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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MUCOADHESIVE MATRIX TABLET OF LAMIVUDINE

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ABSTRACT

The purpose of this study was to formulate sustained release mucoadhesive matrix tablet of antiviral drug lamivudine. Lamivudine matrix tablet was developed to prolong drug release, to enhance the bioavailability, to reduce the chances of dose dumping, so as to reduce the dosing frequency of the tablet. The mucoadhesive matrix tablets were prepared by direct compression technique using different polymers like HPMC K100, Ethyl cellulose and Carbopol 934p as rate retarding polymers. These tablets were evaluated for weight variation, diameter, thickness, hardness, friability, drug content, swelling index, Mucoadhesive strength, drug release and kinetics of release. All the formulations followed the pharmacopeia standards. Through FTIR studies, it was confirmed that there were no interactions between drug, polymers and other excipients. Among the entire formulations F11 batch showed the optimum drug release of 83.38 % for 12 hrs with Mucoadhesive strength of 55 grams.

KEY WORDS: Lamivudine, Sustained release Matrix tablet, hydroxy propyl methyl cellulose, Ethyl cellulose, Carbopol 934p, Mucoadhesive strength.

INTRODUCTION

Oral route most commonly adopted and most convenient route for the drug delivery. Oral route of administration has been receiving more attention in pharmaceutical field because of its flexibility in the designing of dosage form than other drug delivery design through any other routes. The oral drug delivery depends on various factors such as the type of delivery system, the disease being treated, and patient, the length of the therapy and the properties of the drug[1]. The current approach in novel drug delivery system (NDDS) aims to increase efficacy and safety of already used drug molecule by formulating a convenient dosage form for achieving better patient compliance[2].

A Sustained released dosage form; a modern approach in the pharmaceutical sciences has proved its importance and compliance. The oral conventional types of drug delivery system are known to provide a prompt release of the drug. Therefore, to achieve as well as to maintain the drug concentration within the therapeutically effective range needed for treatment, it is often necessary to take this type of drug delivery system.

Drawback of Conventional Dosage Form

1. Poor patient compliance, i.e. the chances of missing the dose is more.
2. There are unavoidable fluctuations in drug concentration which may lead to under medication or over medication.
3. Atypical peak-valley plasma concentration-time profile is obtained which is the main drawback of conventional dosage form.
4. Variation in drug levels can lead to adverse effects mainly with the drug having small Therapeutic Index[3, 4, 5].

Advantages of Sustained Release Dosage Form

1. Patient compliance is increased.
2. Reduced 'see-saw' fluctuation: The 'see-saw' pattern is more often seen in the case of drugs with a biological half-life less than four hour. Sustained release drug delivery system can widely reduce the frequency of drug dosing and maintain a steady drug concentration in blood circulation and target tissue cells.
3. Total dose reduction.
4. Sustained release dosage form leads to better management of the acute or chronic disease condition.
5. Economy: The cost of sustained release products is usually more than that of conventional dosage form because of the unique nature of these compounds but importantly the average cost of treatment over a longer period may be less.[4, 6, 7]

Disadvantages of Sustained Release Dosage Form

1. Dose dumping may occur with defective formulations.
2. The potential for dose adjustment is reduced.
3. Cost of sustained released dosage form is more than conventional dosage form.
4. The potential for first pass metabolism of drug is increased.
5. Patient education is necessary for proper medication.
6. Poor in vivo and in vitro correlations [3, 8, 9, 10].

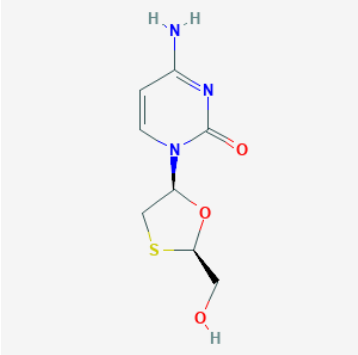
Matrix tablet formulations has been widely accepted oral controlled drug delivery formulations because of its simple nature, ease in the formulation process, highly reproducible, stability of the raw materials and dosage form, ease of scale-up and process validation. The matrix system is the mixture of materials with the drug, which will cause release of the drug to

slow down. This system has subcategories as follows hydrophobic matrices, lipid matrices, hydrophilic matrices, biodegradable matrices, and mineral matrices[11].

Advantages of Mucoadhesive Drug Delivery Systems are [12]

1. A prolonged residence time at the site of action or absorption is achieved,
2. Localization of the drug delivery system at a given target site,
3. An increase in the drug concentration gradient due to the intestine contact of the particles with the mucosal surface,
4. A direct contact with intestinal cells, which is the step earlier to particulate absorption.

Lamivudine



IUPAC name:(−)-L-2′,3′-dideoxy-3′-thiacytidine

Lamivudine is an antiretroviral drug, belongs to class III of the BCS Classification with high solubility and low permeability. It is rapidly absorbed with a bioavailability of over 80% following oral ingestion. The drug half-life in plasma is approximately 5-7 hrs. It is bound to plasma proteins less than 36 %. It can inhibit both types (1 and 2) of HIV reverse transcriptase and the reverse transcriptase of hepatitis B.

MATERIALS AND METHODS

Lamivudine was a gift sample from Aurobindo Pharma Limited, Hyderabad. HPMC K100 were procured from Chemdyes Corporation, Gujarat. Carbopol 934p and colloidal silicon dioxide were procured from Research lab-fine chem. industries, Mumbai. Ethyl cellulose and Magnesium stearate were procured from Thomas Baker Pvt. Ltd, Mumbai. Lactose was procured from Merck specialities Pvt. Ltd. All reagents used were of analytical grade.

Method

All ingredients were collected and weighed accurately as shown in Table 1. Lamivudine USP was sieved with lactose and polymers through sieve no. 60# and then remaining excipients were added. Colloidal silicon dioxide (Aerosil-200) and magnesium stearate were separately sifted, through sieve no. 60#. Pre blend all ingredients (except lubricant- magnesium stearate) for 15 minutes. Add magnesium stearate and then again blend for 5 minutes. Compress Lubricated powder by using 9 station single rotary machine having 9.5 (mm) diameter and circular standard concave shaped punch, with a pressure of 7-8 tons.

PRE FORMULATION STUDIES

Fourier transmission infrared (FT-IR) spectroscopy

The identity of the drug was confirmed by comparing the IR spectrum of drug with a reported spectrum of lamivudine as shown in Figure 2.

Melting point

The melting point of the drug was found to approximately 162˚C.

Construction of Standard Curve of Lamivudine

Spectrophotometrically estimate lamivudine at 270 nm as it obeys beer- Lambert's law. A Stock solution was prepared by dissolving 100mg of lamivudine in 0.1 N HCl buffer to get a solution of 1000 µg/ml concentration[13, 14].

Standard solution

10ml of stock solution was made to 100ml with 0.1 N HCl thus giving a concentration of 100µg/ml. An aliquot of standard drug solutions ranging from 0.25ml to 2ml was transferred into a 10ml volumetric flask and were diluted up to the mark with 0.1 N HCl. Thus the final concentration ranges from 2.5-20µg/ml. Absorbance of these solutions was measured at 270 nm against 0.1 N HCl as a blank. A plot of concentrations of the drug versus absorbance was plotted as shown in figure 3.

Drug excipients compatibility studies (using FT-IR spectroscopy) [15, 16]

A compatibility study should be done to know if any, chemical interactions exist between drug and excipients. Interpretation is done by comparing FTIR spectra of pure drug and drug-excipients mixture. Both the spectra should show that characteristic bands of drug were not altered, indicates no chemical interactions between the drug and excipients used.

Screening of polymers[1, 17]

Screening of polymers was done by calculating swelling index and observing gelling properties of different polymers.

PRECOMPRESSION PARAMETERS OF BLENDS[18]

Angle of repose

Weight accurately the powder blend and take it in the funnel. Funnel height was adjusted in such a way that a tip of the funnel just touches the apex of the powder blend. The powder was passed through the funnel freely. The diameter was measured and angle of repose was calculated using the following formula.

$$\tan \alpha = h/r$$

Bulk density and Tapped density

An accurately weighed quantity of powder blend (W) was taken and carefully poured into the graduated measuring cylinder and the volume (V_0) of the powder was measured. Then graduated measuring cylinder was tapped 50 times and volume (V_T) were measured which was tapped volume of the powder blend. The bulk density and tapped density were calculated by using the following formulas.

$$\text{Bulk density} = W/V_0$$

$$\text{Tapped density} = W/V_T$$

Compressibility index (CI)/ Carr's index

It was obtained from bulk and tapped densities of the powder. It was calculated by using the following formula.

$$CI = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped density}} X\ 100$$

Hausner's ratio

Hausner's ratio is a number that is compared to the flowability of a powder. It is calculated by taking the ratio of tapped density to bulk density.

$$\text{Hausner's ratio} = \text{Tapped Density}/\text{Bulk Density}$$

POST COMPRESSION PARAMETERS [19,20,21,22]

Thickness

Five tablets were selected randomly from each batch were used for thickness determination. The thickness of each tablet was measured in mm using a digital Vernier calliper their values were reported in millimeters. The mean and SD were calculated and reported.

Weight Variation Test

Ten tablets were selected randomly from each batch and individually weighed using an electronic balance. The average weight was calculated. The percentage deviation from average weight was reported.

Hardness

The strength of the tablet which prevents from chipping, abrasion or breakage under conditions of storage, transportation and handling before usage, depends on its hardness. The hardness of five tablets which randomly selected from each batch was measured using Monsanto Hardness tester and expressed in Kg/cm^2. The average mean and SD were calculated.

Friability

Friability of tablets was performed by using Roche friabilator. The tablets should be carefully de-dusted prior to testing. Five tablets were randomly selected from each batch and accurately weigh the tablet sample, and place the tablets in the drum. Rotate the drum 100 times, and remove the tablets, reweighed and percentage loss was determined.

$$\%\ \text{friability} = \{[\text{Initial weight of the tablets} - \text{final weight of the tablets}]/[\text{Initial weight of the tablets}]\} \times 100$$

Uniformity of Drug Content

Matrix tablet of Lamivudine from a batch was taken at random and was crushed to a fine powder and was transferred into a 100ml volumetric flask and add 100ml 0.1 N HCl to it. It was shaken occasionally for about 30 minutes and the volume was made up to 100ml by adding 0.1 N HCl. The resulting solution was set aside for a few minutes and the supernatant solution was collected, filtered by using Whatman filter paper. Then the filtrate was subsequently diluted, and the absorbance was measured at 270nm.

The drug content was calculated as:

$$\%\ \text{Drug Content} = (\text{Analyzed value} / \text{Theoretical Value}) \times 100$$

Swelling Index[22]

Formulated tablets were weighed individually (W_0) and placed separately in a Petri dish containing 50 ml of 1.2 pH HCl Buffer. The Petri dishes were placed in an incubator maintained at 37 ± 0.5^0 C. The tablets were removed from the Petri dish, at predefined intervals of time and reweighed (W_t), and the % swelling index was calculated using the following formula.

$$\%\ W_u = \frac{W_t - W_0}{W_t} \times 100$$

Where: W_u - Water uptake, Wt - Weight of tablet after time t, W_0 - Initial Weight of tablet before immersion in buffer solution.

In-Vitro Dissolution Studies[23]

Dissolution studies on each formulation were performed by using USP type II apparatus, employing 900 ml HCl Buffer of pH 1.2 as a dissolution medium. The paddles were operated at a 50rpm and the temperature was maintained at 37±0.5°C throughout the experiment. 5 ml Samples were withdrawn for 12 hrs at regular interval of time and replaced with an equal volume of same dissolution medium to maintain the constant volume throughout the experiment. Samples withdrawn at various time intervals were suitably diluted with same dissolution medium and the amount of drug released was estimated by double beam UV – VIS spectrophotometer at 270nm. The dissolution studies on each formulation were conducted in triplicate and the average of 3 values was taken from studies.

Evaluation of Kinetics[24]

Dissolution parameters such as the zero order rate constant, the first order rate constant, Higuchi constant, Korsermayer-Peppas constant and Hixson Crowell constant were calculated from the dissolution data obtained from various formulations. The following mathematical expressions were used to calculate various drug release mechanisms from the dissolution data.

1) Zero order equation,

$$Q_t = Q_0 - K_0 t$$

Where, Q_t =Amount of drug dissolved at time t, Q_0= Initial amount of drug in solution, K_0 = Zero order rate constant, t = Time.

2) First order equation,

$$\text{Log } C_t = \log Co - K_1 t/2.303$$

Where, C_0 = Initial concentration of drug, K_1 = First order rate constant.

3) Higuchi equation,

$$\text{Cumulative amount of drug released} = K_H t_{1/2}$$

Where, K_H = Higuchi constant.

4) Korsermayer - Peppas Constant,

$$M_t/M_\infty = Kt^n$$

Where, M_t/M_∞ = Fraction of drug release at time t, n = release exponent.

5) Hixson Crowell constant,

$$Q_0^{1/3} - Qt^{1/3} = K_s t$$

Where, Q_0 =Initial amount of drug, Q_t = Cumulative amount of drug release at time t, K_s = Hixson Crowell release constant, t = time in hrs.

Mucoadhesive Strength Measurement [25, 26, 27]

Modified physical balance was used to measure Mucoadhesive strength of the matrix tablet. The goat gastric mucosal membrane was used as a model membrane for Mucoadhesive strength and 1.2 pH HCl buffer was used as the media for testing. The goat gastric mucosal membrane was placed in Tyrode solution at 37° c for 2 hrs.

The left side arm of the balance was removed, and a thick thread was hanged of suitable height. To this thread a Teflon block was attached, another Teflon block was placed in a 100-ml beaker, which was kept on the left side of the balance. The mucous membrane was washed thoroughly with the buffer solution and was cut into desired size. This membrane was then attached to the Teflon block placed in the beaker and one which was hanged with thread by using cyanoacrylate solution (feviquick). The beaker was filled with the buffer solution of pH 1.2, so that the buffer solution reaches the surface of the mucosal membrane to keep it moist. This was then kept below the left-hand side of the balance. The balance was then adjusted so that the right-hand side of the balance was exactly 5 g heavier than the left side.

The matrix tablet was then placed between the two-mucous membranes. 5 g weight on the right side of the balance was removed, this will lead to an application of 5 g of pressure on the matrix tablet overlying between moist mucosa. The balance was kept as such for 3 min and then the weight was slowly increased on the right-hand side pan, till the tablet gets separated from the membranes. This will give the Bioadhesive strength in grams. The mean value was taken for three such trials. After every single measurement the tissue was washed gently with buffer solution and left for 5 minutes before taking reading for a new tablet.

From the Mucoadhesive strength, the force of adhesion was calculated using the following formula:

$$\text{Force of adhesion (N)} = \frac{\text{Bioadhesive strength}}{100} \times 9.81.$$

Stability studies [28]

The optimized batch of formulation was subjected to accelerated stability studies at 40˚C ± 2˚C/75 % RH ± 5 % RH for three months to investigate the stability of formulation in terms of physical and chemical changes. Stability study of an optimized F11 batch indicates no significant change in physical parameters.

RESULTS AND DISCUSSION

Drug Excipient Compatibility Studies

The results showed that the principle IR peak of pure drug, its physical mixture with polymer were almost similar as shown in figure 4, signifying no interaction was seen between drug and polymer during formulation of tablets.

Pre formulation Studies of Powder blend

The prepared powders were characterized for angle of repose, bulk density, tapped density, Hausner's factor, Carr's index and compressibility index and the values were reported in Table 4. The angle of repose of the different batches of powders was determined as per method mentioned earlier and the results ranged between 22.57° to 25.89°.The powder with the angle of repose 20°-30^0 indicates excellent flow properties. The bulk densities of powder were ranged between 0.430 g/cm^3 to 0.490 g/cm^3. Tapped density ranged between 0.640 g/cm^3 to 0.680 g/cm^3. Compressibility index (%) were in the range of 11.29%-15.19%. The powder in the range of 11%-15% show good flow character. Hausner's ratios of the entire batch were in the range of 1.12-1.65.

Evaluation of tablets

All the tablets passed the weight variation test as the % weight variation was within the Pharmacopoeia limits of ± 5% of the weight. Hardness was found to be between 10.12-13.15 kg per square centimeter. All tablets satisfied friability requirement, as the % friability values were less than 1%. The drug content estimations showed values in the range of 96.94 to 98.91%, which reflects good uniformity in drug content among all formulations. All the values were in Table 5.

Swelling index profiles of all formulations are shown in Table 6 and Figure 5, 6. Swelling index of all formulations varied between 46.55 to 234.66 %. Swelling of the matrix, this is indicated by the transition of the polymer from the glassy to the rubbery state. It is an important parameter in determination of the release characteristics of the matrix system. As swelling process proceeds, the gel layer gradually becomes thicker and therefore the drug concentration gradient along the diffusional path length is decreased results in the slow drug release.

All the sixteen formulations were subjected to in-vitro dissolution studies using a USP type -II Dissolution Test Apparatus. The dissolution medium 1.2 pH buffer was used to study the drug release. The samples were withdrawn at different intervals of time and analyzed at 270 nm using a UV spectrophotometer. The cumulative percentage drug release was calculated. The data obtained from in vitro release for formulations prepared by direct compression technique are tabulated in the Table 7.From the results we can conclude that there was an increase in the extend of the duration of drug release with increase in concentration of polymer in the formula. The F11 batch showed best result as the percent cumulative drug release of F11 is 83.38 % at 12 h. Comparative graphs of In vitro drug release of all the 16 formulations were shown in Figure 7, 8, 9, 10, 11.

The Bioadhesive strength of tablets were dependent on the property of the Bioadhesive polymers,which on hydration adhere to the mucosal surface and also on the concentration of polymer used. Bioadhesive force values ranged from 0.107 to 0.539 N. The results were represented in Table 8 and Figure 12.

Table 1: Composition of lamivudine mucoadhesive matrix tablets formulated with different

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
Lamivudine	159	159	159	159	159	159	159	159	159	159	159	159	159	159	159	159
HPMC K100	70	80	90	-	-	-	-	-	-	90	80	70	80	90	80	70
Ethyl cellulose	-	-	-	70	80	90	-	-	-	70	80	90	-	50	40	30
Carbopol 934p	-	-	-	-	-	-	20	40	60	-	-	-	40	20	40	60
Lactose	163	153	143	163	153	143	213	193	173	73	73	73	73	73	73	73
Mg stearate	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Colloidal Silicon dioxide	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
TOTAL	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400

Table 2: Standard curve of Lamivudine in 0.1 N HCL

Concentration (µg/ml)	Absorbance at 270 nm
0	0
2.5	0.1845
5	0.3205
7.5	0.459
10	0.608
12.5	0.752
15	0.8905
17.5	1.046

Table 3: Swelling index and Gelling property of different polymers in water and 1.2 pH phosphate buffer

Polymer	Swelling index		Gelling	
	water	1.2 pH	Water	1.2Ph
HPMC K100	100	166.66	++	+++
HPMC K4M	100	87.5	++	+++
HPMC E15	87.5	66.6	++	+
Ethyl cellulose	92.3	142.3	+	++
Carbopol 934	140	160	+	+
Xanthan gum	80	100	++	++
Guar gum	86.66	73.3	++	++

Table 4: Evaluation of flow properties of powder blend

Formulation	Bulk density(g/ml)	Tapped density(g/ml)	Angle of repose(^{0})	Compressibility index (%)	Hausner's ratio
F1	0.48±0.005	0.65±0.05	25.89±1.92	13.43±1.16	1.14±0.02
F2	0.46±0.01	0.65±0.01	24.56±0.89	13.21±1.77	1.14±0.02
F3	0.46±0.01	0.68±0.01	25.12±2.98	12.05±1.43	1.17±0.03
F4	0.49±0.02	0.65±0.01	23.88±0.55	13.18±1.27	1.13±0.02
F5	0.45±0.005	0.66±0.01	23.31±1.99	13.96±1.41	1.13±0.02
F6	0.44±0.01	0.64±0.01	23.74±1.60	14.15±1.71	1.16±0.01
F7	0.44±0.005	0.64±0.02	23.41±1.13	14.81±1.40	1.14±0.01
F8	0.46±0.01	0.67±0.03	22.73±1.69	16.08±1.56	1.14±0.02
F9	0.45±0.01	0.67±0.01	23.07±1.65	14.27±1.70	1.12±0.01
F10	0.48±0.01	0.67±0.01	22.57±1.58	14.47±1.37	1.32±0.02
F11	0.48±0.01	0.66±0.02	23.85±1.65	11.29±1.30	1.24±0.01
F12	0.47±0.01	0.65±0.01	23.85±2.85	14.86±1.95	1.33±0.01
F13	0.45±0.05	0.67±0.01	25.35±1.99	15.19±1.15	1.15±0.02
F14	0.47±0.02	0.67±0.02	23.55±1.48	11.98±1.79	1.19±0.01
F15	0.48±0.01	0.66±0.01	25.28±1.59	13.10±1.95	1.65±0.01
F16	0.43±0.005	0.64±0.01	24.23±2.94	13.84±1.78	1.41±0.01

Table 5: Evaluation of lamivudine matrix tablets

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
Uniformity of weight(mg)	400 ±3.8	400±2 .8	400±5 .2	400±3 .7	400±4 .4	400±4 .4	400±3 .7	400±2 .7	400±3 .9	400±1 .7	400±1 .4	400±4 .7	400±6 .3	400±7 .1	400±3 .5	400±7 .6
Thickness (mm)	4.2± 0.03	4.2±0. 04	4.2±0. 09	4.2±0. 04	4.2±0. 03	4.2±0. 07	4.2±0. 02	4.2±0. 02	4.2±0. 02	4.2±0. 01	4.2±0. 03	4.2±0. 06	4.2±0. 04	4.2±0. 05	4.2± 0.07	4.2± 0.02
Diameter (mm)	9.6± 0.01	9.6±0. 02	9.6±0. 08	9.6±0. 02	9.6±0. 01	9.6±0. 01	9.6±0. 01	9.6±0. 03	9.6±0. 01	9.6±0. 01	9.6±0. 03	9.6±0. 01	9.6±0. 01	9.6±0. 02	9.6±0. 03	9.6±0. 04
Friability (%)	0.05	0.06	0.04	0.06	0.03	0.03	0.08	0.06	0.06	0.05	0.03	0.06	0.05	0.05	0.04	0.04
Tablet hardness	11.0 3±0. 01	11.06 ±0.01	11.06 ±0.02	11.04 ±0.02	11.15 ±0.00 5	11.13 ±0.02	11.21 ±0.02	11.09 ±0.07	12.1± 0.05	12.1± 0.05	13.15 ±0.03	10.15 ±0.02	11.1± 0.05	10.12 ±0.06	11.14 ±0.02	11.14 ±0.03
Assay (%)	98.0 2	97.26	98.02	98.24	96.94	98.24	97.91	98.13	98.02	98.13	98.56	98.24	98.13	98.59	98.37	98.91

Table 6: Swelling index of Matrix tablets (%)

Formulation	2 hrs	4 hrs	6 hrs	8 hrs	10 hrs
F1	197.416	202.584	205.9432	209.0439	211.8863
F2	196.7089	205.0633	207.3418	214.1772	220.7595
F3	183.2918	195.0125	197.5062	228.6783	234.6633
F4	25.69975	33.84224	39.18575	48.60051	50.89059
F5	29.72292	36.02015	43.32494	44.83627	46.5995
F6	36.5	41.75	45.5	48.75	50.25
F7	21.93878	31.88776	37.2449	50	57.39796
F8	47.20812	63.19797	70.55838	75.38071	79.18782
F9	38.19095	36.93467	43.46734	46.73367	113.3166
F10	194.6565	209.9237	213.7405	221.374	227.4809
F11	140.5473	147.7612	182.5871	219.6517	221.1443
F12	72.29219	110.0756	130.9824	132.7456	147.6071
F13	92.1519	128.6076	146.3291	170.8861	174.9367
F14	78.73418	133.9241	160.7595	180.2532	185.3165
F15	73.5369	115.0127	149.1094	153.4351	155.7252
F16	65.26055	99.00744	122.5806	125.8065	129.0323

Table 7: Cumulative percent drug release of lamivudine matrix tablets

TIME (hrs.)	1	2	3	4	5	6	7	8	9	10	11	12
F1	4.49	18.00	21.52	29.20	35.22	40.29	48.07	49.80	57.39	58.92	60.95	63.72
F2	1.57	17.25	21.25	29.91	32.27	38.55	40.22	43.13	50.68	57.54	58.34	58.90
F3	0.09	11.35	17.76	22.49	27.01	29.84	39.52	43.89	49.74	54.40	55.67	57.68
F4	40.82	42.98	46.39	47.13	48.12	49.60	58.40	61.89	63.20	66.71	68.77	70.84
F5	23.84	35.64	41.45	42.41	42.37	43.85	50.92	52.66	56.12	59.10	60.39	66.81
F6	6.44	38.38	44.45	45.99	47.63	48.62	49.37	55.50	59.46	61.63	63.28	65.32
F7	30.96	50.39	54.33	57.55	58.36	59.89	67.78	87.66	166.21	206.16	-	-
F8	30.96	50.39	57.25	60.74	69.37	70.23	77.69	89.33	95.67	99.60	-	-
F9	6.47	24.41	34.55	40.60	47.41	56.94	60.43	68.08	71.37	75.42	-	-
F10	9.66	23.00	41.18	53.36	59.47	61.30	63.34	66.37	73.07	73.71	75.82	78.66
F11	7.70	25.90	35.31	43.07	52.09	59.94	64.42	65.01	70.98	71.85	76.87	83.38
F12	4.53	11.43	20.6	27.22	31.76	39.74	44.35	45.82	49.24	52.43	63.21	65.26
F13	1.32	4.96	15.00	16.79	21.03	26.51	29.10	34.38	47.01	55.08	68.80	73.81
F14	4.29	4.94	5.94	10.12	15.30	21.00	26.24	30.78	36.80	41.15	46.75	61.88
F15	0.01	0.02	5.15	9.57	13.53	19.66	23.23	24.33	33.98	34.66	39.00	42.82
F16	0.92	1.22	2.15	7.05	10.02	15.93	18.46	23.68	30.89	34.23	38.81	39.51

Table 8: Bioadhesive strength of matrix tablet

	BIOADHESIVE STRENGTH(gm)	BI0ADHESIVE FORCE(N)
F1	20	0.1962
F2	22	0.21582
F3	28	0.27468
F4	15	0.14715
F5	18	0.17658
F6	25	0.24525
F7	11	0.10791
F8	14	0.13734
F9	15	0.14715
F10	50	0.4905
F11	55	0.53955
F12	50	0.4905
F13	40	0.3924
F14	55	0.53955
F15	55	0.53955
F16	50	0.4905

Table 9: Kinetic modelling data of lamivudine matrix tablets

Formulations	zero order (R^2)	1st order (R^2)	Higuchi (R^2)	Hixson-Crowell (R^2)	Korsermayer-Peppas (R^2)
F1	0.981	0.993	0.948	0.752	0.847
F2	0.964	0.976	0.938	0.744	0.869
F3	0.989	0.982	0.906	0.799	0.804
F4	0.713	0.845	0.888	0.414	0.418
F5	0.797	0.888	0.953	0.475	0.503
F6	0.763	0.851	0.892	0.553	0.680
F7	0.759	0.716	0.639	0.707	0.601
F8	0.903	0.751	0.986	0.557	0.546
F9	0.963	0.995	0.963	0.717	0.798
F10	0.885	0.959	0.949	0.654	0.741
F11	0.930	0.983	0.964	0.684	0.769
F12	0.971	0.989	0.945	0.761	0.870
F13	0.965	0.917	0.833	0.875	0.968
F14	0.969	0.949	0.819	0.877	0.908
F15	0.966	0.954	0.813	0.894	0.717
F16	0.944	0.925	0.762	0.955	0.945

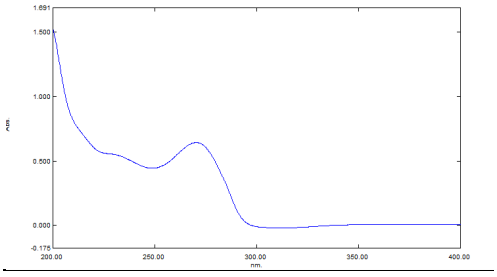


Figure 1: UV-Spectrum of Drug lamivudine

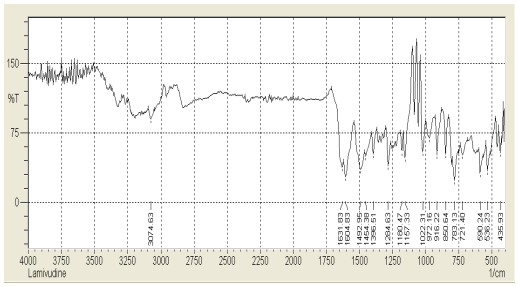


Figure 2: FTIR spectrum of drug lamivudine

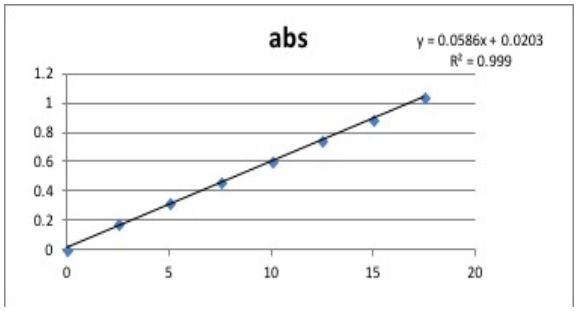


Figure 3: standard curve of lamivudine

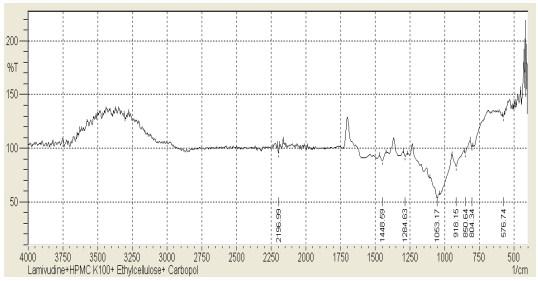


Figure 4: FTIR spectrum of lamivudine, HPMC K100, Ethyl cellulose, carbopol

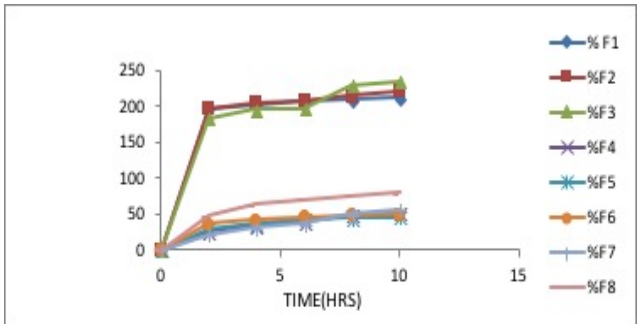


Figure 5: Swelling Index of Formulation F1-F8

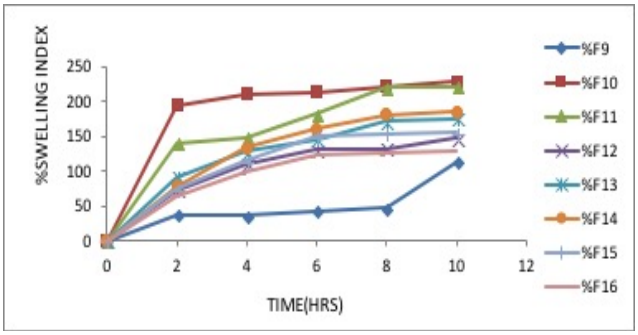


Figure 6: Swelling Index of Formulation F9-F16

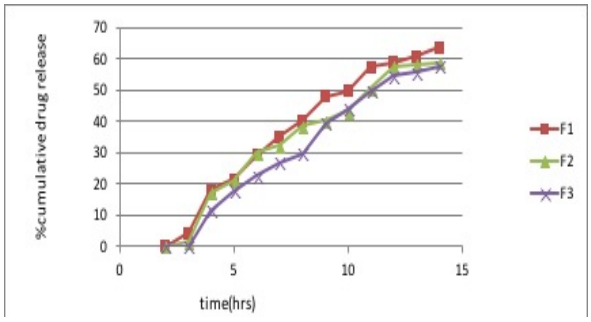


Figure 7: *In vitro* drug release profile of batches (F1-F3)

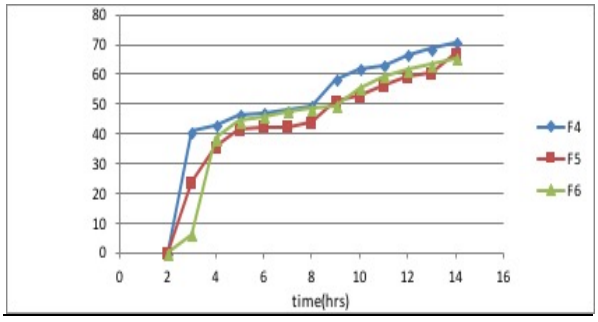


Figure 8: *In vitro* drug release profile of batches (F4-F6)

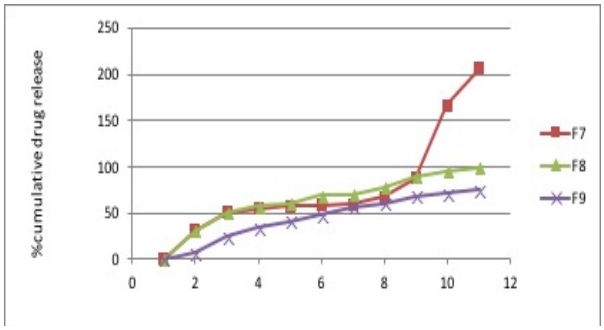


Figure 9: *In vitro* drug release profile of batches (F7-F9)

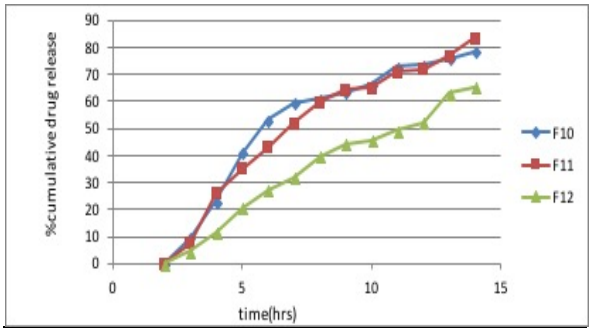


Figure 10: *In vitro* drug release profile of batches (F10-F12)

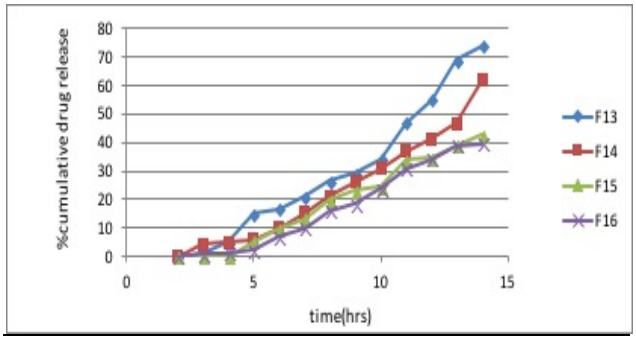


Figure 11: *In vitro* drug release profile of batches (F13-F16)

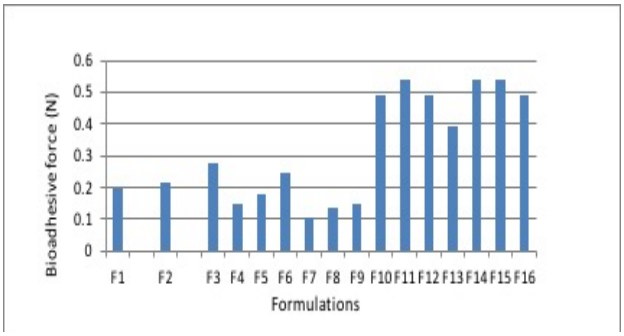


Figure 12: Bioadhesive strength of a tablet in acidic media

To ascertain the mechanism of drug release, the dissolution data were analyzed by zero order, first order kinetics, Higuchi, Hixson-Crowell and Peppas models. The kinetic data were shown in Table 9.

CONCLUSION

The aim of the study was to formulate and evaluate the sustained release Mucoadhesive matrix tablet of Lamivudine using different polymers such as HPMC K100, Ethyl cellulose, Carbopol 934p. Lactose monohydrate was used as filler. Identification and compatibility studies were done by FT-IR. Direct compression method was used for tablet preparation. All the Pre- compression parameters of the powder blend and post compression parameters of tablet were studied.

Amongst the other entire batches F11 batch was selected as an optimized batch because the Pre-and Post-compression parameters results are satisfactory. In-vitro dissolution studies of all 16 batches (F1-F16) were performed, from which we conclude that batch F11 shows % cumulative drug release of 83.38% for 12 hrs. The Bioadhesive strength of F11 batch was found to be 55 gm with Bioadhesive force of 0.53955 N. The swelling index was found to be 221.14 for the optimized batch. Stability study of an optimized F11 batch indicates no significant change in physical and chemical parameters in the tablet. The *in vitro* dissolution studies, drug content uniformity test and Bioadhesive strength of optimized batch F11 shows satisfactory results.

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