FORMULATION DEVELOPMENT AND EVALUATION OF EXTENDED RELEASE MATRIX TABLET OF LAMIVUDINE

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***Abstract*: Oral course of drug administration is most seasoned and most secure method of drug administration. It groups a few benefits. It gives exact dosing without assistantship of administration. In ordinary oral medication conveyance framework, there is next to zero authority over release of drug, and viable fixation at the objective site can be accomplished by administration of horribly exorbitant dosage structure. Extended release technology is somewhat new field and as an outcome, research in the field has been amazingly ripe and has delivered numerous revelations. With many drug, the fundamental objective is to accomplish a consistent state blood level that is remedially viable and non-poisonous for an extended timeframe. The plan of legitimate dosage structure is a significant component to achieve this objective. Lamivudine is Antiretroviral with half-existence of 5 hours and requires numerous every day portions to keep up with sufficient plasma fixations. So it is chosen to set up an extended release Matrix tablet. The target of this current investigation is to foster an extended release Matrix tablet of Lamivudine which releases the drug in an extended way over a time of 12 hours, by utilizing various polymers and study on polymer fixation impact on release design.**

***Keywords*: Extended release, lamivudine, matrix tablet, sustained release.**

1. INTRODUCTION :

Drug administration. It forces a few benefits. It doesn't have the sterility issue and negligible danger of harm at the site of administration. It gives exact dosing without assistantship of administration. In ordinary oral drug delivery framework, there is almost no influence over release of drug, and successful concentration at the objective site can be accomplished by administration of horribly exorbitant dosage structure[1]. This sort of dosing design bring about continually changing, capricious and frequently sub or supra helpful plasma concentration, prompting stamped incidental effects sometimes. Also, the rate and degree of retention from ordinary definition might shift incredibly, contingent upon factor, for example, physiochemical properties of drug, presence of excipients, different physiological factors like presence or nonappearance of food, pH of gastrointestinal lot, G.I. motility and so forth the above issue can be limited by oral controlled drug delivery[2].

In oral controlled drug delivery the measure of drug release is continually predetermined and these steady releases of drug give a consistent blood plasma level of drug for a restorative reaction. The oral controlled drug delivery enjoy many benefit to ordinary delivery. It decline the change of drug plasma concentration, it lessen poisonousness, give a sustained impacts, decreased the dosing recurrence. Aside from other benefit it decreases aggregate sum of drug utilized, work on persistent consistence and diminished patient consideration time.The impediment of oral controlled release item are longer an ideal opportunity to accomplish remedial blood concentration, conceivable increment variety in bioavailability after oral administration, enhanced first pass impact, portion unloading, sustained concentration in oral portion case, absence of dosages adaptability and for the most part grater cost[3-7].

1.1. POTENTIAL ADVANTAGE OF SUSTAINED RELEASE DOSAGE FORM:

i. Avoid patient's consistence issue because of diminished recurrence of dosing.
ii. Blood level oscillation attributes of different dosing of customary dosage structure are decreased in light of the fact that an all the more even blood level is kept up with[8-9].
iii. Employ a less all out drug.
iv. Minimize or dispose of nearby or foundational incidental effects.
v. Minimize drug aggregation with chronic dosing.
vi. Obtained less capability of decrease in drug movement with chronic use.
vii. Improved proficiency in treatment.
viii. Cure or control condition all the more speedily.
ix. Improved control of condition for example diminished change in drug level.
x. Improved bioavailability of certain drugs[10-12].

2. MATERIALS AND METHODS :

2.1. Materials :

Lamivudine Pure Drug was purchased from Invochem Laboratory. Ethyl Cellulose was purchased from Feicheng Rutai Fine Chemicals CO.Ltd. Hydroxy propyl methyl cellulose K-15CR was purchased from Shineltsu LTD Japan. Metalose was purchased from Arihant trading Co.Ltd. PVP-K30 was purchased from Jyoti Associated Indore.

2.2. Methods :

Preparation of matrix tablet:

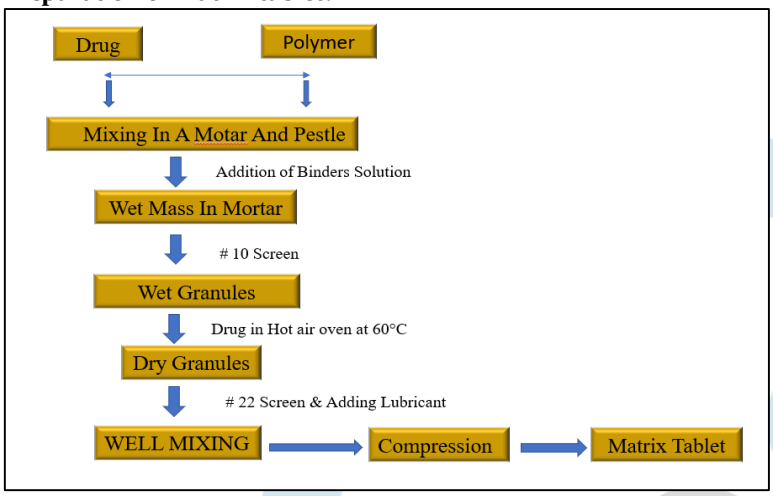


Fig.1. schematic representation of preparation of matrix tablet

Table no.1. Coating formula

S. No.	Ingredients	Quantity
1.	H.P.M.C. 6 cp	15 mg
2.	Etyl Cellulose	3 mg
3.	Polyethylene Glycol	4 mg
4.	Titanium Dioxide	1 mg
5.	Yellow Iron Oxide	1 mg
6.	Talcum	3 mg
7.	I.P.A.	0.5 ml
8	Methylene Chloride	0.3 ml

Procedure: Weigh accurately H.P.M.C 6 CP and Ethyl Cellulose and mixed in half portion of I.P.A. Dissolve titaneous oxide, yellow iron oxide, talc in half portion of I.P.A. mix well half portion of methylene chloride was added in above solution. Dissolve PEG 6000 in half portion of methylene chloride and added to above solution and stirred well[13-14].

3. RESULT AND DISCUSSION :

3.1. Pre-formulation study :

- **Fourier Transform Infra- Red Spectroscopy (FTIR)**

Fig.2. FTIR Spectrum of Lamivudine

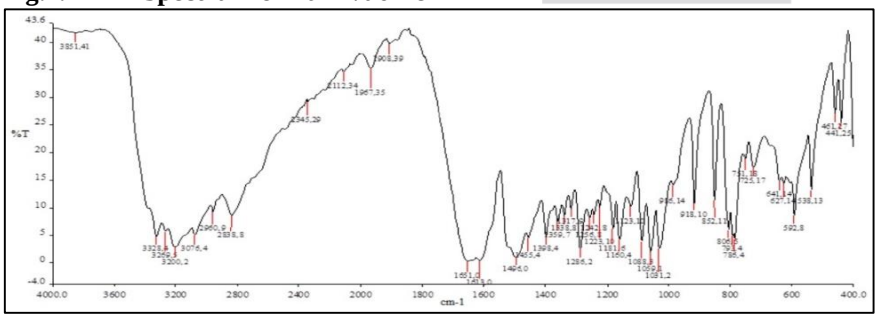


Table.2. FTIR Peak values

Sr. No.	Observed values of peaks (cm^{-1})	Standard Values of peaks (cm^{-1})	Functional Group
1	3328.4	3350-3300	NH_2 Stretch
2	3200.2	3250-3200	O-H stretch
3	1286.2	1300-1250	C-O-C stretch
4	1650.0	1650-1700	C=O stretch

DISCUSSION:

- Infrared spectrum of Lamivudine is shown in fig. The major peaks observed and corresponding functional groups are given in Table. Infra-red spectrum shows peak characteristics of structure of Lamivudine.
- The absorption bands shown by Lamivudine are characteristics of groups present in its structure. The presence of absorption bands corresponding to functional groups present in the structure of Lamivudine confirms the intensity and purity of the sample.

➢ **Characterization of UV Spectrophotometer :**

Detection of λmax :

Spectrum of drug - 0.1 N HCL

λmax – 269 nm

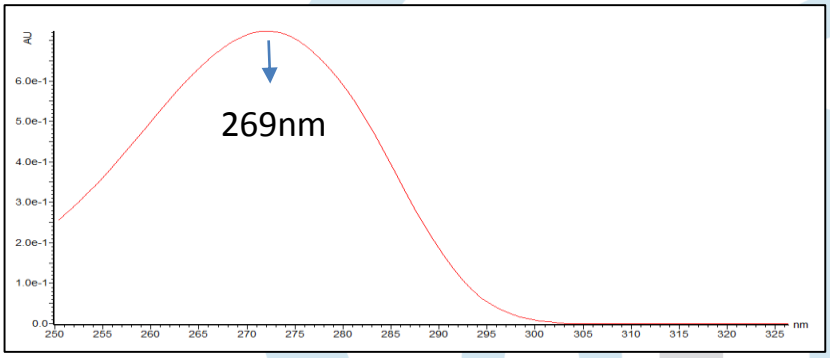


Fig.3. UV Spectrum of lamivudine in 0.1 N HCL

➢ **Calibration curve of Lamivudine**

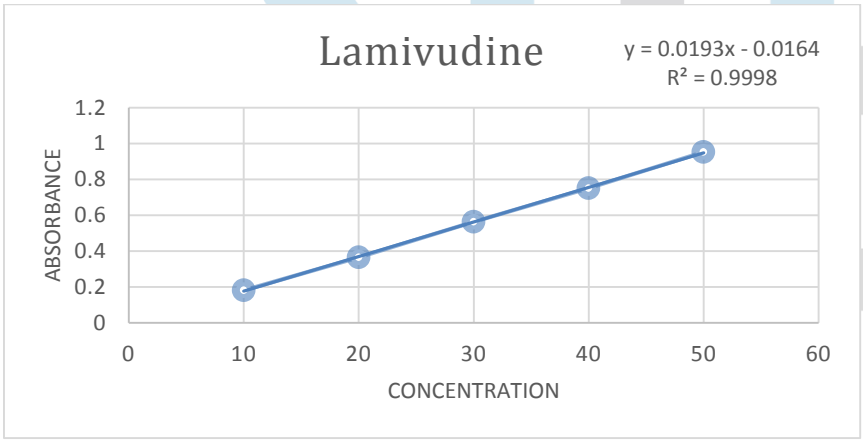


Fig.4. calibration curve of lamivudine

Table.3. concentration/ Abs.

Concentration	Absorbance at 269nm
10	0.1813
20	0.3649
30	0.5631
40	0.7514
50	0.9534

Evaluation of Powder :

Table.4. Pre-formulation studies of pure drug and polymers

Parameter	Result			
	Lamivudine	HPMC-K-15 CR	Maltose	Ethyl Cellulose
Angle of Repose	24	22	19	26
Bulk Density (gm/cm^3)	0.46	0.31	0.35	0.60
Tapped Density (gm/cm^3)	0.72	0.52	0.59	0.77
Compressibility Index	36.11	40.34	40.67	22.07
Hauser's Ratio	1.56	1.60	1.68	1.28

DISCUSSION:

Pre-formulation study was done initially and results directed for the further course of formulation. Based on Pre-formulation studies different polymers and pure drug.

Table.5. Pre-formulation studies of blend

BATCH NO.	BULK DENSITY (g/ml)	TAPPED DENSITY (g/ml)	COMPRSIBILITY (%)	HOUSNER RATIO	ANGLE OF REPOSE (°)
F1	0.314	0.389	19.2	1.237624	25^0
F2	0.368	0.426	13.6	1.157407	18^0
F3	0.399	0.476	16.2	1.193317	20^0
F4	0.354	0.416	17.51	0.86	$29^011'$
F5	0.399	0.476	16.2	1.193317	$20^o12'$
F6	0.421	0.512	17.7	1.215067	23^0
F7	0.458	0.534	14.3	1.166861	20^0
F8	0.316	0.409	29.43	0.77	$31^016'$
F9	0.366	0.457	24.86	0.80	24^0

DISCUSSION:

- Preformulation study was done initially and results directed for the further course of formulation. Based on Preformulation studies different batches of Lamivudine (F1 to F9) were prepared using selected excipients.
- Powders were evaluated for tests Angle of repose, Bulk density, tapped density, compressibility index, Hausner ratio before being punched as tablets.

Fig.6. Physico-Chemical Evaluation of Matrix Tablets

BATCH NO.	WEIGHT VARIATION	FRIABILITY (%)	HARDNESS (kg/cm^2)	THICKNESS (mm)	DRUG CONTENT (%)
F1	375	0.12	4.5	6.0	96.20
F2	379	0.19	5	6.3	97.26
F3	377	0.39	5	6.5	98.93
F4	378	0.14	5	6.0	97
F5	372	0.24	5	6.1	99.89
F6	372	0.11	5.5	6.5	98.53
F7	380	0.43	4	6.4	97.11
F8	379	0.16	5	6.3	97
F9	377	0.18	5.5	6.1	96.00

DISCUSSION:

The weight variation obtained for all the formulations in the range of 372 to 380mg and the thickness of the tablets of all the formulations was found in range of 6.0 to 6.5 mm which is in the good range. The hardness of the tablets of all the formulation was found in the range of 4 to 5.5 kg/cm2 which is excellent or in the acceptable range. The friability was found to be in the range 0.11 to 0.43% and the drug content was found to be in the range 97 to 99.89%.

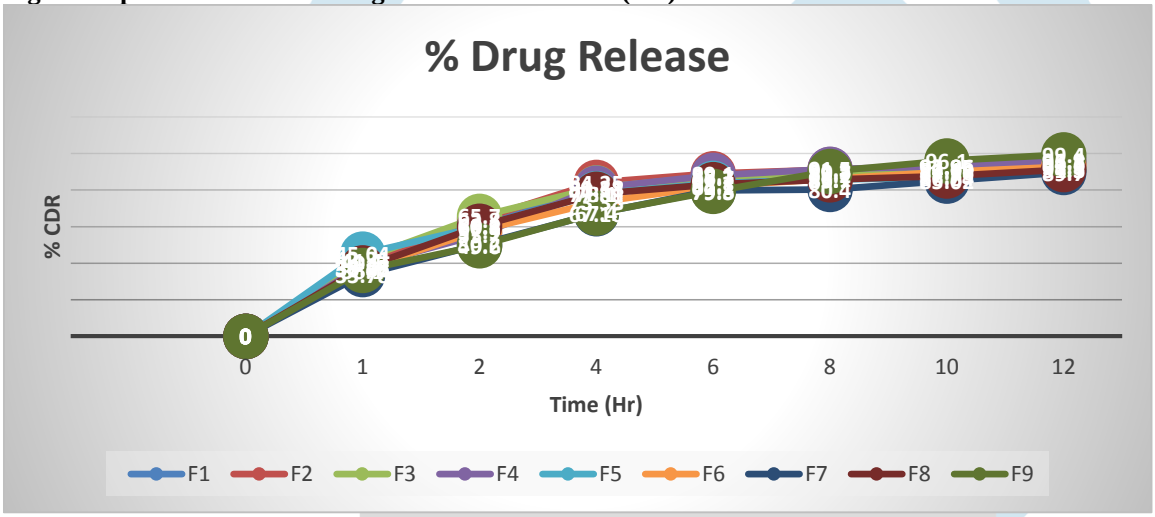
➢ **IN-Vitro Dissolution Studies**

Table.7. Cumulative % Release of Drug of various Formulations

Time (Hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	40.5	41.1	42.31	38.25	45.04	36.83	33.78	37.47	36.1
2	60.3	63.8	65.7	55.7	60.1	57.9	50.2	60.2	49.6
4	80.51	84.25	81.38	81.18	78.1	73.38	67.16	77.81	67.4
6	86.7	89.1	87.3	88.1	83.7	82.1	79.8	83.1	79.3
8	88.2	91.3	89.7	91.5	85.7	86.1	80.4	85.7	90.3
10	91.19	92.86	92.95	92.95	86.84	89.96	85.02	87.75	96.1
12	93.1	94.8	95.8	96.3	91.3	92.8	89.7	91.3	99.4

➢ **Percentage drug Release Profile of F1 to F9**

Fig.5. Graph of the Cum. % drug release versus Time (hrs)

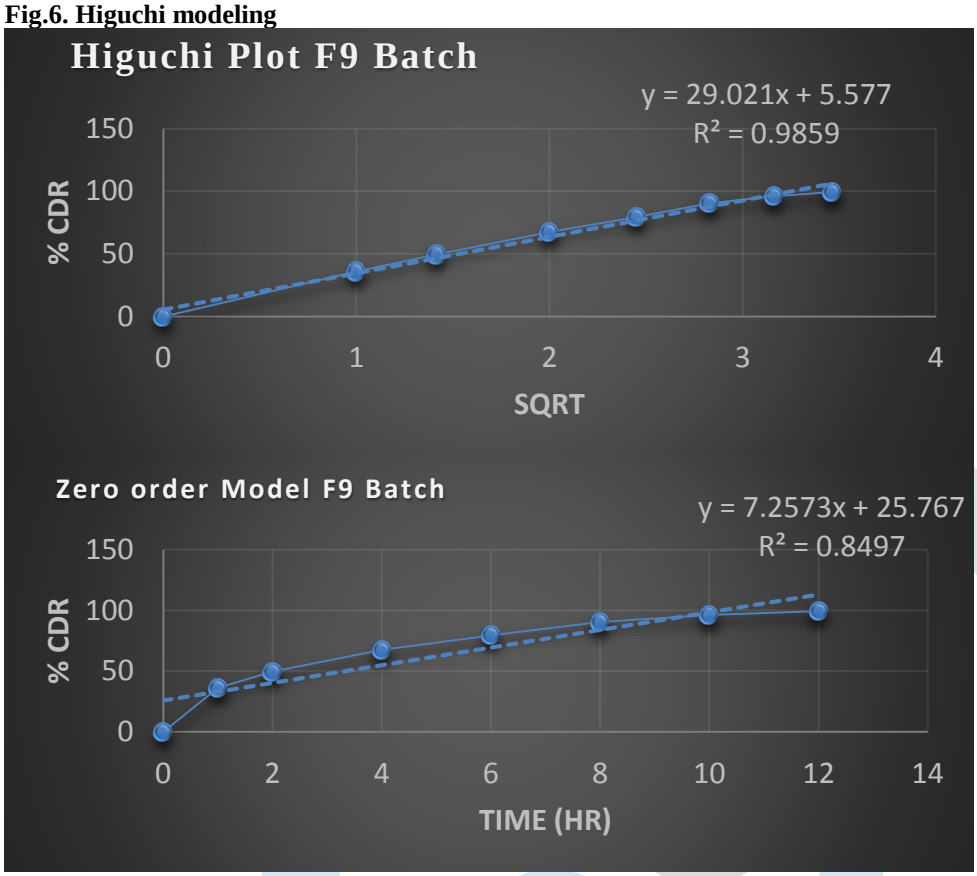


❑ **Kinetic assessment of Extended release Matrix tablet containing Lamivudine :**

Table.8. Higuchi Modeling

BATCHES	R^2 VALUE (ZERO ORDER)	R^2 VALUE (HIGUCHI)
F1	0.809	0.971
F2	0.787	0.961
F3	0.798	0.969
F4	0.802	0.975
F5	0.768	0.955
F6	0.811	0.950
F7	0.825	0.973
F8	0.802	0.968
F9	0.847	0.985

Fig.6. Higuchi modeling



CONCLUSION:

- The present study was undertaken with an aim to formulate develop and evaluate Lamivudine extended release matrix tablets using different polymers as release retarding agent.
- Pre-formulation study was done initially and results directed for the further course of formulation. Based on Pre-formulation studies different batches of Lamivudine were prepared using selected excipients. Powders were evaluated for tests Angle of repose, Bulk density, tapped density, compressibility index, and Hausner ratio before being punched as tablets.
- IR spectra studies revealed that the drug and polymers used were compatible.
- Various formulations of Extended release matrix tablets of Lamivudine were developed using various polymers viz, HPMC K-15CR, Hypermellose, Ethyl Cellulose in different proportions and combinations by Wet Granulation technique.
- From the above results and discussion it is concluded that formulation of Extended release matrix tablet of Lamivudine containing HPMC K-15 (9.28%) and Hypermellose (5.57%), Ethyl cellulose (5.57%) batch F9 can be taken as an ideal or optimized formulation Extended release matrix tablet for 12 hour release as it fulfills the requirements for extended release matrix tablet.

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