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Formulation and In-Vitro Evaluation of Lamivudine Sustained Release Tablets

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Abstract: *The main objective of the present work was to formulate and evaluate sustained release lamivudine tablets using different polymers viz. Microcrystalline cellulose (MCC),Poly vinylpyrrolidine K30 (PVP K30) and gums like Chitosan,Guar gum,Xanthum gum .Then the release rates were modulated. After evaluation of physical properties of tablet, the in-vitro drug release study was performed in 0.1N HCl for 2 hours and in phosphate buffer pH 6.8 upto 12 hours. Dissolution data were analysed by Higuchi plot.Among all the formulations, formulation F9 which contains chitosan release the drug which follows First order kinetics was showing highest drug release retarding capacity*

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I. Introduction

SUSTAINED RELEASE DOSAGE FORMS[5,6]:

Sustained release, sustained action, prolonged action, controlled release, extended action, timed release, depot, and repository dosage forms are terms used to identify drug delivery systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. In this case of orally administered forms, however, this period is measured in hours and critically depends on the residence time of the dosage form in the gastrointestinal (GI) tract. The term "controlled release" has become associated with those systems from which therapeutic agents may be automatically delivered at predefined rates over a long period of time. Products of this type have been formulated for oral, injectable, and topical use, and include inserts for placement in body cavities[5].

Controlled release also denotes systems which can be provide some control whether this is of a temporal or spatial nature of both for drug release in the body. The system attempts to control drug concentration in the target tissue or cells. Prolonged or sustained release systems only prolong therapeutic blood or tissue level of the drug for extend period of time[6].

Advantages of sustained release dosage forms

- Implicit in the design of sustained release forms, is that the total amount of drug administered can be reduced, thus maximizing availability with a minimum dose.
- In addition, better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a high availability drug can be reduced by formulation in an extended action form.
- The safety margin of high-potency drugs can be increased, and the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
- Overall, administration of sustained release forms enables increased reliability of therapy.

Disadvantages of sustained release dosage forms

- Administration of sustained release medication does not permit the prompt termination of therapy. Immediate changes in drug need during therapy, such as might be encountered if significant adverse effects are noted, cannot be accommodated.
- The physician has less flexibility in adjusting dosage regimens. This is fixed by the dosage form design.
- Sustained release forms are designed for the normal population, i.e., on the basis of average drug biologic half-lives. Consequently, disease states that alter drug disposition, significant patient variation, and so forth are not accommodated.

  Not all drugs are suitable candidates for formulation as prolonged action medication.

Table 1: Characteristics of Drugs Unsuitable for Peroral Sustained Release Forms

Characteristics	Drugs
Not effectively absorbed in the lower intestine	Riboflavin, Ferrous salts
Absorbed and excreted rapidly; short biologic half-lives (<1 hr)	Penicillin G, Furosemide
Long biologic half-lives (>12 hr)	Diazepam, Phenytoin
Large doses required (>1 g)	Sulfonamides
Cumulative action and undesirable side effects; drugs with low therapeutic indices	Phenobarbital, Digitoxin
Precise dosage titrated to individual is required	Anticoagulants, Cardiac glycosides

SELECTION OF DRUG FOR SUSTAINED-RELEASE DRUG DELIVERY SYSTEMS[14]

Judicious choice of the drug substance is the most important decision in the successful development of a sustained-release product, Several categories of drug have potential for their therapeutics improvement of efficacy via sustained-release oral routes e.g.Antianginal, Anti-inflammatory, Antihistaminic, Antigastric resistant agents, Antipsychotic agents and Antidiabetic drugs or agents.

The common goal for increased duration is twice a day, or when feasible, once a day. Several properties of the drug itself can lead to the achievement of a 12 to 24 hours oral prolonged release dosage form. Some of the characteristics mitigating against success are the following:

1. Very short half-life and/or a relatively large single dose.
2. Long half-life.
3. Potent drug with a low margin safety.
4. Poorly soluble and/or poorly absorbed.
5. Biological activity not a function of core in blend.
6. Absorption primarily active through a 'window'.
7. Large first-pass metabolism.

The selection of both the drug and retardant polymers along with the filler excipients will impact on the mechanism and rates of drug release from monolithic systems. Cellulose derivatives and acrylic resin polymers comprise the group of polymers that are presently available as aqueous coatings for pharmaceutical dosage forms. These polymers in the dry state, have been utilized in matrix type tablet formulations by directly compressing.

SCOPE OF POLYMERS IN CONTROLLED DRUG DELIVERY SYSTEMS [15, 16, 17]

Various synthetic and natural polymers have been examined in drug delivery applications. The three key advantages that polymeric drug delivery products can offer are:

- **Localized delivery of drug:** The product can be implanted directly at the site where drug action is needed and hence systemic exposure of the drug can be reduced. This becomes especially important for toxic drugs, which produce various systemic side effects such as the chemotherapeutic drugs.

- **Sustained delivery of drug:** The drug encapsulated is released over extended periods and hence eliminates the need for multiple doses. This feature can improve patient compliance especially for drugs for chronic indications, requiring frequent administrations.

- **Stabilization of the drug:** The polymer can protect the drug from the physiological environment and hence improve its stability in-vivo. This particular feature makes this technology attractive for the delivery of labile drugs such as proteins.

II. Material and Methodology

Table 2: List of Materials and Suppliers

S.NO	INGREDIENTS	SUPPLIERS
1	Lamivudine	Supplied By Pharma Train
2	Chitosan	SD Fine Chemicals, Mumbai
3	Guargum	SD Fine Chemicals, Mumbai
4	Xanthum Gum	SD Fine Chemicals, Mumbai
5	PVP K3o	SD Fine Chemicals, Mumbai
6	MCC	SD Fine Chemicals, Mumbai
7	Talc	SD Fine Chemicals, Mumbai
8	Magnesium stearate	SD Fine Chemicals, Mumbai

Table 3: List of equipment

S.NO	NAME OF THE EQUIPMENT
1	Electronic weighing balance
2	Friabilator
3	Laboratory oven
4	Compression machine
5	Tablet hardness tester
6	UV
7	Dissolution apparatus
8	Vernier calipers

I. Analytical Method Development in 0.1N HCL:
Preparation of 0.1 N Hydrochloric Acid (pH 1.2)
8.5 ml of concentrate hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

Determination of λ_{max} of Lamivudine in 0.1N HCL:

Procedure:
Working standard: 100mg of Lamivudine was weighed and dissolved in 10ml mithanol and then make up to the volume of 100ml with 0.1N HCL it give 1000µg/ml concentrated stock solution.

Dilution 1: From the working standard, 10ml solution was diluted to 100ml with 0.1NHcl it will give 100 µg/ml concentrated solution.

Dilution 2: From the dilution1, 10ml solution was diluted to 100ml with 0.1NHcl it will give 10 µg/ml concentrated solution.
This solutions was scanned at range of 200-400nm wavelength light corresponding scan spectrum curve was noted .the corresponding wavelength having highest absorbance is noted as λ_{max}

II Construction of calibration curve of Lamivudine in 0.1N HCL:
Procedure:
Working standard: 100mg of Lamivudine was weighed and dissolved in 10ml methanol and then make up to the volume of 100ml with 0.1N HCL it give 1000µg/ml concentrated stock solution.

Dilution 1: From the working standard, 10ml solution was diluted to 100ml with 0.1NHcl it will give 100 µg/ml concentrated solution.
From dilution 1, take 0.2, 0.4, 0.6, 0.8, and 1ml of solution was diluted up to mark in 10ml volumetric flask to obtain 2, 4, 6, 8 and 10µg/ml concentrated solutions. This solutions absorbance was noted at 280nm.

III. Analytical Method Development in 6.8 phosphate buffer:
Preparation of 6.8 phosphate buffer:
6.8gms of potassium di hydrogen ortho phosphate was taken in a 1000ml volumetric flask and dissolved with distilled water and make up to 1000 ml with distilled water and adjust pH upto 6.8 with Sodium hydroxide solution.

Determination of λ_{max} of Lamivudine in 6.8 phosphate buffer:
Procedure:
Working standard: 100mg of Lamivudine was weighed and dissolved in 10ml mithanol and then make up to the volume of 100ml with 6.8 phosphate buffer it give 1000µg/ml concentrated stock solution.

Dilution 1: From the working standard, 10ml solution was diluted to 100ml with 6.8 phosphate buffer it will give 100µg/ml concentrated solution.

Dilution 2: From the dilution-1, 10ml solution was diluted to 100ml with 6.8 phosphate buffer it will give 10µg/ml concentrated solution.
This solution was scanned at range of 200-400nm wavelength light corresponding scan spectrum curve was noted .the corresponding wavelength having highest absorbance is noted as $\lambda_{max.}$

Construction of calibration curve of Lamivudine 6.8 phosphate buffer:
Procedure:
Working standard: 100mg of Lamivudine was weighed and dissolved in 10ml mithanol and then make up to the volume of 100ml with 6.8 phosphate buffer it give 1000µg/ml concentrated stock solution.

Dilution 1: From the working standard, 10ml solution was diluted to 100ml with 6.8 phosphate buffer it will give 100 µg/ml concentrated solution.
From dilution 1, take 0.2, 0.4, 0.6, 0.8 and 1ml of solution and was diluted up to mark in 10ml volumetric flask to obtain 2, 4, 6, 8 and 10µg/ml concentrated solutions. This solutions absorbance was noted at $\lambda_{max=270}$

II. Formulation of Extended release tablets of Lamivudine by direct compression method
Processing steps involved in direct compression method:
The matrix tablets were prepared by following the General Methodology as given below:
1. All ingredients (Lamivudine + MCC + polymer + PVP K30) were weighed accurately and co sifted by passing through #22 sieve, blended in a Poly Bag for 5 min.
2. The above blend were lubricated with Talc and Magnesium stearate and passed through # 40 Sieves.
3. The final blend was then compressed into tablets using 16 station tablet compression machine with an average hardness of 5.0 - 7.0Kg/cm^2, by using 8-12mm die.

Table 4: Formulation of Lamivudine SR tablets by wet granulation method

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Lamivudine	200	200	200	200	200	200	200	200	200
Guargum	50	100	150	-	-	-	-	-	-
Xanthum gum	-	-	-	50	100	150	-	-	-
Chitosan	-	-	-	-	-	-	50	100	150
PVP K30	30	30	30	30	30	30	30	30	30
MCC	180	130	80	180	130	80	180	130	80
Talc	10	10	10	10	10	10	10	10	10
Mg.stearate	10	10	10	10	10	10	10	10	10
Total Weight(mg)	480	480	480	480	480	480	480	480	480

EVALUATION OF TABLETS

The formulated tablets were evaluated for the following Pre and Post compression quality control studies

A) Pre Compression studies:
1. Angle of Repose: It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.
Angle of Repose of granules was determined by the funnel method. Accurately weighed powder blend was taken in the funnel. Height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel freely on to the surface. Diameter of the powder cone was measured and angle of repose was calculated using the following equation[17].

$$\theta = \tan^{-1} (h/r)$$

Where:

θ = angle of repose
h = height in cms
r = radius in cms

The angle of repose has been used to characterize the flow properties of solids. It is a characteristic related to inter particulate friction or resistance to movement between particles.

III. Angle of repose limits

Table 5: Flow Properties and Corresponding Angles of Repose

Flow Property	Angle of Repose (degrees)
Excellent	25–30
Good	31–35
Fair—aid not needed	36–40
Passable—may hang up	41–45
Poor—must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

2. Density:

a. Bulk density (BD): It is the ratio of total mass of powder to the bulk volume of powder Weigh accurately 25 g of granules, which was previously passed through 22#sieve and transferred in 100 ml graduated cylinder. Carefully level the powder without compacting, and read the unsettled apparent volume. Calculate the apparent bulk density in gm/ml by the following formula[18].

Bulk density = weight of powder/ Bulk volume.

$$\mathbf{D_b} = \frac{M}{V_0}$$

M = mass of the powder

V_0 = bulk volume of the powder.

b. Tapped density (TD): It is the ratio of total mass of powder to the tapped volume of powder Weigh accurately 25 g of granules, which was previously passed through 40# sieve and transferred in 100 ml graduated cylinder of tap density tester which was operated for fixed number of taps until the powder bed volume has reached a minimum, thus was calculated by formula[18.]

Tapped density = Weigh of powder / Tapped volume

Dt = $(M) / (V_f)$.)

M = mass of the powder

V_f = tapped volume of the powder.

3. Carr's Index:

Compressibility index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down[19]. The formula for Carr's index is as below:

Compressibility index=100 x $tapped\ density - Bulk\ density/tapped\ density$

4. Hausner's Ratio:

Hausner's Ratio is a number that is correlated to the flow ability of a powder[19.]

Hausner's Ratio = $tapped\ density/\ bulk\ density$

IV. Compressibility index limits

Table 6: Scale of Flow ability (USP29-NF34)

Compressibility Index (%)	Flow Character	Hausner's Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59
> 38	Very, very Poor	> 1.60

B) Post compression studies:

1. General appearance: The formulated tablets were assessed for its general appearance and observations were made for shape, colour, texture and odour.

2. Average weight/Weight Variation: 20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg tablets and none by more than double that percentage.

$$Average\ weight = weight\ of\ 20\ tablets\ /\ 20$$

% weight variation = 100 * average weight – individual weight / average weight

Weight variation tolerance for uncoated tablets

Table 7: Acceptance criteria for tablet weight variation (USP 29-NF 34)

Average weight of tablet(mg)	% difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

3. Thickness: Thickness of the tablets (n=3) was determined using a Vernier calipers

4. Hardness test: Hardness of the tablet was determined by using the Monsanto hardness tester (n=3) the lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

5. Friability test: This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting.
Initial weight of 20 tablets is taken and these are placed in the Friabilator, rotating at 25rpm for 4min.
The difference in the weight is noted and expressed as percentage.
It should be preferably between 0.5 to 1.0%.

%Friability = $[(W_1-W_2)/W_1]$ X 100

Where, W_1= weight of tablets before test,
W_2 = weight of tablets after test

6. Content uniformity test

Ten tablets were weighed and powdered, a quantity of powder equivalent to 100 mg of Lamivudine was transferred to a 100 ml volumetric flask and 10 ml methanol is added. The drug is dissolved in methanol by vigorously shaking the volumetric flask for 15 minutes. Then the volume is adjusted to the mark with distilled water and the liquid is filtered. From prepared solution take 0.1ml solution in 10ml volumetric flask and make up to mark with distilled water. The Lamivudine content was determined by measuring the absorbance at 270nm after appropriate dilution. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

Calculate the quantity in mg of drug in the portion taken by the formula

$$\%assay = \frac{test\ absorbance}{standard\ absorbance} * \frac{standard\ concentration}{sample\ concentration} * \% \frac{purity\ of\ drug}{100} * 100$$

7. In vitro Dissolution Study:

900 ml of 0.1N HCl was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of $37^0C \pm 0.5^0C$. A tablet was placed in the vessel and was covered; the apparatus was operated up to 2hours at 50 rpm. After completion of 2hours remove the 0.1N HCL and add 6.8 phosphate buffer then continue the apparatus up to 12hours. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium and were analyzed spectrophotometrically at λ_{max} =280 nm using a UV-spectrophotometer (Lab India).

Table 8: Dissolution parameters

Parameter	**Details**
Dissolution apparatus	USP -Type II (paddle)
Medium	0.1N HCl and 6.8 Phosphate buffer
Volume	900 ml
Speed	50rpm
Temperature	37± 0.5 ºC
Sample volume withdrawn	5ml
Time points	1, 2, 4, 6, 8, 10 and 12 hours
Analytical method	Ultraviolet Visible Spectroscopy
Amax	280nm

C) In vitro Release Kinetics Studies:

The analysis of drug release mechanism from a pharmaceutical dosage form is important but complicated process and is practically evident in the case of matrix systems. The order of drug release from ER was described by using zero order kinetics or first order kinetics. The mechanism of drug release from ER was studied by using Higuchi equation and the Peppa's-Korsemeyer equation.

1. Zero Order Release Kinetics:

It defines a linear relationship between the fractions of drug released versus time.

$Q=k_0t$.

Where, Q is the fraction of drug released at time t and k_o is the zero order release rate constant. A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

2. First Order Release Kinetics:

Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that the drug release from most of the slow release tablets could be described adequately by the first-order kinetics. The equation that describes first order kinetics is

Log C= Log C_o-kt/2.303

Where C is the amount of drug dissolved at time t,

C_o is the amount of drug dissolved at t=0 and

k is the first order rate constant.

A graph of log cumulative of log % drug remaining Vs time yields a straight line. Will be linear if the release obeys the first order release kinetics.

3. Higuchi equation:

It defines a linear dependence of the active fraction released per unit of surface (Q) and the square root of time.

$Q=K_2t^{1/2}$

Where K_2 is release rate constant. A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependent[20].

4. Peppa's-Korsemeyer equation (Power Law):

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analysed by Peppa's-Korsemeyer equation (Power Law).

$$Mt/ M_\infty = K.t^n$$

Where, Mt is the amount of drug released at time t

M_α is the amount released at time α,

M_t/M_α is the fraction of drug released at time t,

K is the kinetic constant and n is the diffusion exponent.

To characterize the mechanism for both solvent penetration and drug release n can be used as abstracted. A plot between log drug release upto 60% against log of time will be linear if the release obeys Peppa's-Korsemeyer equation and the slope of this plot represents "n" value[21].the kinetic data of the formulations were included.

Nature of release of the drug from the designed tablets was inferred based on the correlation coefficients obtained from the plots of the kinetic models. The data were processed for regression analysis using MS EXCEL

Table 9: Drug release kinetics mechanism

Diffusion exponent(n)	Mechanism
0.45	Fickian diffusion
0.45 < n <0.89	Anomalous(Non- Fickian) diffusion
0.89	Case II transport
n > 0.89	Super Case II transport

V. Results and Discussion

1. Construction of Standard calibration curve of Lamivudine in 0.1N HCL:

The absorbance of the solution was measured at 280nm, using UV spectrometer with 0.1N HCL as blank. The values are shown in table. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml

Table 10: Standard Calibration graph values of Lamivudine in 0.1N HCL

Concentration (µg/ml)	Absorbance
0	0
2	0.136
4	0.283
6	0.409
8	0.546
10	0.683

Standard plot of Lamivudine plotted by taking absorbance on Y – axis and concentration (µg/ml) on X – axis, the plot is shown fig

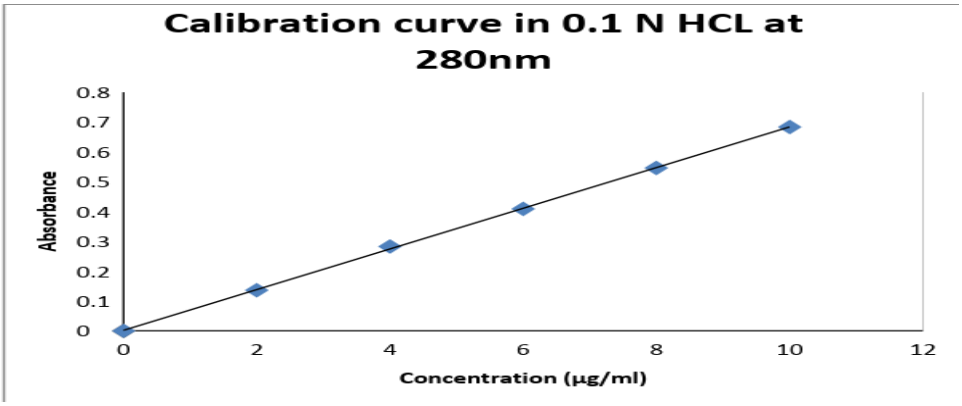

Figure: Standard calibration curve of Lamivudine in 0.1N HCL

Inference: The standard calibration curve of Lamivudine in 0.1N HCL showed good correlation with regression value of 0.999

2. Construction of Standard calibration curve of Lamivudine in 6.8 phosphate buffer:

The absorbance of the solution was measured at 270nm, using UV spectrometer with 6.8 phosphate buffer as blank. The values are shown in table. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml

Table11: Standard Calibration graph values of Lamivudine in 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
2	0.089
4	0.178
6	0.261
8	0.365
10	0.447

Standard plot of Lamivudine plotted by taking absorbance on Y – axis and concentration (µg/ml) on X – axis, the plot is shown fig

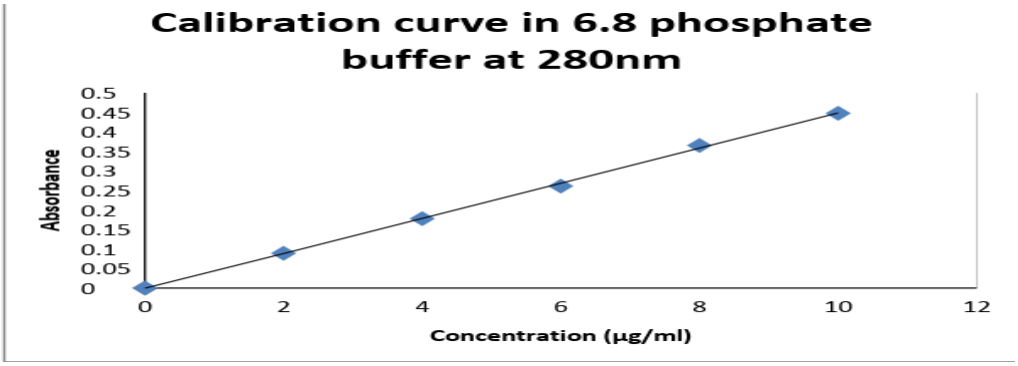

Figure: Standard calibration curve of Lamivudine in 6.8 phosphate buffer

Inference: The standard calibration curve of Lamivudine in 6.8 phosphate buffer showed good correlation with regression value of 0.999

Table12: Pre compression studies of Lamivudine SR tablets

Formulation Code	Bulk density (Kg/cm^3)	Tapped density (Kg/cm^3)	Cars index	Hausners ratio	Angle of repose (°)
F1	0.49	0.52	5.76	1.06	26.82
F2	0.41	0.47	12.76	1.14	33.13
F3	0.43	0.49	12.24	1.13	32.68
F4	0.46	0.51	9.80	1.10	29.32
F5	0.50	0.56	10.71	1.12	31.75
F6	0.45	0.53	15.09	1.17	37.83
F7	0.4	0.45	11.11	1.12	32.14

F8	0.48	0.55	12.72	1.14	34.38
F9	0.45	0.50	10	1.11	30.42

Table13: Post compression studies of Lamivudine SR tablets

Formulation Code	% weight vaiation	Thickness (mm)	% friability	% Drug Content	Hardness (Kg/cm^2)
F1	pass	5.06±0.11	0.142	101.3 ±1.2	5.56 ±0.057
F2	pass	5.06±0.15	0.151	102.3 ±1.7	5.03 ±0.115
F3	pass	5.03±0.057	0.62	100.1 ±1.2	5.01 ±0.1
F4	pass	5.1±0.1	0.154	100.7 ±1.1	5.63 ±0.05
F5	pass	5.03±0.05	0.132	99.6±1.5	5.63 ±0.03
F6	pass	5.03±0.15	0.143	98.9 ±2.3	5.5 ±0.05
F7	pass	4.93±0.05	0.110	100.2± 1.7	5.7 ±0.1
F8	pass	5.1±0.1	0.133	100.5± 1.4	5.53 ±0.04
F9	pass	5.02±0.2	0.13	99.2±1.1	5.69 ±0.05

Inference:

- The variation in weight was within the limit
- The thickness of tablets was found to be between 3.18 – 4.97 mm.
- The hardness for different formulations was found to be between 5.93 to 6.34 kg/cm^2, indicating satisfactory mechanical strength
- The friability was < 1.0% W/W for all the formulations, which is an indication of good mechanical resistance of the tablet.
- The drug content was found to be within limits 98 to 102 %.

Table14: In-vitro Dissolution results for Lamivudine SR tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	**0**
1	35	23	18	25	22	18	26	22	**14**
2	59	41	32	39	34	29	38	31	**23**
3	84	62	46	55	47	43	53	43	**31**
4	100	83	65	73	62	56	67	55	**39**
6		99	89	87	81	74	85	68	**56**
8			100	99	98	97	100	84	**73**
10								99	**89**
12									**100**

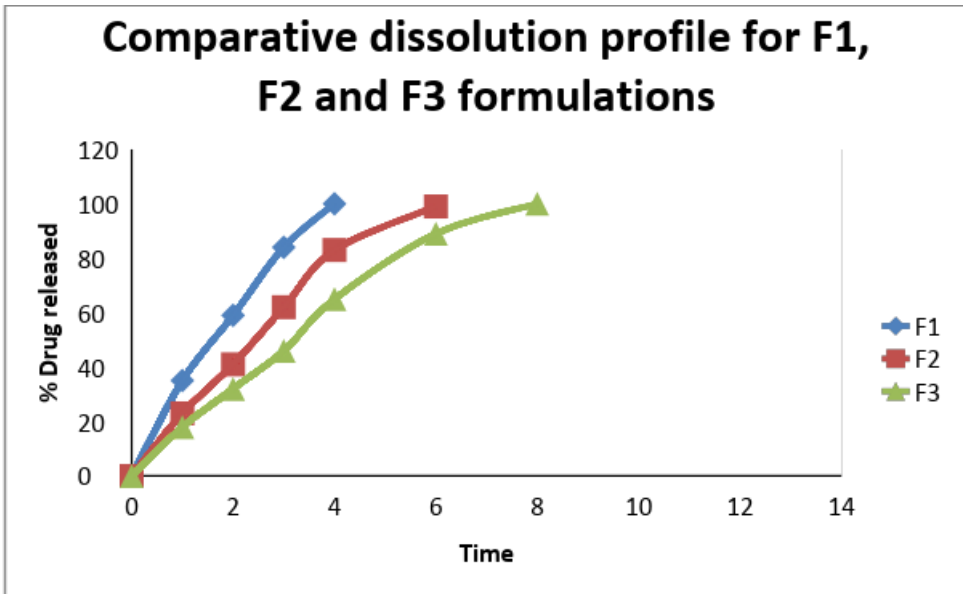

Figure : Comparative dissolution profile for F1, F2 and F3 formulations

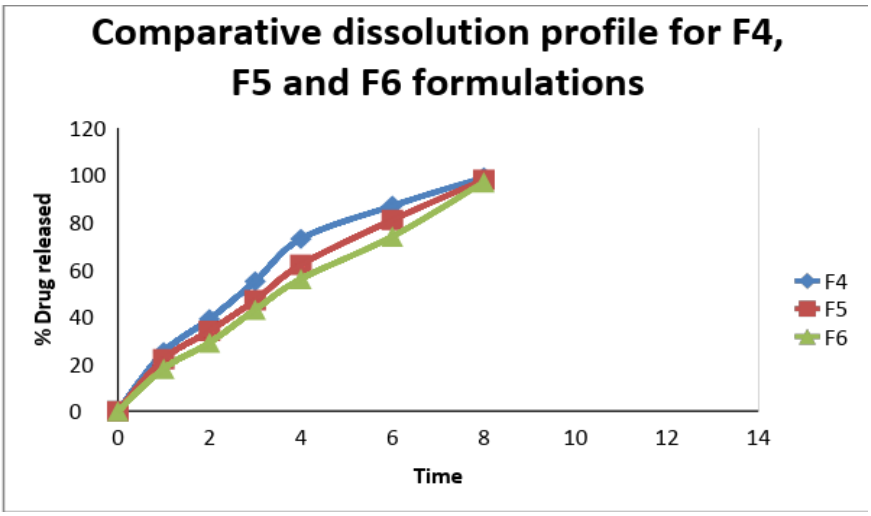

Figure : Comparative dissolution profile for F4, F5 and F6 used formulations

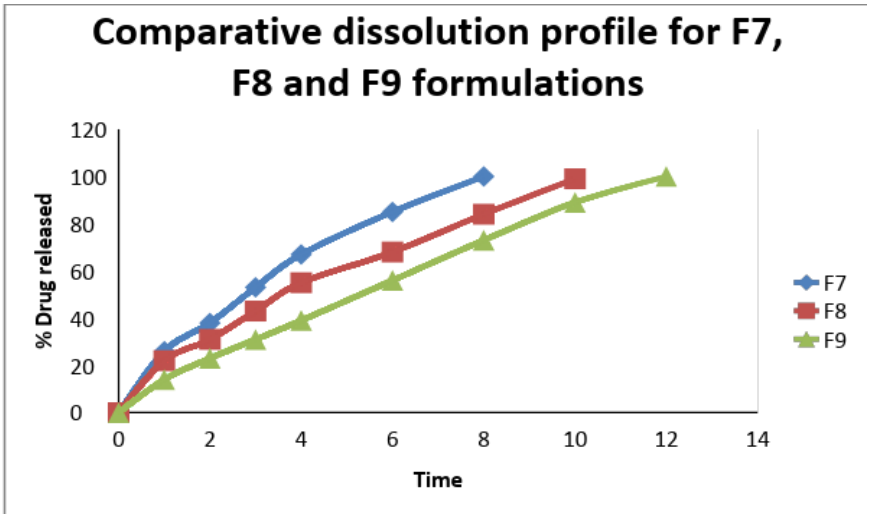

Figure : Comparative dissolution profile for F7, F7 and F9 formulations

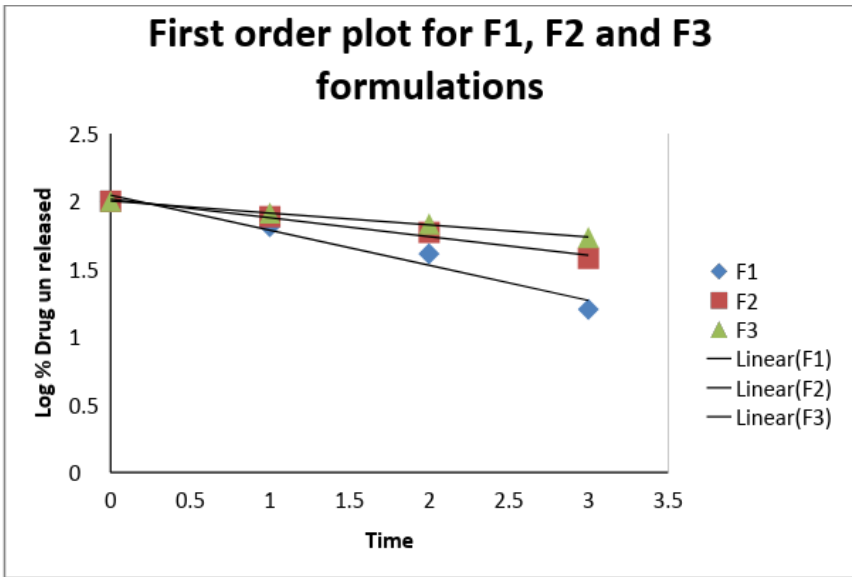

Figure : First order plot for F1, F2 and F3 formulations

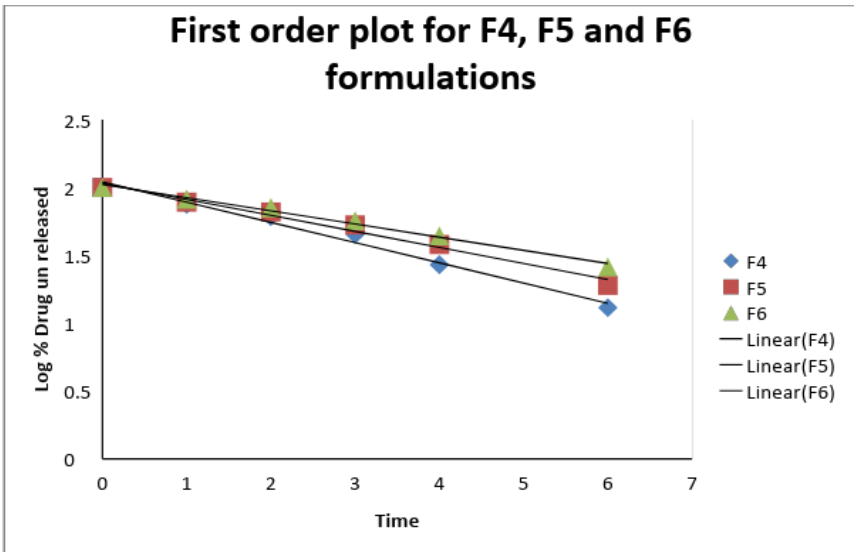

Figure : First order plot for F4, F5 and F6 formulations

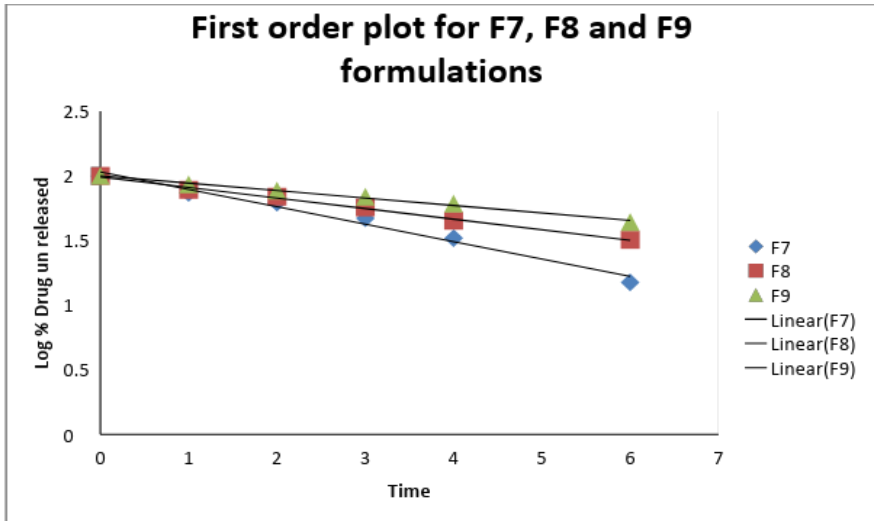

Figure : First order plot for F7, F8 and F9 formulations

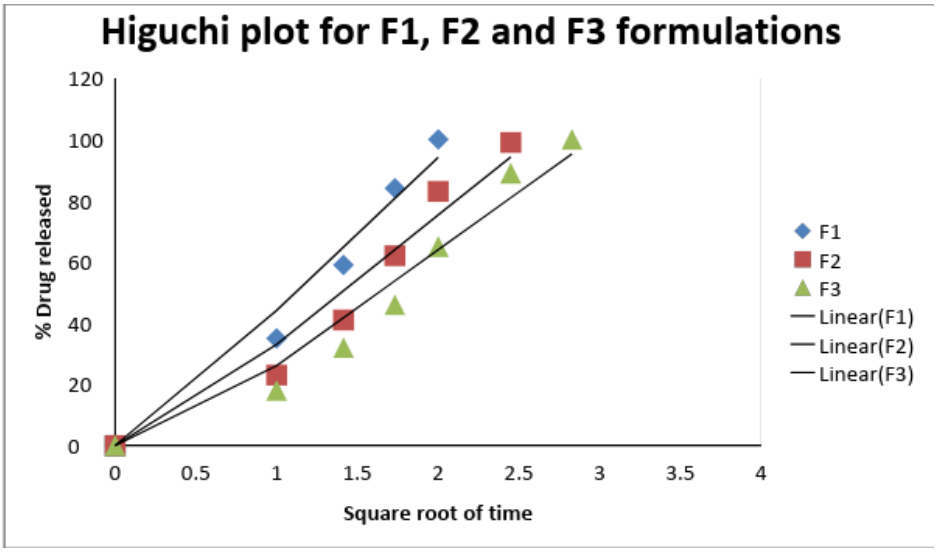

Figure: Higuchi plot for F1, F2 and F3 formulations

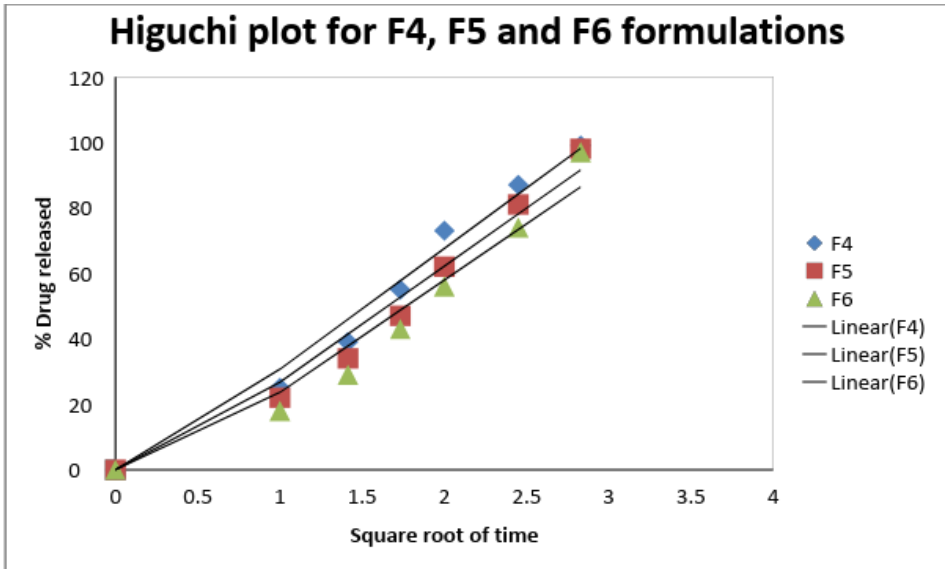

Figure: Higuchi plot for F4, F5 and F6 formulations

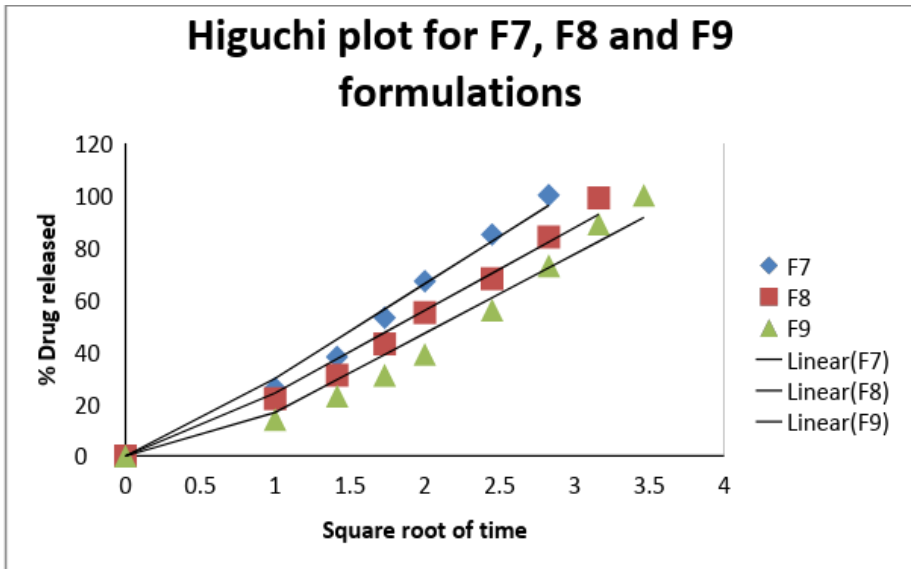

Figure: Higuchi plot for F7, F8 and F9 formulations

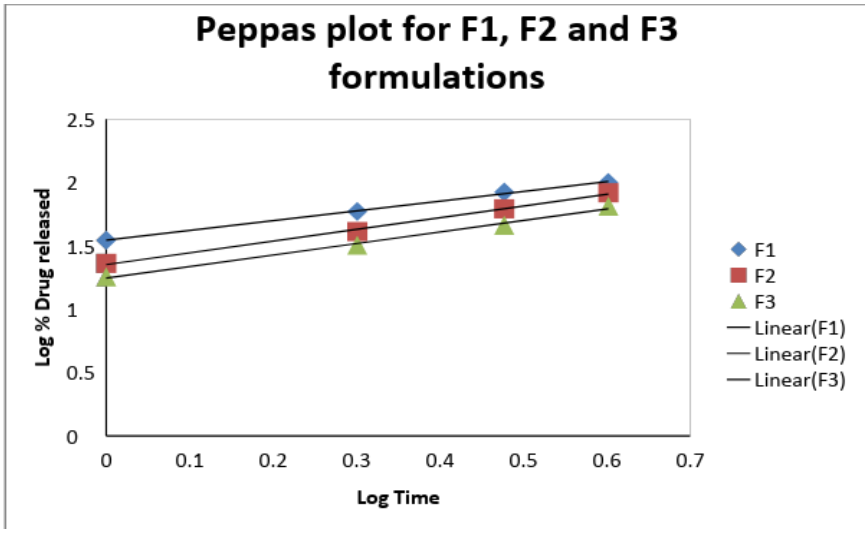

Figure: Korsmayers pepas plot for F1, F2 and F3 formulations

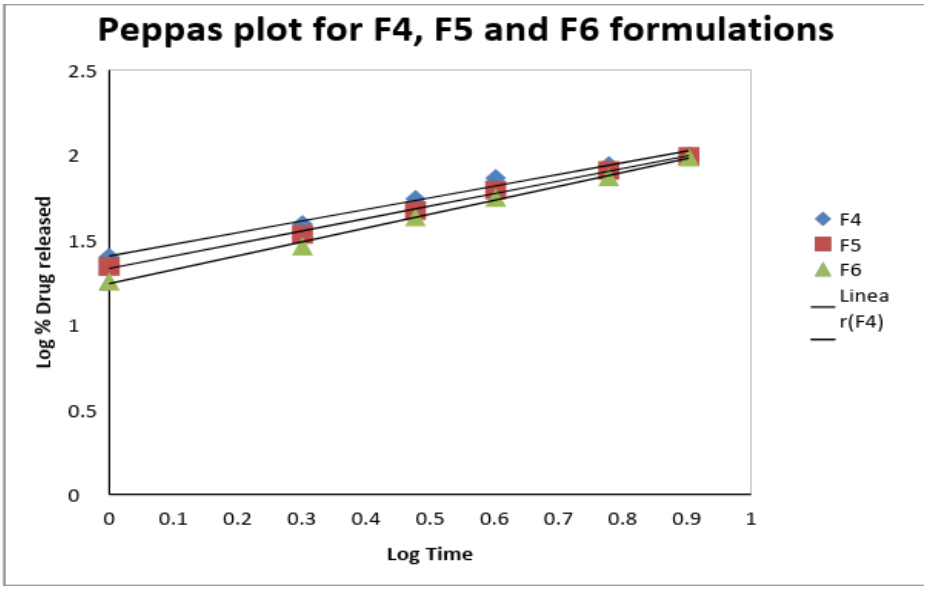

Figure: Korsmayers pepas plot for F4, F5 and F6 formulations

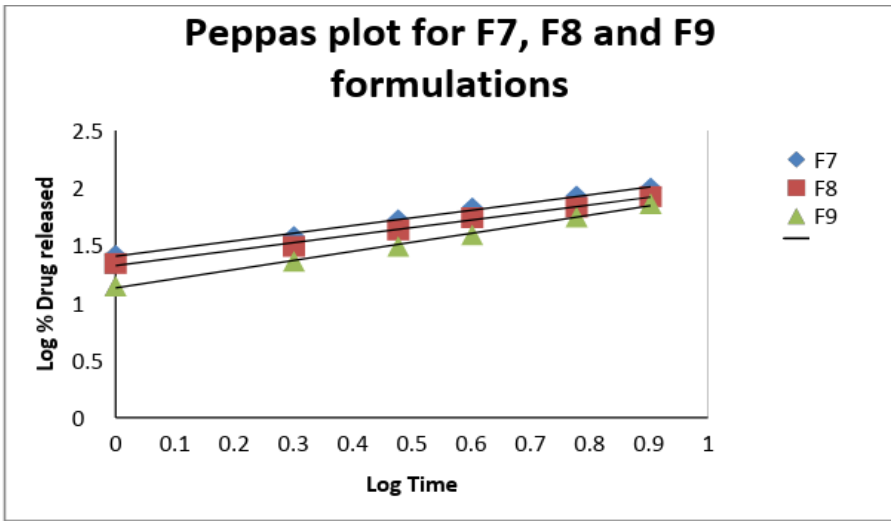

Figure: Korsmayers pepas plot for F7, F8 and F9 formulations

Table 15: R^2 value and n result table for best formulation

Formulation Code	R2 Values				"N" Values
	Zero Order	First Order	Higuchi	Peppas	
F9	0.994	0.992	0.947	0.996	0.791

Inference

- ➢ Among the different control release polymers Chitosan was showing highest drug release retarding capacity
- ➢ F9 was showing the satisfactory results.
- ➢ For the F9 formulation diffusion exponent n value is in between 0.45 to 0.89 so they are following non fickian anomalous diffusion modeol.
- ➢ Higuchi plots for F9 formulations are having good correlation values so the drug is releasing diffusion mechanism.

VI. Summary And Conclusion

The approach of the present study was to make a comparative evaluation among these polymers (Chitosan, Guargum and Xanthum gum) and to assess the effect of physico-chemical nature of the active ingredients on the drug release profile.

The angle of repose, bulk density, tapped density and compressibility index results shown that the formulation is suitable for direct compression method.

Formulated tablets showed satisfactory results for various Post compression evaluation parameters like: tablet thickness, hardness, weight variation, content uniformity and *in vitro* drug release.

This study have been showed that Lamivudine could be used in extended release drug delivery system by formulating it has extended drug delivery system, provides extend duration of action in therapeutic range without reaching toxic levels as in the case of conventional dosage forms. These dosage forms have the ability to reduce the dosing frequency.

By increasing the polymer, release rate of the drug decrease Formulations F9 gave better release i.e., 100% when compared to all formulation

By the results we can confirm that order of drug release first order and the mechanism of drug release from extended release tablets is Higuchi model.

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