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FORMULATION DESIGN, DEVELOPMENT AND CHARACTERIZATION OF MATRIX TABLETS OF LAMIVUDINE BY USING NOVEL TECHNIQUE FOR CONTROLLED RELEASE

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ABSTRACT

Extending or controlling the release of highly water soluble drugs from matrix tablets is always a challenge. The research attempt was aimed to explore the embedment technique for the development of controlled release (CR) matrix tablets of highly water soluble drug i.e., lamivudine. Lamivudine controlled release matrix tablets were developed to prolong drug release time and prepared by embedment technique by employing anacardium occidentale tree gum, Moringa oleifera tree gum and delonix regia seed endosperm gum in different ratios as drug release-retarding polymers. Lamivudine granules were prepared and evaluated for the angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. All the formulations showed good flow properties. The compressed tablets were evaluated for the hardness, uniformity of weight, friability, tensile strength, swelling index, wetting time, drug content and *In-vitro* dissolution studies. All the formulations were in compliance with pharmacopeial standards. Through FTIR & DSC studies, it was confirmed that there was no interaction between drug, polymer and other excipients. Among all the formulations LET10 showed prolong release when compare to the other formulations. The drug release kinetics followed zero order. The diffusion exponent (n) values are found to be more than 0.9 (n>0.9) which indicated that the drug release was predominantly controlled by super case II transport system.

Keywords: Controlled Release, Lamivudine, Embedment technique, Moringa oleifera gum, Anacardium occidentale gum, Delonix regia seed

INTRODUCTION:

The oral route is the route most often used for administration of drugs. Tablets are the most popular oral formulations available in the market and are preferred by patients and physicians.

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In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses and therefore have several disadvantages (1). Controlled drug delivery technology is fast growing because of its many potential advantages like minimum fluctuations in plasma drug concentration and a reduced frequency of dosing when compared to the conventional dosage forms. Many newer technologies are also emerging for designing controlling drug delivery systems with improved efficiency and *embedment* (2) is one such novel technique. Lamivudine (Figure.1) is a potential anti- HIV agent, used for the long term treatment of HIV-1 infection as well

as for the treatment of chronic Hepatitis B. It has an elimination half-life of around 5-7 hours (3) Lamivudine requires multiple daily drug dosage in order to maintain adequate plasma concentrations. Therefore, it is a suitable candidate for making controlled release formulation. Matrix based CR formulations are the most popular and easiest to formulate on commercial scale. Extensive research was published on Lamivudine ER formulations, some of them are, mucoadhesive microspheres using Xanthan gum & SCMC with sodium alginate by ionic gelation method (4), extended-release matrix tablets using HPMC K100M & PEO by direct compression (5); controlled release matrix tablets using cross-linked sago starch (6); floating bioadhesive tablets using cellulosic polymers (7); sustained release matrix tablets using natural polymers by wet granulation technique (8); lamivudine CR tablets by using HPMC derivatives by direct compression (9).

The main objective of the present research work was to develop CR matrix tablets of Lamivudine for once–a–day dosing using natural gums by embedding technique. The matrix tablets were prepared as of two batches. In the first batch formulations, natural gums as the rate controlling polymer, was incorporated in the increasing quantities. The second batch formulations contained fixed quantity of natural polymers (at which the maximum controlling of the drug release was observed) and the method of granulation/manufacturing was altered i.e., by using wet granulation and comparing the drug release profiles of the tablets obtained from both the techniques.

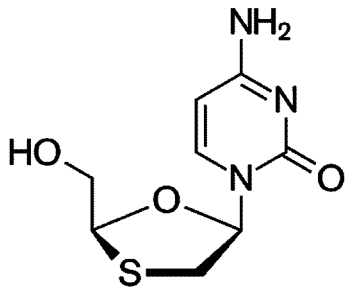

Fig.1: Structure of Lamivudine

MATERIALS AND METHODS:

MATERIALS: Lamivudine was a gift sample from Hetero Drugs Pvt. Ltd., Hyderabad. The gums were collected from Bapatla (anacardium occidentale gum), Tenali (moringa oleifere gum) & Guntur (delonix regia seed gum) regions. PVP K30, Lactose, Talc and Magnesium stearate were purchased from Merck Specialities Pvt. Ltd., Mumbai, India.

METHODS:

A) ISOLATION, PURIFICATION AND CHARACTERIZATION OF NATURAL GUMS

a) Isolation and purification of natural gums

Occasionally plant polysaccharides are available naturally in a relatively pure form. This is true of the various gums and mucilages exuded from the bark of trees and also from the seeds and fruits (10). Such gums can often be purified by dissolving in water, dialysing to remove low molecular weight compounds, precipitating by pouring into ethanol and collecting and drying.

***i) Delonix regia* seeds endosperm gum (DR) (11):**

Gulmohar seeds (100 g) (delonix regia seeds) were soaked in 800 mL of warm water for 24 hr. The water was discarded and the seeds were immersed in 800 mL of fresh boiling water for 4–5 hrs. The seeds were then removed from water, washed and the tegument broken and separated manually from the seed coat. The thick transparent cotyledon portion was separated from the seed coat and the embryonic axis. The cotyledon portions were milled and squeezed using several folds of muslin cloth to separate the marc from the filtrate. Absolute alcohol was then added to the filtrate to precipitate the polysaccharide. The polysaccharide was separated by filtration and dried in an oven at 60 ^{0}C until getting constant weight. The dried polysaccharide film was milled and sifted with a #80 to obtain the flour and was used as gum.

***ii) Anacardium occidentale gum (AO)* (12):**

The gum was extracted from exudates by a modified method of that reported by Okoye *et al.* (2010). Clean cashew exudates were pulverized and screened through #60. Thereafter, 100 g of the powder was soaked in 50 mL of distilled water at room temperature

with intermittent stirring for 24 hrs. At the end of the 24 hr, the dispersion was strained through a muslin bag and the resulting mucilage was precipitated by mixing it with thrice its volume of 96% ethanol. The precipitated gum was filtered using a filter cloth, heated in a hot-air oven at 50 ^{0}C for 12 hrs and at the end, it was pulverized and passed through #80 and stored in air tight container over silica gel for further use.

iii) *Moringa oleifera gum* (MO) (13):

The gummy extracts from the injured sites of moringa trees were collected, dried, pulverized and passed through #80. The dried gum was stirred in distilled water (10 g in 250mL) for around 6-8 hrs at room temperature using magnetic stirrers. The Supernatant was obtained by centrifugation and kept separately, the residue was washed with water and this water was added to the separated supernatant. This process was repeated for 4-5 times. The finally obtained supernatant was made up to 500 ml with water and then treated with ethanol by continuous stirring. The precipitated material was washed with distilled water and further dried at 50-60 ^{0}C in an oven. Later the dried portion was pulverized and passed through #80 and stored in an air tight container for further use.

b) Physicochemical characterization of natural gums (11, 14, 15)

The three natural gums were subjected to the following characterization studies**.**

i) ***pH determination:*** pH was determined by shaking a 1% w/v solution of the sample in water for 5 min and the reading were noted by digital pH meter.

ii) ***Viscosity Determination:*** The viscosity of 1% w/v gum solution was measured using Brookfield DV-E Viscometer.

iii) ***Swelling index (SI):*** About 1 g of gum powder was weighed accurately and transferred to a 100 mL measuring cylinder. The initial volume of the powder in the measuring cylinder was noted. The volume occupied by the gum sediment was shaken gently and set aside for 24 hrs. The volume occupied by the gum sediment was noted after 24 hrs. Swelling capacity of the gum was expressed in terms of swelling Index. Swelling Index was expressed as a percentage and calculated according to the following equation:

$$SI = [Xt - Xo)/Xt] \times 100$$

Where, Xo is the initial height of the powder in graduated cylinder,

Xt denotes the height occupied by swollen gum after 24 hrs.

iv) ***Water retention capacity:*** The contents from the measuring cylinder from the above test (SI) were filtered through a muslin cloth and the water was allowed to drain completely into a dry 100 mL graduated cylinder. The volume of water collected was noted and the difference between the original volume of the water and the volume drained was taken as water retained by the sample referred as water retention capacity or water absorption capacity of the gum.

v) ***Moisture sorption capacity:*** Moisture sorption study was performed using programmable environmental test chamber (Remi Labs, Mumbai, India). 1g of powdered gum was taken in a petri dish and spread uniformly. Then it was kept in programmable environmental test chamber 37±1^{0}C and 100% relative humidity for two days. The moisture sorption was calculated by recording weight difference of the sample before and after exposure to programmable environmental test chamber.

vi) ***Preliminary phytochemical screening*****:** The preliminary phytochemical screening of gum powder was carried out for the detection of various phyto constituents. The presence of carbohydrate (Molisch's test), reducing sugar (Fehling's solution), alkaloid (Wagner test), gum (Ruthenium red test), flavonoids (Shinoda test), steroids (Liberman Burchard test), and tannins (Ferric chloride test) were analyzed.

B) DRUG-EXCIPIENTS COMPATIBILITY STUDIES

a) Fourier transforms infrared spectroscopy (FT-IR)

The physicochemical compatibility between lamivudine and natural gums used in the research was carried out by subjecting to IR spectral studies using Bruker Fourier Transform infrared Spectrophotometer, USA. The samples were prepared by mixing the 100 mg of the drug with the100 mg of polymers (1:1 ratio). These samples were scanned under diffuse reflectance mold and plotted the graph

by the KBr pellet method and spectra were recorded in the wavelength region between 4000 $cm^{-1}$to 400 cm^{-1}. The spectra obtained for the pure drug was compared with that of the physical mixtures of the drug with polymers.

b) Differential scanning calorimetry (DSC)

The thermal behavior of the drug alone (lamivudine) and with polymers was analyzed by using DSC instrument. The drug and its physical mixture with polymers were weighed, crimped in aluminum pans and analyzed at a scanning temperature range from 50 to 400 ^{o}C at the heating rate of 10 ^{o} C/min in nitrogen atmosphere [10].

C) DESIGN & DEVELOPMENT OF CONTROLLED RELEASE MATRIX TABLETS OF LAMIVUDINE

a) Preparation of matrix tablets using Embedment method

In this technique, tablets were prepared in two successive steps.

Step 1: Embedment of the drug in polymer matrix

The embedment of the drug in polymer matrix was done by, weighed quantities of polymer(s), according to the formulae as shown in the table 3, was transferred into a porcelain dish. To this, ethanol was added slowly with continuous trituration until a smooth paste was formed. Then the weighed quantities of the drug i.e., lamivudine and lactose as diluent, according to the formulae, were incorporated into the smooth paste of the polymer(s) by levigation technique. Then the obtained semisolid mass was spreaded over the walls of the porcelain dish and was dried in a hot air oven until complete drying. Then the dried material was scrapped and passed through #20. The granules obtained were studied for their densities, flow properties and compressibility prior to the compression.

Step 2: Lubrication & Compression

The above obtained drug entrapped polymer matrix granules were properly lubricated with previously screened (through #100) and weighed quantities of magnesium stearate and talc. Then the blend was subjected to compression into tablets weighing 720 mg each using 10 stage rotary tablet press equipped with 12 mm round, flat punches. The obtained tablets were stored properly until further use.

b) Matrix Tablets using Wet granulation method

In this method, 2% PVP K30 solution was used as binder. To prepare the binder, 2g of PVP K30 powder as slowly added to the distilled water in 100 mL volumetric flask with continuous stirring until all of the powder was dissolved, then made the volume upto 100 mL with distilled water. The mixture was kept aside for further use.

The drug, polymer(s) and other excipients were screened (through #80) before processing and weighed according to formulae as shown in the table 3. Initially, the drug and polymer(s) were transferred into a clean mortar and mixed thoroughly. The powder mixture was made into wet mass by adding 2% PVP K30 solution as granulation fluid (binder) and triturated with pestle. Then the wet mass was passed through sieve #16 and the obtained granules were subjected to drying in hot air oven at 60 °C. Then dried granules were passed through mesh #20. The granules thus obtained were transferred to a tray. Magnesium stearate and talc were added and the blend was subjected to mixing for 5 min. The lubricated granules were further subjected to compression. The lubricated granules were transferred into the hopper of a rotary tablet press and die volume and hardness of the tablets were adjusted. The granules were compressed into tablets weighing 720 mg each using 10 stage rotary tablet press equipped with 12 mm round, flat punches. The obtained tablets were stored properly until further use.

D) EVALUATION OF MATRIX TABLETS OF LAMIVUDINE

i) **Flow properties**

The prepared granules were evaluated for flow properties. Different tests that were carried out are angle of repose, bulk density, tapped density, compressibility index, and Hausner ratio was calculated. The results were shown in table-4.

ii) **Evaluation of physical parameters**

The physical evaluation parameters like thickness, hardness, tensile strength were measured for all the formulations. The measurement of tensile strengths provides a more fundamental measure of the mechanical strength of the compacted material and takes into account the geometry of the tablet. If tablets fail in tension, the breaking force can be used to

calculate the tensile strength. Tensile strength of tablets was calculated using the following formula and the results were given in table-6.

$$T = 2F_c / \pi d\ t$$

Where, F_c - Crushing strength/Hardness, d – Diameter & t - Thickness of tablet.

iii) **Friability**

Ten tablets were carefully weighed and loaded into the drum of a friabilator and operated for 4 min at 25 rpm. Then tablets were collected, dedusted between tissue towels and reweighed. Percentage friability was calculated and given in table-6.

$$\%\ Friability = \frac{Initial\ Wt. - Final\ Wt.}{Final\ Wt.}\ X\ 100$$

iv) **Weight Variation**

Twenty tablets from each batch at random were taken and weighed. The average weight was calculated, then each tablet was weighed individually and weights of each tablet were noted. The weights of individual tablets were then compared with the average weight that was already calculated. The deviation if any in the weight of individual tablets from the average weight was checked. If any weight variation is there, that should be within the I.P limits. The test was considered correct if not more than two tablets fall outside the I.P limits out of twenty tablets taken for the test. Results were given in the table-6.

$$\%\ Weight\ Variation = \frac{Avg.\ Wt. - Individual\ Wt.}{Avg.Wt.}\ X\ 100$$

v) **Uniformity of Drug Content**

5 tablets were taken and grinded to powder. 100 mg of the drug equivalent tablet powder was taken and dissolved in 10 mL of methanol and the volume was made up to 100 mL with distilled water in a 100 mL volumetric flask. Then the solution was filtered to remove any insoluble matter and the filtrate was taken, made suitable dilutions. Then drug content was estimated by using the UV spectroscopic method and the drug content was calculated by using the standard calibration curve. The results were given in table-6.

vi) ***In-Vitro*** **Dissolution Studies**

Dissolution studies on each formulation were performed by using USP type II apparatus, employing 900ml of 0.1N HCl for first 2 hrs and followed by phosphate buffer 6.8 pH as a dissolution medium. The paddles were operated at a 50rpm and the temperature was maintained at 37±0.5°C throughout the experiment. Samples were withdrawn at regular intervals for 18hrs and replaced with 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 'thermo scientific' double beam UV – VIS spectrophotometer at 270nm. The dissolution studies on each formulation were conducted in triplicate and the average of 3 values were taken for studies.

vii) **Evaluation of Kinetics**

Various dissolution parameters such as zero order rate constant, first order rate constant, Higuchi constant and Peppas constant were calculated from the dissolution data obtained from various formulations. The results were given in table-5.

RESULTS AND DISCUSSION:

The spectrophotometric method used for the estimation of lamivudine in the dissolution medium (0.1N HCl & Phosphate buffer pH 6.8) were found to be linear and reproducible. The standard calibration curve yields a straight line, which shows that the drug follows Beer's law in the concentration range of 2-14 µg/mL. Reproducibility of the method was tested by analyzing 6 separately weighed samples of drug lamivudine. The results were shown in figures 2. Thus, the method was found to be suitable for the estimation of lamivudine in dissolution medium.

Drug – Excipient compatibility studies:

The preformulation studies performed on lamivudine alone and along with excipient admixtures were found to be stable with no physical changes in the color and amorphous nature.

- **FTIR Studies:**

FTIR studies of lamivudine alone and admixtures with excipients were carried out to study the interaction between the drug and excipients used. The results were shown in figure 3a – 3d. C=O stretching, O-H stretching, N-H stretching, Asymmetrical C-O-C stretching and Symmetrical C-O-C stretching of pure lamivudine and the

optimized formulations were almost in the same region of wave number ranging from 3326.95cm^{-1} to 1160.39cm^{-1}. It showed that IR spectrum of lamivudine and excipients admixtures were having similar fundamental peaks and pattern. This indicated that there were no drug excipients interactions in the formulations.

- **Differential Scanning Calorimetry:**

DSC studies of Lamivudine alone and admixtures with excipients were carried out to study the interaction between the drug and excipients used and the results of the study were shown in figures 4a – 4d. The DSC Thermogram of Lamivudine showed sharp endothermic peak at 180.5^{0}C. The DSC Thermograms of drug excipient admixtures showed sharp endothermic peaks for Lamivudine with AO gum, MO gum & DR gum at the temperatures 182.8^{0}C, 182.2^{0}C and 181.4˚C respectively. This indicated that there were no drug excipients interactions in the formulations. Based upon these studies suitable excipients were selected and Lamivudine controlled release matrix tablets were formulated.

Physicochemical & Phytochemical characterization of natural gums:

The gums were kept for physicochemical analysis, the results for each parameter were found to be within the limits and also satisfy the need of formulations. The results were given in table 1. The purified gums that are obtained were subjected to their phytochemical characterization that is to evaluate the nature of the gums. All the three gums passed the molish test, fehlings test and rheuthenium red test confirming that the three gums contain carbohydrates, reducing sugars and gum properties respectively and the results were shown in the table 2.

Evaluation parameters:

The thickness of the tablets was found to be in between 4.39-4.52mm and the hardness was found to be in between 5.02 – 5.78 kg/cm^2. The tensile strength of the tablets was found to be in between 5.81*10^5 – 6.76*10^5 N/m^2. The tablets satisfied friability requirement, as the % friability values were less than 1% (0.32-0.57). The drug content estimations showed values in the range of 97.89 to 102.34%, which reflects good uniformity in drug content among all formulations. All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeia limits of ± 5% of the weight. All the formulations showed values within the prescribed limits for tests like hardness, friability and weight variation which indicate that the prepared tablets are of standard quality. These values were shown in table-6. The results of the in vitro drug release studies for formulations containing natural gums were shown in figure-5. Among all the formulations LET10 formulation showed the prolonged drug release up to 18 hrs. The controlled drug release may be due to increased proportion of polymer. Based on the release rate constant and % of drug release at the end of 18 hours the release retarding capacities of the polymers were arranged in the following order, Endo sperm gum of Delonix Regia seeds > Cashew nut tree gum> Moringa oleifera tree gum. As the concentration of gum or the rate retarding polymer increased the drug release from the controlled release matrix tablets was found to be decreased in case of all the formulations. The results were shown in figure-5 & 6.

Dissolution parameters such as zero order rate constant, first order rate constant, Higuchi constant and Peppas constant were calculated from the dissolution data and the results were given in table 5. The 1st order plots for the matrix tablet formulations prepared by embedment technique were not linear when compared to the zero order. All the matrix tablet formulations were found to be linear with zero order release rate with R^2 values in the range of 0.95 - 0.99. Thus the rate of drug release from all the matrix tablet formulations was concentration independent and was linear with zero order release rate constant. The Higuchi plots i.e., the amount of drug released *vs* square root time plots were found to be linear with R^2 values in the range of 0.80 – 0.95.The drug release from the matrix tablet formulations was not by fickian diffusion process. The release exponent (n values) for all the matrix tablet formulations were in the range of >0.9 which are obtained from peppas plot indicated that the drug release was by super case II transport system.

Table No 1: Physicochemical Properties of Gums

S. No	Property	Delonix regia seed gum	Anacardium occidentale tree gum	Moringa oleifera tree gum
1	pH of 1% w/v solution	7.6	7.4	6.8
2	Viscosity of 1% w/v solution	1400cps	1250cps	900cps
3	Swelling index%	700	600	450
4	Water retention capacity	3.8ml	3.2ml	2.7ml
5	Hydration capacity	1.5±0.03	1.2 ± 0.06	1.3±0.02
6	Moisture sorption capacity	1.57±0.52	1.44±0.21	1.41±0.32

Table No 2: Phytochemical Analysis of Natural Gums

S. No	Name of the test	*Delonix regia* seed gum	*Anacardium occidentalis* tree gum	*Moringa oleifera* tree gum
1	Test for carbohydrates (Molish test)	+	+	+
2	Test for Gums (Ruthenium red test)	+	+	+
3	Test for Reducing sugars (Fehling's test)	+	+	+
4	Test for Alkaloids (Wagner test)	-	-	-
5	Test for Steroids (Salkowski test)	-	-	-
6	Test for Flavonoids (Shinoda test)	-	-	-
7	Test for Tannins (Ferric chloride test	-	-	-

+ Present, - absent

Table No. 3: Formulae of controlled release matrix tablets of Lamivudine

Formulation Code / Ingredients (in mg)	LE T1	LE T2	LE T3	LE T4	LE T5	LE T6	LE T7	LE T8	LE T9	LE T10	LE T11	LE T12	LW G1	LW G2	LW G3
Lamivudine	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
DR gum	100	-	-	200	-	-	300	-	-	400	-	-	400	-	-
AO gum	-	100	-	-	200	-	-	300	-	-	400	-	-	400	-
MO gum	-	-	100	-	-	200	-	-	300	-	-	400	-	-	400
PVP K30	-	-	-	-	-	-	-	-	-	-	-	-	6	6	6
Lactose	306	306	306	206	206	206	106	106	106	6	6	6	-	-	-
Talc	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Magnesium stearate	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Total weight	720	720	720	720	720	720	720	720	720	720	720	720	720	720	720

Table No. 4: Flow properties of lamivudine granules

Formn. Code	Results (Avg. ± SD; n=6)				
	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (^{0})
LET1	0.909 ± 0.008	1.020 ± 0.012	10.688 ± 0.542	1.121 ± 0.017	23.67 ± 0.324
LET2	0.934 ± 0.009	1.039 ± 0.011	10.418 ± 0.871	1.118 ± 0.018	20.08 ± 0.456
LET3	0.910 ± 0.014	1.038 ± 0.013	12.121 ± 0.852	1.140 ± 0.023	23.35 ± 0.843
LET4	0.925 ± 0.012	1.038 ± 0.014	10.766 ± 0.438	1.128 ± 0.021	19.91 ± 0.432
LET5	0.911 ± 0.011	1.028 ± 0.012	11.201 ± 0.652	1.121 ± 0.015	19.46 ± 0.612
LET6	0.935 ± 0.015	1.039 ± 0.016	10.934 ± 0.728	1.111 ± 0.014	20.98 ± 0.651
LET7	0.918 ± 0.013	1.032 ± 0.013	11.236 ± 0.673	1.126 ± 0.016	21.55 ± 0.648
LET8	0.918 ± 0.013	1.023 ± 0.011	12.583 ± 0.743	1.119 ± 0.021	19.08 ± 0.743
LET9	0.943 ± 0.013	1.041 ± 0.015	09.764 ± 0.996	1.106 ± 0.023	19.80 ± 0.721
LET10	0.943 ± 0.013	1.046 ± 0.019	09.167 ± 0.761	1.111 ± 0.016	24.31 ± 0.754
LET11	0.927 ± 0.015	1.029 ± 0.016	09.202 ± 0.732	1.110 ± 0.015	22.29 ± 1.342
LET12	0.932 ± 0.012	1.034 ± 0.011	09.984 ± 0.842	1.109 ± 0.021	23.08 ± 0.650
LET10A	0.929 ± 0.015	1.041 ± 0.015	12.511 ± 0.974	1.121 ± 0.015	21.29 ± 0.874
LET11A	0.938 ± 0.011	1.043 ± 0.018	10.581 ± 0.974	1.118 ± 0.019	24.36 ± 1.632
LET12A	0.917 ± 0.016	1.034 ± 0.018	11.245 ± 0.632	1.129 ± 0.012	24.03 ± 1.182

Table No. 5: Dissolution kinetics of lamivudie CR matrix tablets of all formulations

Formulation	Regression coefficient (R^2) value			Dissolution rate constant (%dose/hr)	Peppas 'n' value
	Zero – order	First – order	Higuchi		
LET1	0.991	0.674	0.852	32.46	1.499
LET2	0.993	0.655	0.901	49.11	1.709
LET3	0.955	0.870	0.981	71.83	1.883
LET4	0.991	0.744	0.850	13.54	1.136
LET5	0.968	0.718	0.902	22.54	1.407
LET6	0.995	0.752	0.878	34.12	1.533
LET7	0.994	0.752	0.866	7.51	0.943
LET8	0.997	0.659	0.834	10.34	1.026
LET9	0.984	0.641	0.874	13.71	1.170
LET10	0.999	0.677	0.842	5.65	0.749
LET11	0.998	0.617	0.836	6.47	0.805
LET12	0.996	0.621	0.805	8.41	0.894
LET10A	0.747	0.939	0.990	7.63	1.318
LET11A	0.710	0.902	0.993	8.80	1.375
LET12A	0.696	0.920	0.982	12.81	1.451

Table No. 6: Results of various evaluation parameters of lamivudine CR tablets

Formn. Code	Results (Avg. ± S.D.; n=6)					
	Thickness (mm)	Hardness (Kg/cm^2)	Tensile Strength (N/m^2)	Average Weight (mg)	Friability (%)	Assay (%)
LET1	4.46 ± 0.012	5.26 ± 0.16	$6.144*10^5$ ± 0.041	719.45 ± 0.63	0.47 ± 0.033	100.12 ± 0.52
LET2	4.41 ± 0.023	5.19 ± 0.21	$6.168*10^5$ ± 0.031	720.67 ± 0.66	0.55 ± 0.027	101.32 ± 0.46
LET3	4.49 ± 0.026	5.02 ± 0.23	$5.841*10^5$ ± 0.045	719.45 ± 0.42	0.57 ± 0.026	102.34 ± 0.24
LET4	4.42 ± 0.021	5.47 ± 0.14	$6.474*10^5$ ± 0.044	719.36 ± 0.76	0.44 ± 0.025	98.76 ± 0.42
LET5	4.48 ± 0.017	5.24 ± 0.18	$6.024*10^5$ ± 0.041	720.12 ± 0.72	0.43 ± 0.030	99.89 ± 0.32
LET6	4.51 ± 0.013	5.14 ± 0.18	$5.967*10^5$ ± 0.051	720.33 ± 0.33	0.52 ± 0.029	101.21 ± 0.11
LET7	4.41 ± 0.011	5.56 ± 0.19	$6.515*10^5$ ± 0.054	718.96 ± 0.47	0.41 ± 0.013	99.46 ± 0.14
LET8	4.39 ± 0.011	5.31 ± 0.22	$6.247*10^5$ ± 0.051	719.72 ± 0.32	0.36 ± 0.025	98.76 ± 0.46
LET9	4.46 ± 0.019	5.26 ± 0.13	$6.126*10^5$ ± 0.049	719.16 ± 0.33	0.46 ± 0.019	98.72 ± 0.34
LET10	4.39 ± 0.012	5.72 ± 0.22	$6.761*10^5$ ± 0.043	720.41 ± 0.65	0.39 ± 0.019	100.21 ± 0.11
LET11	4.42 ± 0.018	5.46 ± 0.26	$6.468*10^5$ ± 0.054	719.11 ± 0.56	0.31 ± 0.031	97.89 ± 0.62
LET12	4.48 ± 0.022	5.38 ± 0.24	$6.212*10^5$ ± 0.055	720.47 ± 0.45	0.43 ± 0.016	99.34 ± 0.22
LET10A	4.52 ± 0.016	5.79 ± 0.15	$6.616*10^5$ ± 0.054	719.33 ± 0.49	0.38 ± 0.023	98.22 ± 0.58
LET11A	4.51 ± 0.021	5.54 ± 0.14	$6.334*10^5$ ± 0.056	718.56 ± 0.52	0.32 ± 0.024	98.92 ± 0.41
LET12A	4.51 ± 0.014	5.46 ± 0.18	$6.268*10^5$ ± 0.059	719.66 ± 0.45	0.42 ± 0.028	102.68 ± 0. 12

Figure No 1: Chemical structure of lamivudine

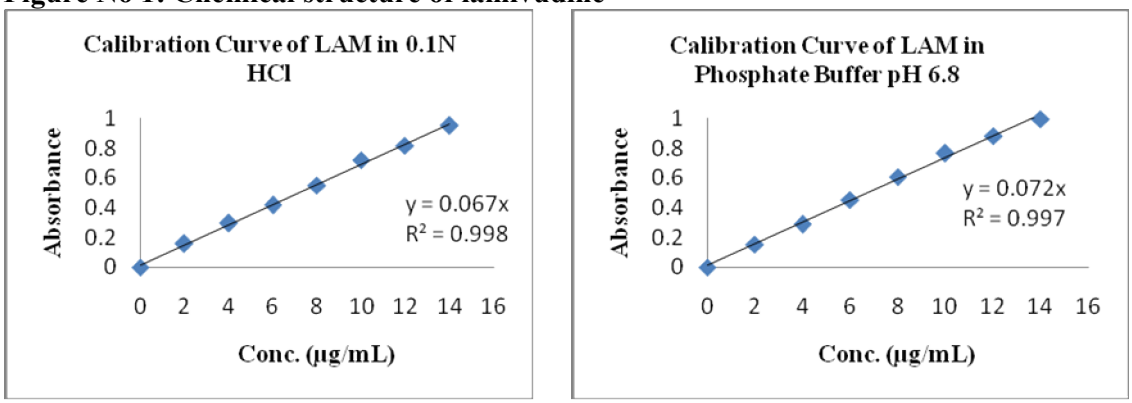

Figure No 2: Calibration curves of lamivudine in 0.1N HCl & Phosphate buffer pH 6.8

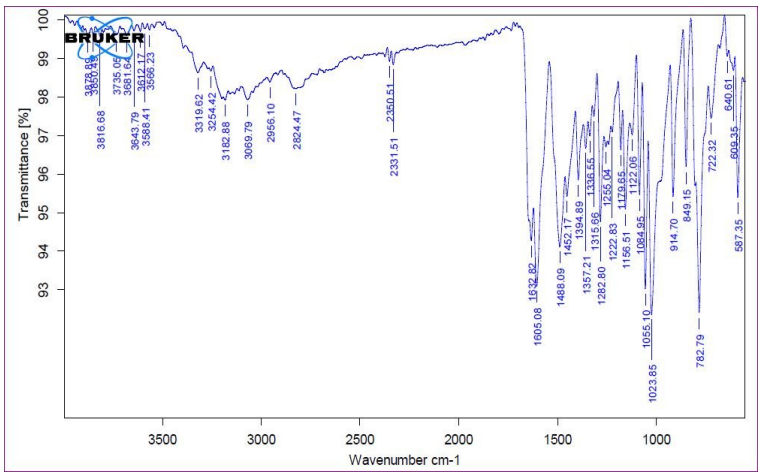

Figure No 3a: FTIR Spectrum of Lamivudine

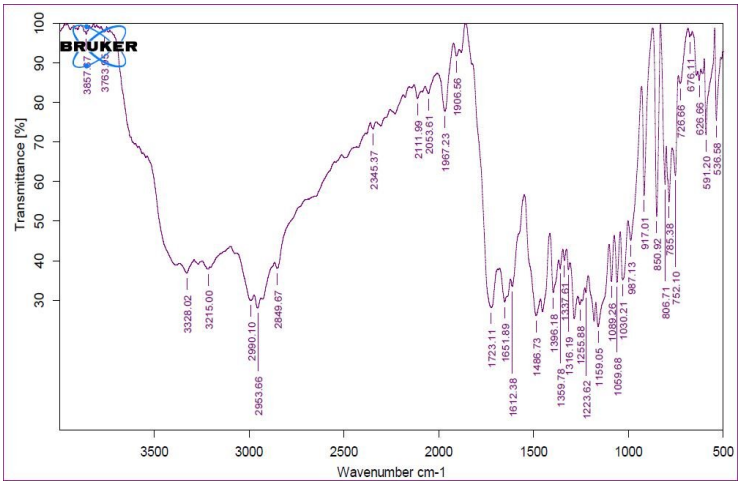

Figure No 3b: FTIR Spectrum of LAM + Anacardium Occidentale gum

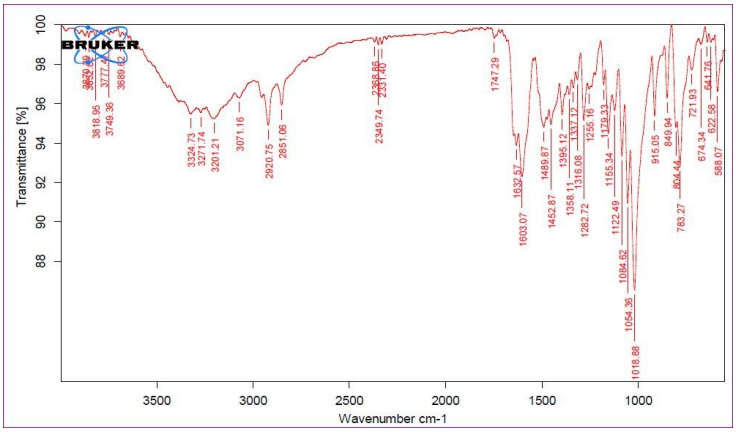

Figure No 3c: FTIR Spectrum of LAM + Delonix Regia seed endosperm gum

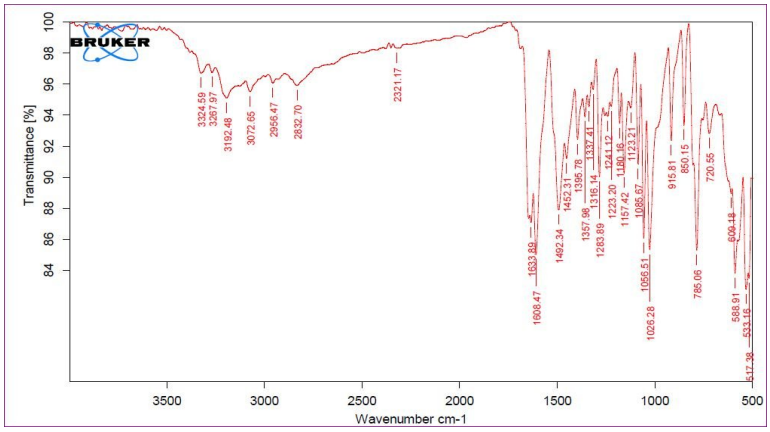

Figure No 3d: FTIR Spectrum of LAM + Moringa Oleifera gum

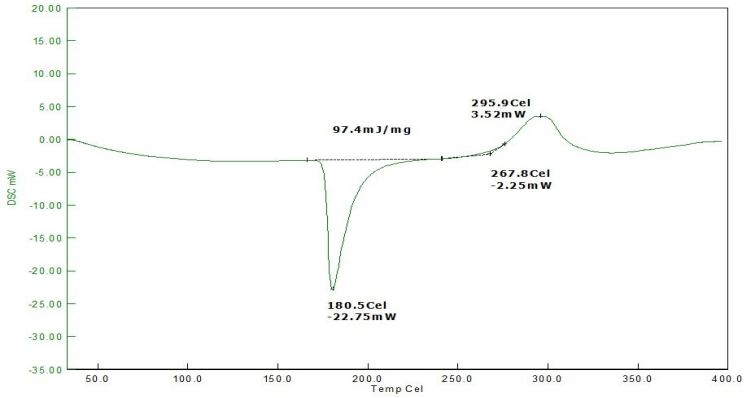

Figure No 4a:: DSC Thermogram of LAM

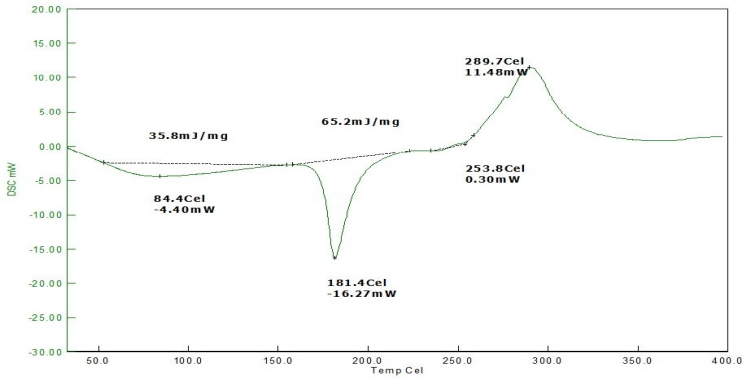

Figure No 4b: DSC Thermogram of LAM + MO gum

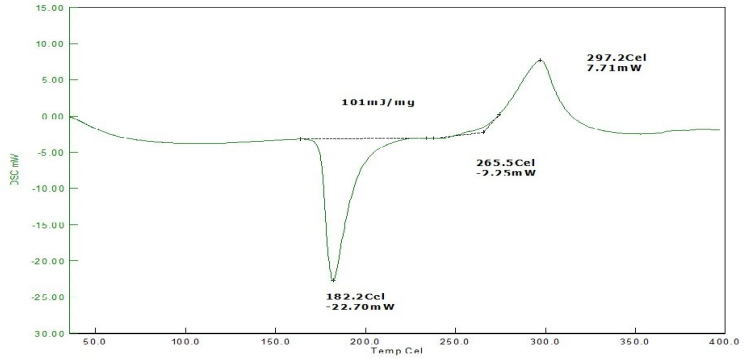

Figure No 4c: DSC Thermogram of LAM + AO gum

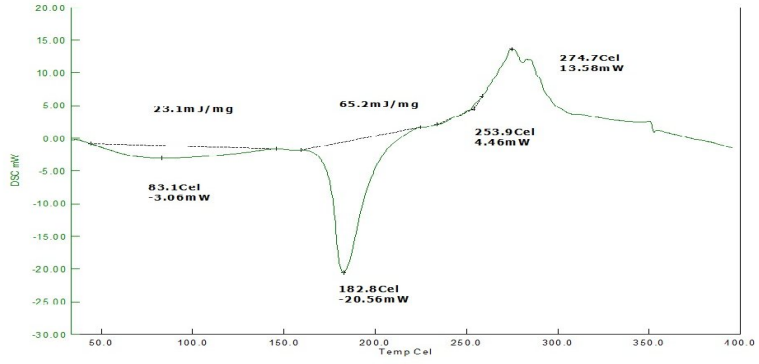

Figure No 4d: DSC Thermogram of LAM + DR gum

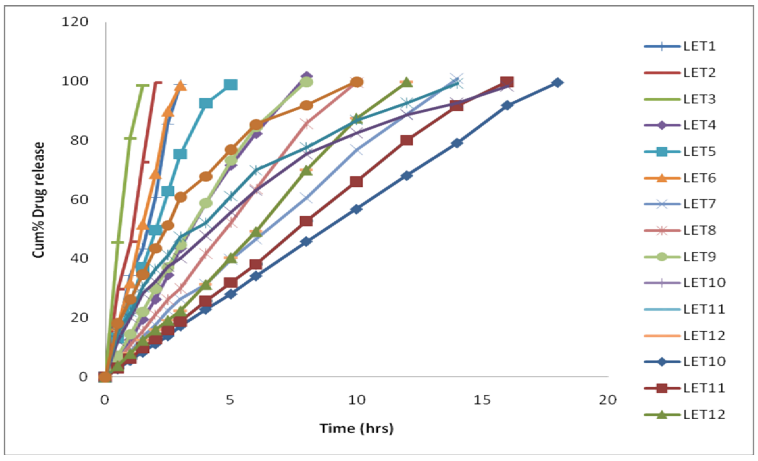

Figure No 5: Drug release profiles of lamivudine CR matrix tablets of all formulations

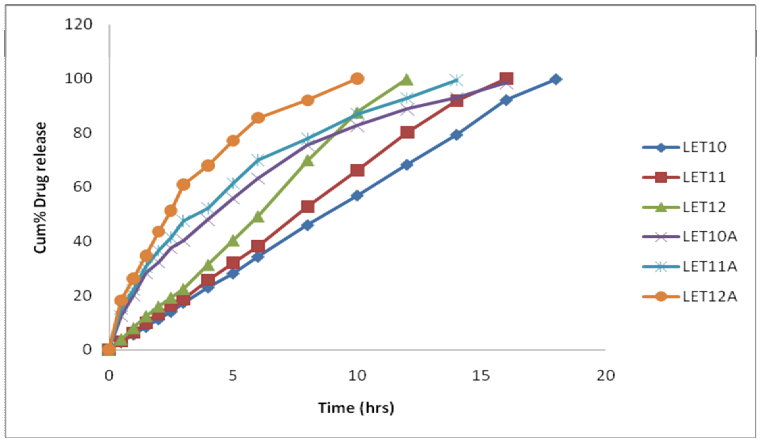

Figure No 6: Drug release profiles of formulations of lamivudne CR matrix tablets prepared from embedment (LET10, LET11 & LET12) and wet granulation (LET10A, LET11A & LET12A)

CONCLUSION

The results of the drug release studies on the prepared matrix tablets revealed that the embedment technique was more effective for the efficient incorporation of drug in the polymer matrix than wet granulation technique for the preparation of CR formulations to get the desired control release. Therefore, it can be concluded that even for the high water soluble drugs like lamivudine, extended or controlled release matrix tablets can be effectively prepared by the embedment technique.

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