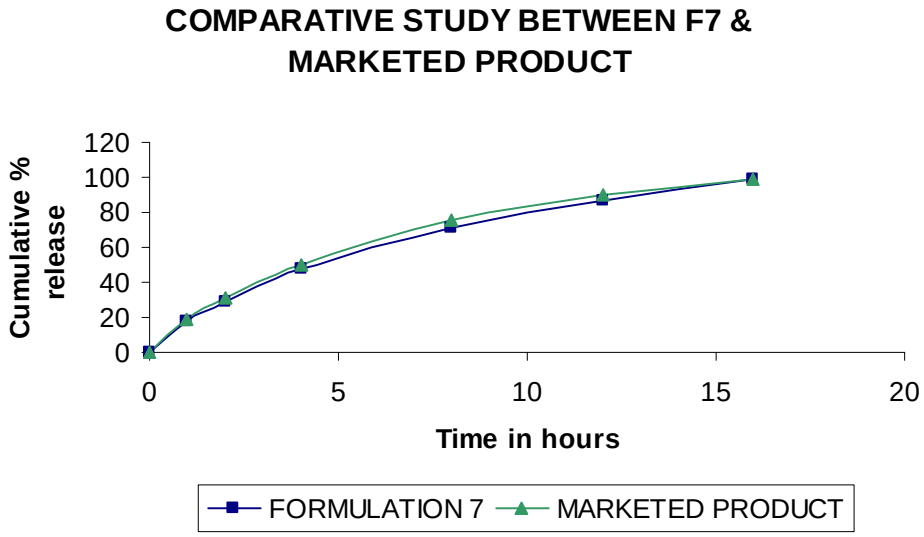
Parameters	Formulation F-7	Epivir HBV Tablets
Appearance	Circular standard concave round shaped uncoated tablets.	Capsule shaped uncoated tablets
Colour	White	Light Brown
weight ± SD%	400 mg ± 1.63%	465 mg ± 0.85
Thickness	4.90 ± 0.02 mm	4.2 ± 0.06 mm
Hardness	11 Kp ± 0.61	10 Kp ± 0.69

*Average of three determination

Table 5: percentage drug release of f7 vs marketed product (EPIVIR HBV tablets)

S.No.	Time (hrs.)	F- 7*	Epivir HBV Tablets
1	0	0.00	0.00
2	1	18.06	19.34
3	2	29.34	31.66
4	4	47.54	50.44
5	8	71.56	75.67
6	12	86.36	89.70
7	16	98.85	99.01

*Average of three determination



CONCLUSION

The study was undertaken with an aim to formulation development and evaluation of Lamivudine sustained release tablets using polymers hydroxypropylmethylcellulose and ethylcellulose. Lactose monohydrate was used as channeling agent and or as filler. FT-IR study was performed for the identification and compatibility study of drug with polymers and the characteristics peaks of various groups were found.

Tablets were prepared by direct compression method by using 9 station single rotary tablet compression machine with application of 6-7 tons pressure. After evaluation, tablets are packed in a well closed moisture proof, light resistance container, labeled, and kept at dry place. Employing direct compression technique, the cost of production is reduced as this process requires less labor and doesn't involve numerous steps like wet granulation technique. If any other granulation technique was to be employed, the drug might get degraded in the presence of water or any other solvent.

Tablets were tested for official and unofficial tests like- weight variation test, thickness, hardness, friability and *In vitro* drug release as per official procedure was performed to observe diffusion and release mechanism of drug through polymeric membrane.From the above results and discussion it is concluded that formulation of sustained release tablet of Lamivudine containing 80 mg of hydroxypropyl-methylcellulose E15 (high viscosity grade) and 80 mg of ethylcellulose i.e. formulation F7 can be taken as an ideal or optimized formulation of sustained release tablets for 16 hours release as it fulfills all the requirements for sustained release tablet.

REFERENCES

[1] A. Sandberg, B. Abrahamson, A. Svenheden, B. Olofsson, R. Bergstrand, *Pharm. Res*. **1993**;10(1):28–34.
[2] G. Ragnarsson, A. Sandberg, MO. Johansson, J. Sjogren, *Drug. Dev. Ind. Pharm.* **1987**,l3,1495.
[3] MJ. Kendall, VA. John, CP. Quarterman, PG. Welling, *Eur. J. Clin. Pharmacol*. **1980**,17(2),87.
[4] YSR. Krishnaih, RS. Karthikeyan, V. Satyanarayan, *Int. J. Pharm*. **2002**,241,353.
[5] C. Nastruzzi, R. Cortesi, E. Esposito, A. Genovesi, A. Spadoni, C. Vecchio, *AAPS. Pharm.Sci.Tech*. **2000**,1(2),14.
[6] MVS. Varma, AM. Kaushal, A. Garg, S. Garg, *Am. J. Drug. Deliv*. **2004**,2(1),43.
[7] SB. Tiwari, A. Rajaji-Siahboomi, Extended release oral drug delivery technologies: Monolithic matrix systems, vol. 437, USA, Humana Press, **2008**.
[8] J. Liu, S. Lin, L. Li, E. Liu, *Int. J. Pharm*. **2005**,298,117.
[9] R. Bettini, P. Colombo, G. Massimo, PL. Cartellani, T. Vitali, *Eur. J. Pharm. Sci*. **1994**,2,213.
[10] K. Tahara, K. Yamamoto, T. Nishihata, *J. Control. Release*. **1995**,35,59.
[11] AP. Rokhade, SA. Agnihotri, SA. Patil, NN. Mallikarjuna, PV. Kulkarni, TM. Aminabhavi, *Carbohydr. Polym.* **2006**,65,243.
[12] MH. Amaral, JMS. Lobo, DC. Ferreira, *AAPS Pharm.Sci.Tech*. **2001**,2(2),E6.
[13] ML. Vueba, LAE. Batista De Carvalho, F. Veiga, JJ. Sousa, ME. Pina, *Pharm. Dev. Technol*. **2006**,11 (2),213.

[14] LJ. Lucisano, JA. Breech, LA. Angel, RM. Franz, *Pharm. Tech*. **1989**,13,88.
[15] J. Siepmann, H. Kranz, R. Bodmeier, NA. Peppas, *Pharm. Res*. **1999**,16,1748.
[16] K. Nakamura, E. Nara, Y. Akiyama, *J. Control. Release*. **2006**,111 (3),309.
[17] TD. Reynolds, SH. Gehrke, AS. Hussain, LS. Shenouda, *J. Pharm. Sci*. **1998**,87,1115.
[18] S. Malamataris, D. Ganderton, *Int. J. Pharm*. **1991**,70,69.
[19] S. Kiortsis, K. Kachrimanis, T. Broussali, S. Malamataris, *Eur. J. Pharm. Biopharm*. **2005**,59,73.
[20] AM. Lowmen, NA. Peppas, E. Mathiowitz, Encyclopedia of controlled drug delivery, New York, John Wiley and sons Inc, **1999**.
[21] NS. Barakat, IM. Elbagory, AS. Almurshedi, *Drug. Deliv*. **2009**,16(1),57.
[22] SB. Tiwari, TK. Murthy, RM. Pai, PR. Mehta, PB. Chowdary, *AAPS Pharm. Sci. Tech*. **2003**, 4(3), article 31.
[23] A. Kuksal, AK. Tiwari, NK. Jain, S. Jain. *AAPS Pharm.Sci.Tech*. **2006**,7(1),E1–9.

[24] S. Klein, JB. Dressman, *Dissolution Technol*. **2006**,13(1),6.
[25] SF. Anthony, HL. Clifford, Harrison's Principles of Internal Medicine. Human immunodeficiency virus (HIV) disease: AIDS and related disorders. New York, McGraw-Hill, **2001**.
[26] JD. Betty ,Textbook of Therapeutics: Drug and Disease Management. Human immunodeficiency virus (HIV)—antiretroviral therapy , Lippincott Williams & Wilkins, Philadelphia, **2000**.
[27] G.Moyle ,*Clin Ther(Pub Med*), **2000**,22,911.