FORMULATION AND EVALUATION OF LAMIVUDINE MOUTH DISSOLVING THIN FILMS

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ABSTRACT

A reverse transcriptase inhibitor, lamivudine is used to treat hepatitis B and HIV. To help patients who have trouble swallowing traditional dosage forms and to improve the drug's bioavailability and start of action, the current study aimed to formulate Lamivudine films that dissolve in the mouth using different polymers to achieve a faster disintegration time and better drug release. Mentally ill, young, old, and developmentally disabled persons all benefit from the increased accessibility that MDFs give. Using a solvent casting technique, MDFs were produced. Physical appearance, drug content uniformity, thickness, folding endurance, surface pH, in vitro disintegration time, tensile strength, percent elongation, scanning electron microscopy, in vitro dissolution studies, stability studies, comparison with marketed formulations, in vitro disintegration, spitting, and evaluation of taste are all criteria that the optimised MDF satisfies. Within 12 minutes, the enhanced MDF obtained a % CDR of 78.54±1.05%, whilst the ideal formulation reached 99.25±1.20% in only 10 minutes. The findings confirmed that the Lamivudine-infused MDFs were effective.

Keywords: Mouth Dissolving Film, Lamivudine, FTIR, XRD, DSC and SEM, Solvent casting method.

INTRODUCTION

Oral administration of pharmaceuticals is preferred due to its many advantages, including its low invasiveness, flexibility, and high rates of patient compliance and acceptability. Oral medicine administration in young, elderly, ill, or otherwise disobedient patients is an ongoing difficulty, but new, innovative technology has been progressively producing a variety of alternatives. Thanks to recent technological developments, bioadhesive mucosal dosage forms such patches, gels, and tablets have been developed. There has been encouraging progress in the use of polymeric films for buccal cavity medicine administration. Quickly hydrating upon contact with the tongue, orally disintegrating films (ODFs) release the active medicinal component from the dose form. They aid in disintegration and/or degradation by absorbing saliva. The hydrophilic polymers that make up most ODFs allow them to dissolve rapidly when they come into contact with saliva. Oral disintegrating tablets (ODTs) and oral disintegrating films (ODFs) are two options for administering medications that disintegrate in the mouth. As an alternative to the more typical fast-dissolving tablets and capsules, these systems were developed in the late 1970s for patients of any age who have difficulty swallowing normal pills. In most cases, an average ODF is about the size of a postage stamp. The release of ODT onto the market was closely associated with patient education on correct administration. As part of this training, students learnt things like "do not chew/do not swallow." However, mastication and deglutition occurrences were still often documented, despite these instructions.

Patients were given instructions on how to use MDFs when they were available for purchase, along with cautions like "do not chew/do not swallow." Despite these recommendations,

there were still several cases of swallowing and chewing. The public, however, was freed from these undesirable results by MDFs. Solvent casting and hot-melt extrusion are two typical methods for making films that dissolve in the mouth. When opposed to the hot melt extrusion method, the solvent casting technique has significant downsides, such as the presence of solvent residues and the potential environmental risks linked to organic solvents. Mouth dissolving films (MDF) are a relatively new kind of medication administration system that has lately become rather popular. Anyone, from young children to the elderly, who has problems swallowing may benefit from these videos. Rapid medication delivery to the circulation is made possible by the hydrophilic polymers used to create MDF, which dissolve rapidly in the mouth when they come into contact with saliva. Place the strip on the buccal or sublingual area of the tongue for oral delivery, which is a usual technique of delivering MDF. Sublingual and buccal passageways are the most common entry points for medicine into the circulation when the strip dissolves.

Lamivudine, a NRTI, is commonly the first drug in many antiretroviral therapy plans (3TC). Lamivudine is usually well-tolerated by patients, however a few do have mild side effects such nausea and headaches. A black box warning for NRTIs is the very unusual adverse effect of lactic acidosis. In 2021, a 70-year-old Swiss man was reported to have necrotising fasciitis, an extremely unusual complication that typically occurs about one month after a kidney transplant. He was undergoing antiretroviral treatment (ART) that consisted of long-term NRTIs. Metabolic acidosis was the untimely cause of death for the guy. The patient was given norepinephrine as a supportive drug at a rate of 2-4 μg/min after the fasciitis regions biopsy was finished. The patient's haemodynamic state deteriorated during the next several days, necessitating the oral administration of broad-spectrum antibiotics and an increase in norepinephrine dosage to 12μg/min. The patient's lactate levels spiked from 1.2 to 6.3 mmol/L five days after admission to the critical care unit, leading to the diagnosis of metabolic acidosis. After discontinuing ABC/3TC, the medical team began intermittent high-flux haemodialysis. Plasma lamivudine values of 2035 ng, 52 times the normative limit, were seen in individuals with normal renal function. Using NRTI-sparing regimens may provide individuals with sepsis a chance to prevent hyperlactatemia.

MATERIALS AND METHODS

Materials An "anti-retroviral agent" called Lamivudine was received as a gift. This aspertame, PVA, PVP, citric acid, and propylene glycol was purchased from S.D. fine chemicals. Indian city of Mumbai Our supplier, INR chem, supplied the gelatin. Lycoat received in Mumbai from Signet Chemical Corp. in Mumbai International Flavours of Fragrances India Ltd. supplied the Trusil mixed flavour R.S.V. The remaining components were all of analytical quality and were not altered in any way.

Preparation Method

Formulation of Mouth Dissolving Films of Lamivudine by Using Solvent Casting Method[6]

The Mouth Dissolving Films were made using film forming ingredients such as gelatin, PVA, and PVP. Citric acid, like Lycoat, promotes saliva production and functions as a super disintegrant, while propylene glycol is helpful as a plasticiser. After adding distilled water to adjust the final volume, we continued to mix the polymer solution using a magnetic stirrer for three quarters of the volume. After adding the expected amount of Lamivudine, the polymeric solutions were levitated with the appropriate volumes of Propylene Glycol, Aspertame, and Flavour. The mixture was brought to a temperature of 400 degrees Celsius in a hot air oven after being cast onto a glass plate. Each film contained 100 milligrammes of Lamivudine and was punched into a 9 square centimetre area. Various concentrations of

film-forming polymers, such as PVA, PVP, and gelatin, were tested using the trial-and-error approach. In 30 ml of water, varying amounts of film-forming polymers were dissolved to create the film concentrations.

Table.No.1 Formulation details of Lamivudine Mouth Dissolving Films by using PVA

Formulation Code / Ingredients	F1	F2	F3	F4	F5
Lamivudine (mg)	400	400	400	400	400
PVA	200	250	300	350	400
PVP	-	-	-	-	-
Gelatin	-	-	-	-	-
Lycoat	25	50	75	100	
Citric acid	40	40	40	40	40
Aspertame	10	10	10	10	10
Trusil Flavor(mg)	10	10	10	10	10
Propylene Glycol(ml)	25	25	25	25	25
Distilled Water	Q.S	Q.S	Q.S	Q.S	Q.S

Table.No.2 Formulation details of Lamivudine Mouth Dissolving Films by using PVP

Formulation Code / Ingredients	F6	F7	F8	F9	F10
Lamivudine (mg)	400	400	400	400	400
PVA	-	-	-	-	-
PVP	200	250	300	350	400
Gelatin	-	-	-	-	-
Lycoat	25	50	75	100	125
Citric acid	40	40	40	40	40
Aspertame	10	10	10	10	10
Trusil Flavor(mg)	10	10	10	10	10
Propylene Glycol(ml)	25	25	25	25	25
Distilled Water	Q.S	Q.S	Q.S	Q.S	Q.S

Table.No.3 Formulation details of Lamivudine Mouth Dissolving Films by using Gelatin

Formulation Code / Ingredients	F11	F12	F13	F14	F15
Lamivudine (mg)	400	400	400	400	400
PVA	-	-	-	-	-
PVP	-	-	-	-	-
Gelatin	200	250	300	350	400
Lycoat	25	50	75	100	125
Citric acid	40	40	40	40	40
Aspertame	10	10	10	10	10
Trusil Flavor(mg)	10	10	10	10	10
Propylene Glycol(ml)	25	25	25	25	25
Distilled Water	Q.S	Q.S	Q.S	Q.S	Q.S

Calculation of dose for Lamivudine

Lamivudine 400 mg is the recommended dosage. Hence, 100 mg of Lamivudine is needed for a 3cm*3cm=9 cm^2 film.

- Length of glass plate =6 cm.
- Width of glass plate =6 cm.
- Area of the plate =36 cm^2.
- No. of 9 cm^2 films present whole plate =36/9 =4 films.
- Therefore, each films contains 50 mg of drug
- 4 films contain 100 mg drug (4/400=100mg).
- So, the Labelled claim of drug = 100 mg.

Evaluation Parameters of Mouth Dissolving Film

Organoleptic Properties of Pure Drug
The pure medicine's organoleptic properties, such as its colour, smell, taste, and texture, have been noted.

Determination of melting point

By sealing one end of a capillary tube and inserting a little amount of the drug inside, its melting point may be determined. The temperature at which the medicine melted was measured after positioning the capillary tube in the thermionic melting point apparatus. Thermodynamic melting point measurements compared to literature

Solubility studies of pure drug

The drug's solubility was investigated by testing it with various buffers. The following solutions were prepared in glass-capped tubes: 0.1 N hydrochloric acid, 10 mL of distilled water, and phosphate buffer solutions with a pH of 6.8. All of these liquids contained the medicine. Each flask was tightly sealed with a stopper and then wrapped in cellophane to keep the solvent inside. A water bath was used to shake them at 37ºC for a whole day. Once the samples had achieved equilibrium, a German Hermle Z 200 A centrifuge was used to spin them at 3000 rpm for 5 minutes. The liquid on top was extracted by means of a 0.45 µm membrane filter. One millilitre of saturated solution was diluted with suitable solvents before examination using a UV spectrophotometer set at 257.0 nm (Single Beam Spectrophotometer, YIS-294).
Drug-polymer compatibility studies:
Because the medicine and polymer are in such close proximity during tablet manufacturing, there is a risk that they may interact, rendering the drug unstable. Consequently, choosing the right polymers requires thorough pre-formulation research on the drug-polymer interaction. To determine if the chosen polymers were compatible with Tenofovir disoproxil fumarate, FT-IR spectroscopy was used. Two distinct batches of medication, one without an excipient and one with it, were scanned.

FT-IR studies
Sample/KBr ratio

It is recommended that the sample be concentrated in KBr between 0.2% and 1%. Due to the fact that the pellet is much thicker than a liquid film, Beer's Law states that a lower concentration in the sample is necessary. Typically, getting clear pellets becomes

challenging at concentrations that are too high. Extremely noisy spectra are produced when the infrared beam is either entirely absorbed or dispersed by the material.

Differential scanning calorimetry (DSC)

TA Instruments' DSC Q20 Universal V4.5A was used for DSC. After the samples had equilibrated for 1 minute, they were subjected to temperatures ranging from 0 to 300°C in a nitrogen environment. We used the 2000 universal analysis program from TA Instruments to get the thermograms.

X-Ray diffraction (XRD)

The XRD (PW 1729, Philips, Amsterdam, Netherlands) was used to record the samples. XRD patterns were captured by using monochromatic Cu Ka radiation with a Ni filter. The measurements were taken at 10° to 80° 20 values, with a voltage of 40 kV and a current of 30 mA. Diffrac Plus V1.01 was used to process the data.

Experimental Methods

Analytical method development by U.V. Spectroscopy

One of the most common methods used for analysing pharmaceuticals is ultraviolet-visible spectrophotometry. It is a method for determining how much light, either UV or visible, material in a solution can absorb. Spectrophotometers that measure the ratio of two U.V.-visible light beam intensities are known as ultraviolet-visible spectrophotometers. Quantitative spectrophotometric analysis determines the number of molecular species absorbing the light, whereas qualitative analysis uses a spectrophotometer to identify organic substances (if any recorded data is available). When working with low concentrations of substances, the spectrophotometric method is ideal since it is quick, easy, and somewhat selective. In quantitative spectrophotometric analysis, the Beer-Lambert law is the guiding principle.

Differential scanning calorimetry (DSC)

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Physical appearance and surface texture of film:[7]

In order to confirm this criteria, only visual inspection of films and tactile evaluation of tack were used.

Weight uniformity of films

We used a digital scale to measure the individual weights of three films, each measuring 3*3 cm2 (9 cm square), and then we averaged them.

Drug content uniformity study of films

Using a UV-Spectrophotometric technique, the films were examined for homogeneity drug content. The cast films were divided into three separate sections, each with a diameter of 3×3 cm2. After dissolving the films in a 6.8 pH Phosphate Buffer solution, 0.2 ml was taken and diluted with buffer until it reached a volume of 10 ml. The solution was then added to a 100 ml volumetric flask. A UV-Visible Single Beam Spectrophotometer (YIS-294) was used to test the solution's absorbance at 257 nm. For all three films, we used the same method to calculate the drug content % using the standard graph.

Moisture content of film

To guarantee dryness, testing were conducted on the moisture content. Before being placed in the desiccators with calcium chloride, the prepared films were weighed. To find the percentage of moisture loss, the films were reweighed after 3 days. For this experiment, we employed three different formula films.

$$\%\ \mathbf{Moisture\ content} = \frac{\boldsymbol{initial\ weight - final\ weight}}{\boldsymbol{initial\ weight}} * \mathbf{100}$$

The thickness of films[8,9,10]

We used a calibrated vernier calliper (Mitutoyo, Japan) to measure the film's thickness. A dosage-equivalent sample was collected. The film was inserted after the anvil of the thickness gauge was raised and the pointer was adjusted to zero. We measured the dial reading while the film was resting on the anvil. We took thickness readings at three separate locations. Average thickness was determined by averaging the results of six measurements.

Folding endurance of films[11]

One way to measure the pliability of films is by looking at their folding durability. To test the films' capacity to withstand repeated folding, a small (8 cm2) section was bent in the same direction until it snapped. The number of rip-free folds in a given area is one indicator of a film's folding endurance.

Surface pH of films[12,13]

One millilitre of distilled water was allowed to touch the films in order to determine the surface pH. To measure the surface pH, we brought a glass electrode and pH paper next to the films' surfaces and let them equilibrate for one minute.

In vitro disintegration time of films[14,15]

The disintegration test was conducted using a 6.8pH phosphate buffer solution, which is the recommended medium according to the USP disintegration time testing device. The disintegration time of the films was measured after placing them in the container's tubes.

Tensile strength and Percentage elongation

Following the steps outlined below, the films' tensile strengths were measured using a TAXT Plus Texture Analyser (Texture Technologies, Scarsdale, NY) in conjunction with micro tensile grips TA-96B. The texture analyser was used to hold a 3 x 3 cm2 sheet that was free of air bubbles and physical flaws in a tensile grasp throughout its length. At an initial grip separation of 6 mm from both sides, the test was run at a crosshead speed of 2 mm/sec until the film broke. For every film, the measurements were taken three times.

$$\boldsymbol{Tensile\ strength} = \frac{\textbf{Force at break (N)}}{\textbf{Initial cross sectional area of the film (mm2)}}$$

The following equation was used to compute percentage elongation

$$\%\ \boldsymbol{Elongation} = \frac{\textbf{Increase in length}}{\textbf{Original length}} * \mathbf{100}$$

Scanning electron microscopy (SEM)

A scanning electron microscope (Quanta-200, Thermo Fischer Scientific, USA) was used to test the formulations' surface properties. Carbon tape with two sides was applied to an aluminium stick. We dipped the stab in the sample and used an air blower to get rid of any loose particles. A bio-radpolaran sputter coater was used to apply a layer of gold particles on the sample. After positioning the sample in an evacuated chamber, an electron beam was used to scan it in a regulated pattern. Comparisons were made between images of uncoated KCl and those of the coated ones.

Taste Evaluation Study by Spitting:[19]

A taste panel (n=5) was used to test the acceptability of the medication's flavour. A film sample containing 150 mg of the drug was kept in the mouth until it disintegrated, then spit out and the amount of bitterness was recorded. Gargling with distilled water was instructed by the participants in between the delivery of the medicine and the film samples. Here is the scale that was used for the bitter study:

- → + = very bitter
- → ++ = moderate to bitter
- → +++ = slightly bitter
- → ++++ = tasteless/taste masked
- → +++++ = excellent taste masking

In-vitro Dissolution Study [20]

Lamivudine Mouth Dissolving Films were studied for their in vitro dissolving using the USP dissolution apparatus (Type II). The dissolving agent was a phosphate buffer solution with a pH of 6.8, with a volume measurement of 900 ml. The stirrer was set to spin at a speed of fifty revolutions per minute. The temperature of the dissolving media was maintained at

37±0.5ºC throughout the experiment. A singular film was used in each experiment. To determine the rate of drug release, we measured the absorbance at 257 nm after withdrawing 5 ml of dissolution media using a syringe equipped with a pre-filter at 1, 3, 5-, 7-, 10-, and 12-minute intervals. Every time a volume was removed, the same number of dissolving media was added to replace it. A graph was created showing the cumulative % release of Lamivudine over time.

Comparison of optimized formulation with marketed formulation

The optimised T15 formulation containing Lamivudine was compared in a dissolving trial with 50 mg of commercially available Lamivudine tablets. Lamivudine 50 mg tablets in a 6.8 pH phosphate buffer were the subjects of an in vitro drug release investigation using the optimised formulation (T15).

Drug Release Kinetics[21,22]

A kinetic analysis of the dosage form's drug release rate was performed by plotting the acquired data as:

Zero order model

The optimal way to accomplish a pharmacological extended effect is using pharmaceutical dose forms that follow these characteristics, as they release the same quantity of medication per unit of time.

$$Qt = Q0 + K0t$$

First order model

The application of this model to drug dissolution studies was first proposed by Gibaldi and Feldman (1967) and later by Wagner (1969).

$$\log Qt = \log Q0 + (K1/2.303)$$

Higuchi model

In 1961, Higuchi put forth the first mathematical model that explains the release of drugs from a matrix system.

$$f\,t = Q = KH \surd t$$

Korsemeyer- peppas model

A straightforward equation describing drug release was developed by Korsemeyer et al. (1983) from a polymeric system. In some experimental settings, the releasing mechanism acts in a way that is not consistent with Ficks equation. It is possible to apply a more general equation in these instances:

$$Mt/M\infty = at^{n}$$

Stability studies[23]

The created oral dissolving films were subjected to stability testing in a variety of environmental settings. The film was placed in an aluminium foil container and kept in a stability chamber for a month at 2-8°C (45% RH), then again at 400C/75% RH after three

months. During the stability investigation, the patches were examined for characteristics such as their appearance, drug content homogeneity, surface pH, tensile strength, and In-vitro dissolution studies.

RESULTS AND DISCUSSION

Organoleptic Properties of Pure Drug

Discussion: The drug's texture was silky smooth, and its colour was pure white. It had an awful taste and a distinct aroma, and it was amorphous in shape.

Determination of Melting Point:

The capillary technique was used to estimate the melting point of the pure medication Lamivudine.

Discussion: According to the results of the capillary technique, the pure medication Lamivudine has a melting point of 162°C.

Solubility studies

At 25^0C, we tested Lamivudine's solubility in filtered water, 6.8 pH phosphate buffer, and 7.4 pH phosphate buffer.

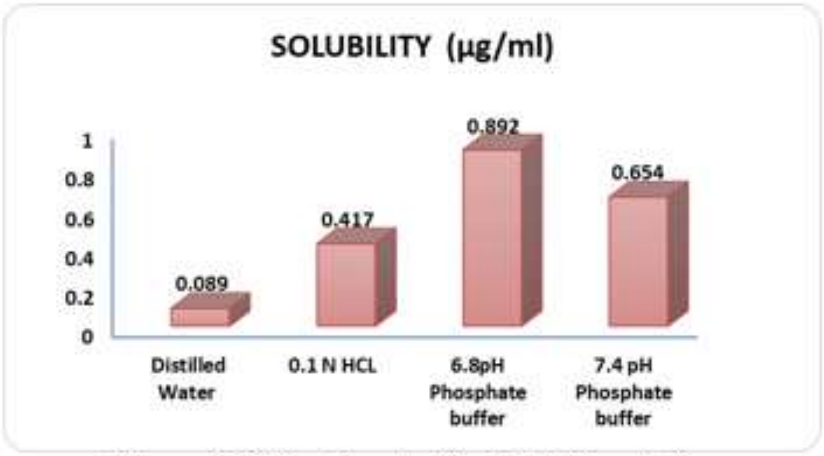

Figure No.1 Bar Graphs for Solubility studies

Discussion: A variety of buffers, including acidic (0.1N HCL) and basic (6.8pH phosphate buffer, 7.4pH phosphate buffer, and water), were used to perform the solubility investigations. According to the solubility tests that were performed in different buffers, it was found that the medication was more soluble in 6.8 pH phosphate buffer than in the other solutions.

Drug excipient compatibility: By comparing the spectra of the FT-IR analysis of the pure drug with those of the different excipients used in the trial, the compatibility of the drug and excipient was validated.

FTIR Studies

Pure Drug

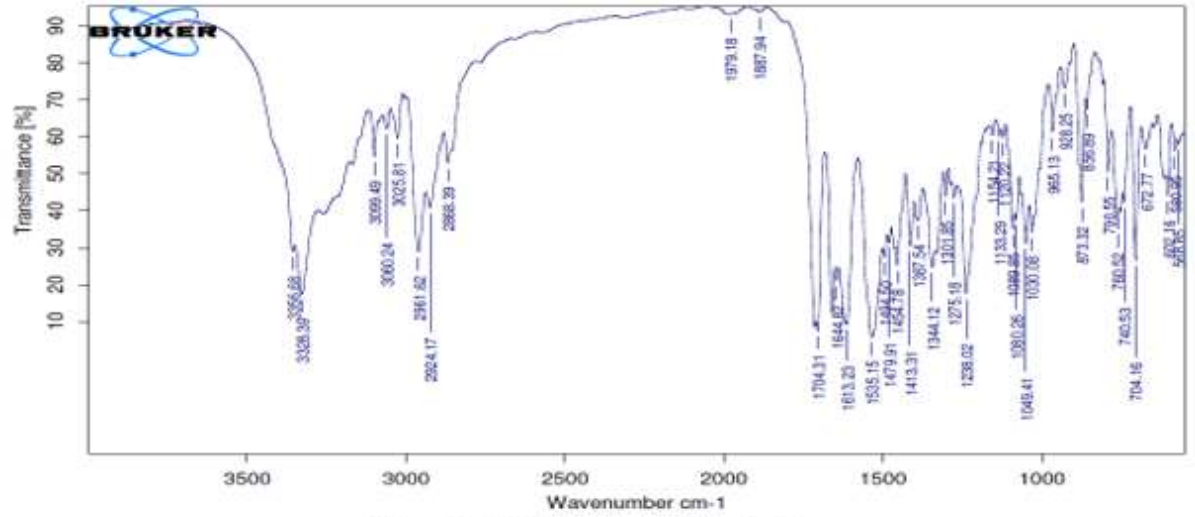

Figure No.2 IR spectrum of Lamivudine

Optimized

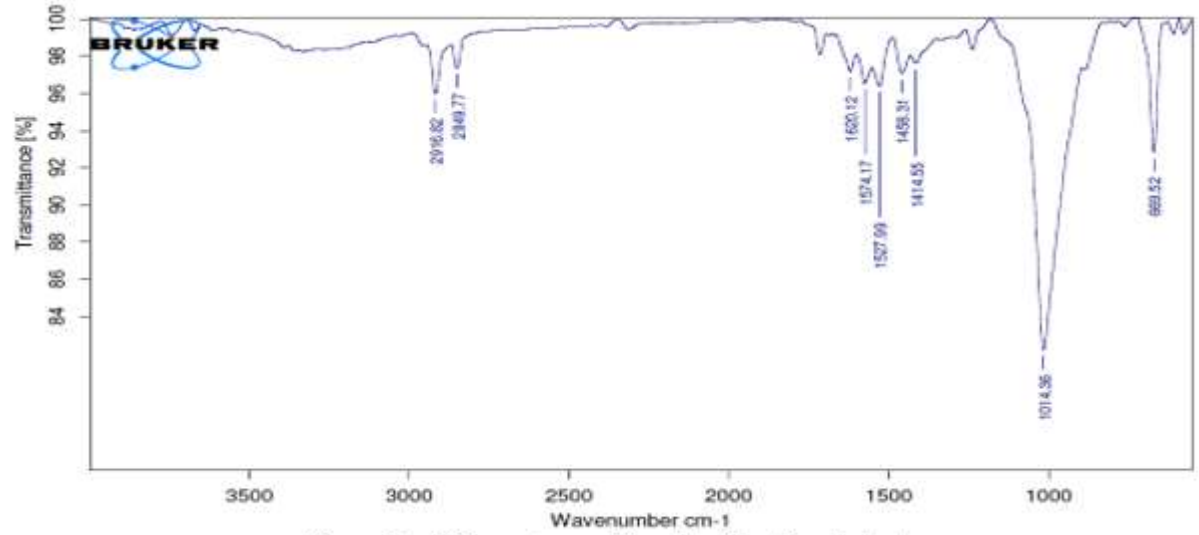

Figure No.3 IR spectrum of Lamivudine & excipients

Differential scanning calorimetry: By use of a differential scanning calorimeter, the pure medication and optimised trail DSC curves were acquired.

Pure Drug

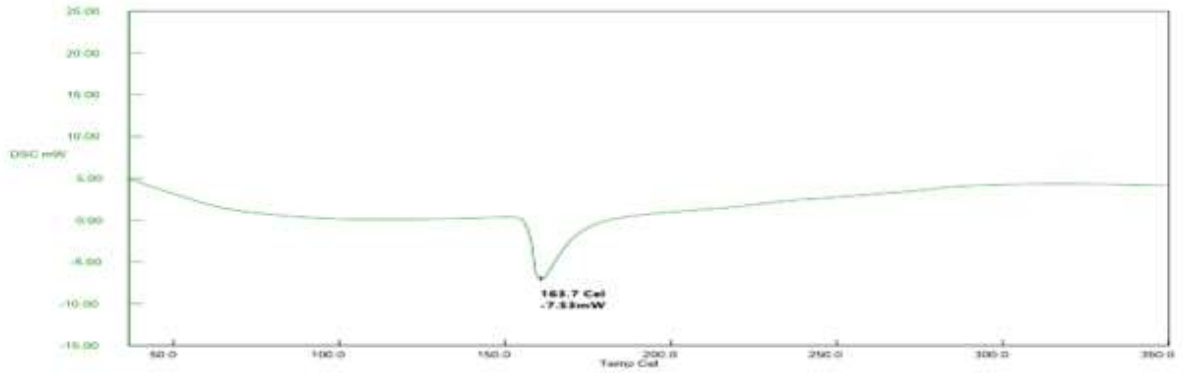

Figure No.4 DSC of the Pure Drug

Optimised :

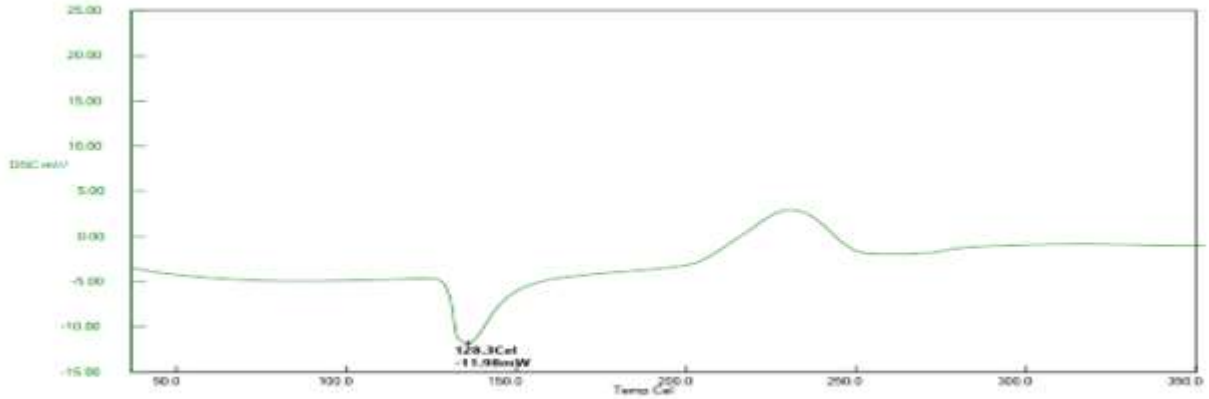

Figure No.5 DSC of the Optimized trail

X-Ray diffraction: Even when mixed, the level of crystallinity of the pure medicine remains constant. On the other hand, the peak intensity was lower since there was less pure drug in the combination compared to the pure version.

Pure Drug:

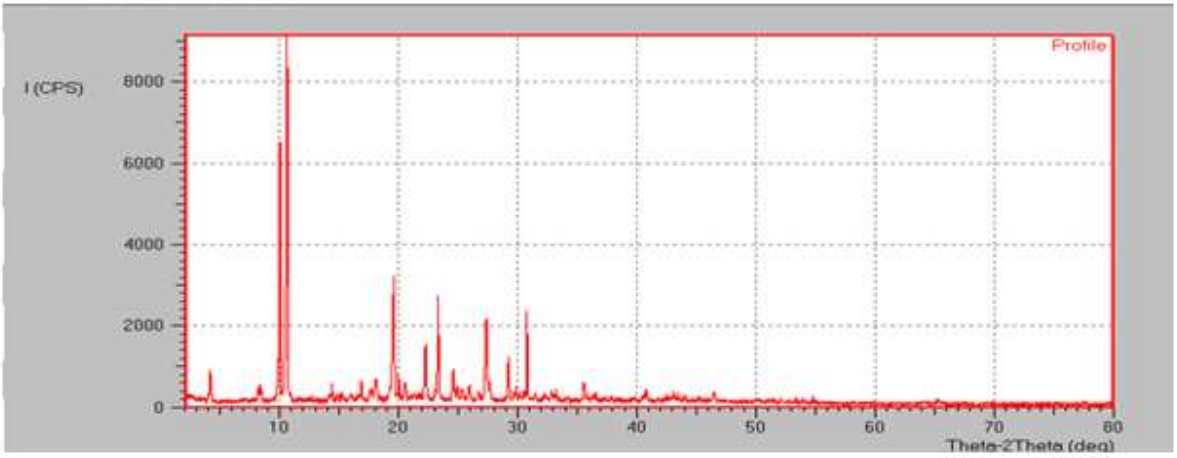

Figure No.6 XRD of Pure Drug

Optimized Trail:

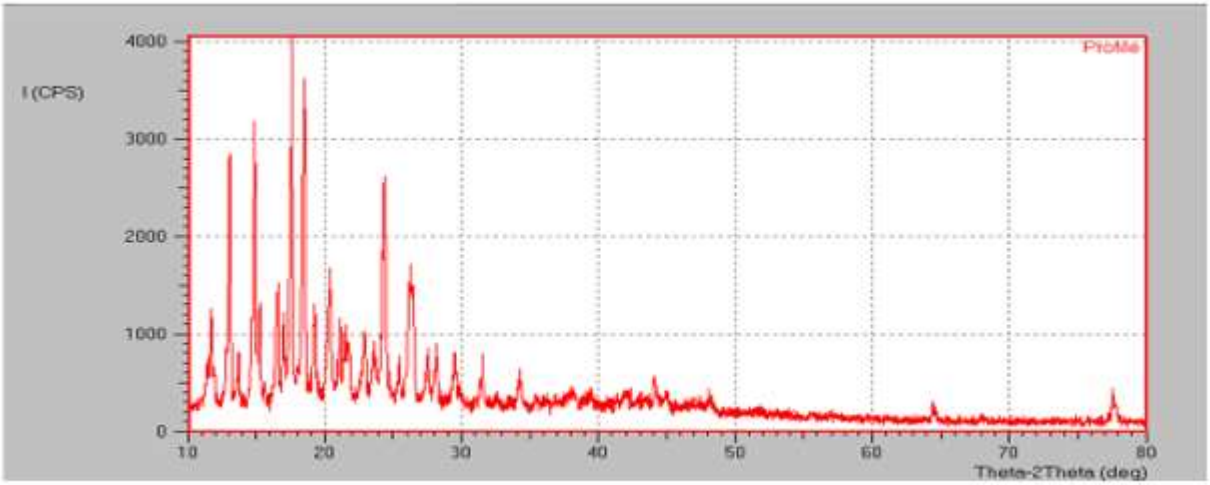

Figure No.7 XRD of Optimized Trail

Discussion

FTIR The absorption peaks in the pure drug lamivudine were observed at approximately 3356.68 cm-1 for the O-H bond (stretching), 3328.39 cm-1 for the N-H bond (stretching), 3099.49 aromatic cm-1 for the C-H bond (stretching), 1887.94 cm-1 for the C=O bond (stretching), 1644.82 cm-1 for the N=C bond (stretching), 1613.23 cm-1 for the C=C bond, 1238.02 cm-1 for the O-S bond (stretching), and 1049.41 cm-1 for the O=C bond (stretching), respectively. The absorption peaks measured in the Optimised Trail were 2916.82 aromatic cm- 1 for the C-H bond (Stretching), 1620.12 cm-1 for the N=C bond (Stretching), 1574.17 cm-1 for the C=C bond (Stretching), and 1014.36 cm-1 for the O=C bond (Stretching), in that order. We can see that there are no physical changes from the drug excipient compatibility experiments because the pure drug (Lamivudine) and optimised trail (Lamivudine + excipients) do not interact with each other.

DSC Conducting trials on Optimised Trail and pure Lamivudine was the standard procedure. The exact temperature range for the melting point of the medication Lamivudine was found to be 100–200 degrees Celsius. The melting point of pure lamivudine, as indicated in the differential scanning calorimetry (DSC) thermograms (Figures 7.87 and 7.88), is 163.7 degrees Celsius, where a prominent peak is seen. A loss of the peak in the enhanced trail suggests that the film component has achieved 128.3 Cel complete homogeneity and that an amorphous form of Lamivudine has developed. Lamivudine, Lamivudine + Gelatin, and disintegrate mixtures' DSC thermograms show their melting points as peaks. As a result, the DSC analysis did not uncover any interactions between the selected medicine Lamivudine and any combinations of Gelatin and Lycoat.

XRD The crystalline structure of lamivudine was revealed by its strong peaks seen at various diffraction angles. While the Optimised trail's X-ray diffractogram did not reveal any Lamivudine peaks, the physical combination exhibited the key characteristic peaks of the drug, gelatin, and lycoat polymer at lesser intensities. Lycoat is an amorphous structure as its X-ray diffraction pattern does not exhibit any peaks. Lycoat was determined to be a unique super disintegrant for use in trailing mouth dissolving films since it exhibited all the properties of a film producing agent and a free-flowing, amorphous powder.

Determination of λ_{max}: -

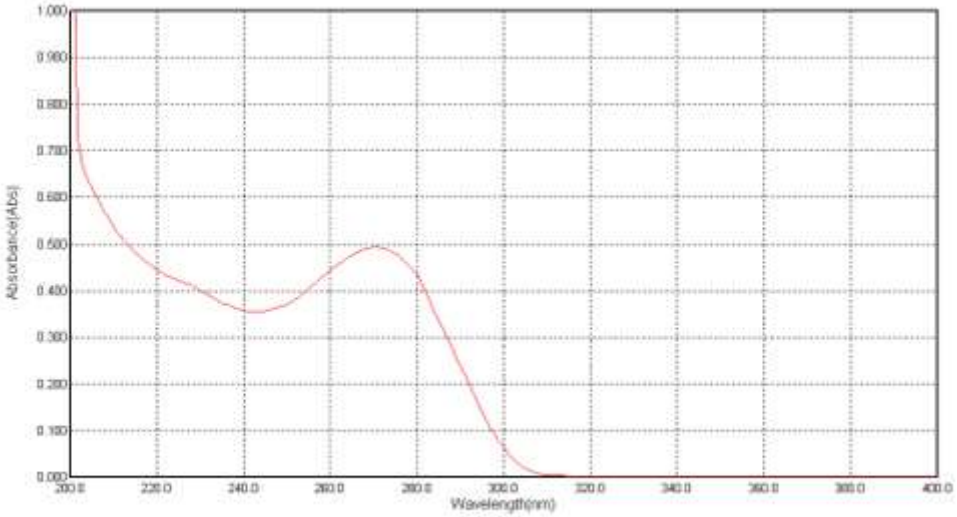

Figure No.8 UV Spectrum curve of Rilpivirine

Discussion: Using a microprocessor-based UV visible single beam spectrophotometer, the maximum absorption peak (abbreviated as 0.615 Abs) at 259.0 nm was recorded for the standard dissolving solution of Tenofovir disoproxil fumarate, which is a 100% concentration solution with a concentration of 10 ppm (10 µg/ml).

Calibration curve of Rilpivirine in 7.4 pH phopshate Buffer

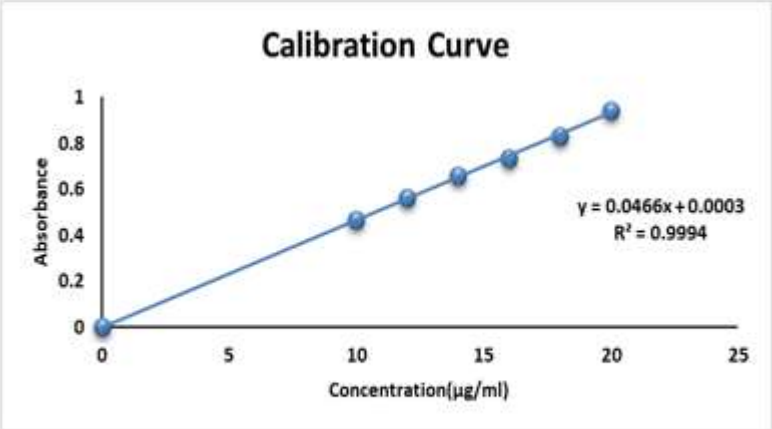

Figure No.9 Standard graph of Rilpivirine

Discussion: Absorption peaks at 257.0 nm were seen in the Lamivudine calibration curve in a phosphate buffer with a pH of 6.8. The absorption data points were used for linear regression analysis using the Microprocessor UV Visible single beam spectrophotometer, since the UV spectrophotometric showed a linearity range of 10-20 µg/ml. When determining the dosage, a straight-line equation was used, y= 0.0466x+0.0003. Based on the results, the R2 value is 0.9994.

Physical appearance and surface texture

Discussion: All the trails seemed non-tacky, semi-transparent, and flexible based on their surface texture and physical appearance.

Determination of Weight uniformity and Drug content uniformity of the Trails:

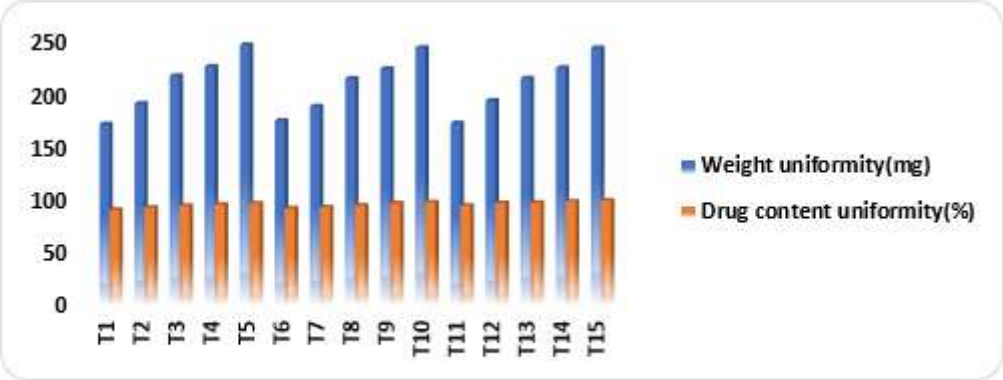

Figure No.10 Graphs of weight uniformity and drug content uniformity

Determination of Moisture content of film

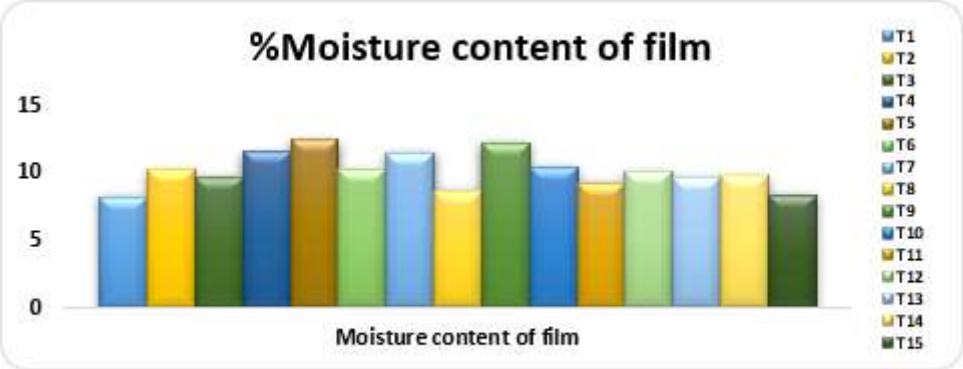

Figure No.11 % Moisture content of films

Determination of Thickness:

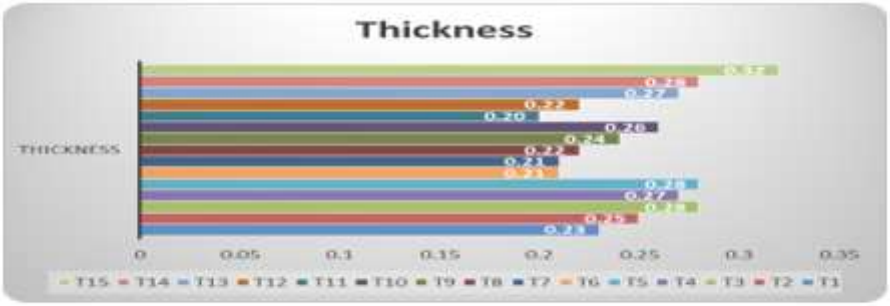

Figure No.12 Thickness of Films

Determination of folding endurance:

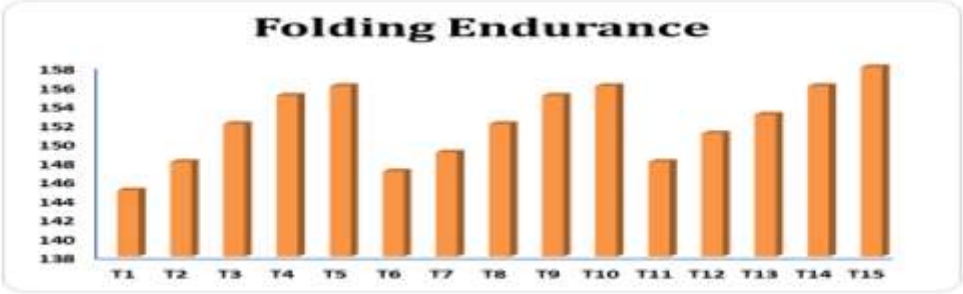

Figure No.13 Folding endurance of the films

Discussions: No substantial difference from the average was seen among trails, and all batches were of equal weight. For films made, the weight consistency varied between 171.14±1.17 mg and 245.84±1.24 mg. The homogeneous mixing was indicated by the drug content uniformity tests, which showed results ranging from 90.24±1.17% to 99.17±1.49% for all the films that were made. The drug content values ranged from 85 to 110%, as per the criteria provided by IP. We ran the % moisture content test in a humid environment to make sure the film was physically stable. The films' physical strength is assessed by measuring how much moisture they absorb in conditions with high moisture content; the results range from 8.24±0.03% to 11.56±0.16%. It is very important to keep the film thickness consistent as it affects the precision of dosage distribution. The films' thickness was discovered to range from 0.23±0.01mm to 0.32±0.06mm, and it reduced as the amount of polymer rose. The film's brittleness can be determined by its folding endurance. The results shown that the folding durability of the oral dissolving film increased with increasing concentrations of polymer and plasticiser. To test folding endurance, a film was folded in the same spot until it snapped. The films that were made had folding endurance values that fell between 145±1 and 158±1. All of the numbers are within the range of 100 to 200.

Determination of Surface pH:

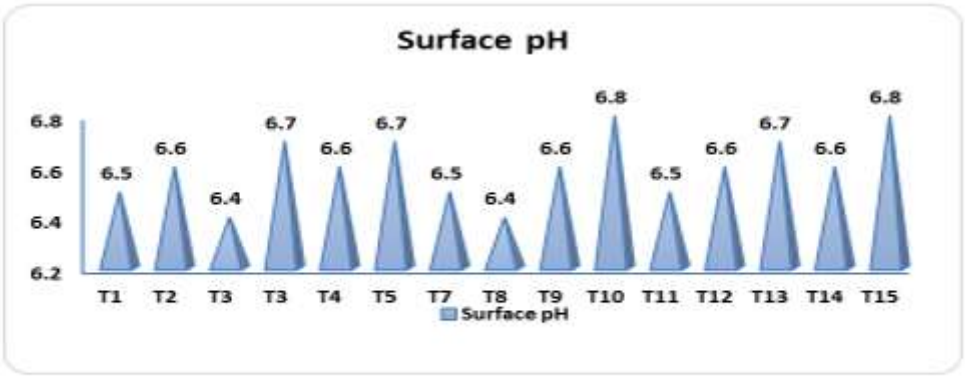

Figure No.14 Graphs of Surface pH

Discussion: Because acidic or alkaline pH variations in vivo might irritate the oral mucosa, we measured the films' surface pH to evaluate potential negative effects. The films' surface pH ranged from 6.4±0.2 to 6.8±0.2, falling within the range of 6-7 pH. This meant that the mouth-solving films were neutral in pH and wouldn't irritate the mouth when placed there.

Determination of Disintegration Time of Films:

Discussion: The durations of disintegration for each trail varied between 35±1 and 16±1 seconds. It was found that the film's thickness and, by extension, the time needed for the film to dissolve, were both affected by the amount of polymer used. Because the hydrophilic plasticiser quickly absorbed water, swelled, and immediately broke down H-bonds, Mouth Dissolving Films disintegrated rapidly as the plasticiser concentration rose.

Determination of Tensile strength and Percentage elongation:

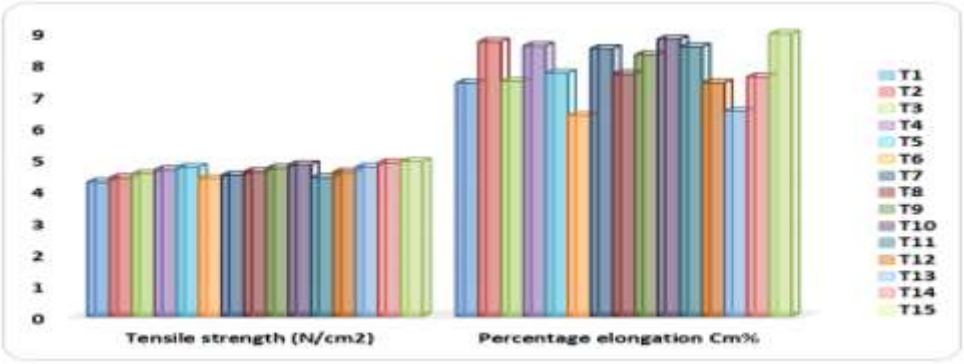

Figure No.15 Tensile strength and percentage elongation of films

Discussion: With the use of a TAXT Plus Texture Analyser from Texture Technologies in Scarsdale, NY, tensile strength was also enhanced. T1 had the lowest tensile strength and Trail T15 had the highest. The addition of a plasticiser, which forms strong hydrogen bonds with the polymer, likely contributed to this by making the polymer more flexible. The range of percentage elongation seen in the films was 6.34±0.3 cm% to 8.92±0.7 cm%.

Scanning electron microscopy (SEM)

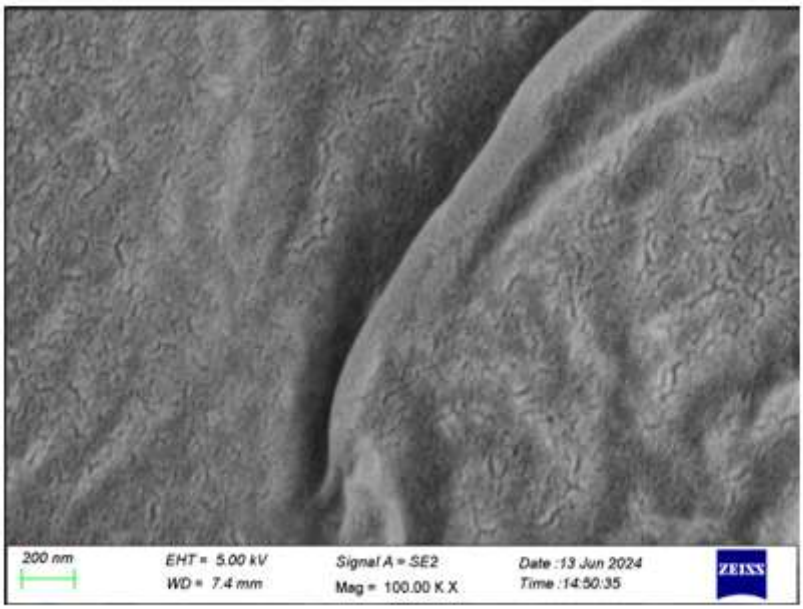

Figure No.16 SEM image of Optimized Trail

Discussion: The decreased particle size indicated the optimised trail. Scanning electron microscopy (SEM) of dissolved Lamivudine MDF reveals a surface that is both rough and

uneven, devoid of particles, which is consistent with the drug's presence in the polymer Gelatin.

Taste Evaluation Study by Spitting

Discussions: Volunteers from a human panel assessed the effectiveness of taste masking. On this study, human panel participants assessed the efficacy of each trail's flavour masking. With the exception of a small number of trials that just disguised the drug's harsh taste, the results demonstrate that all trails achieved effective taste masking.

In-vitro Dissolution Studies:

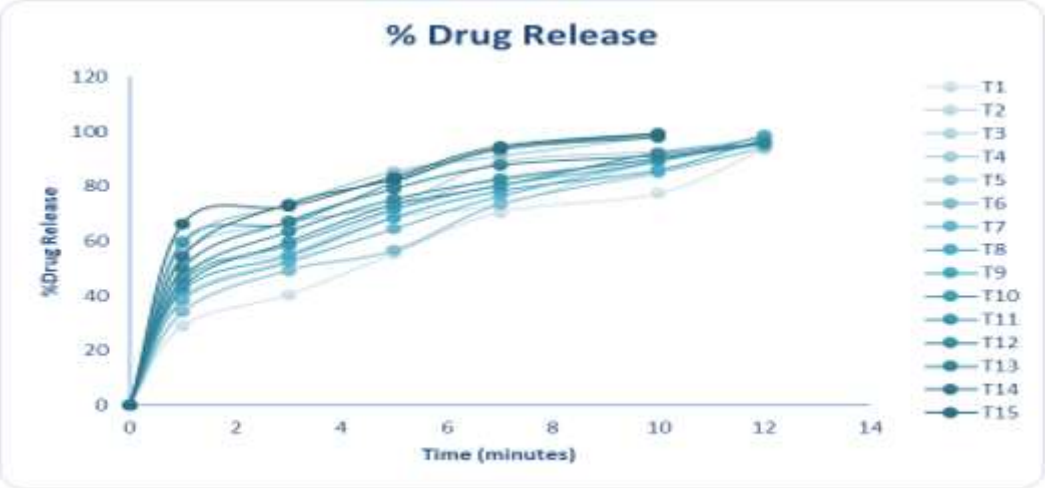

Figure No.17 % Drug Release of Trails from T1 to T15

Discussions: At the end of 10 minutes, the following trails were noticed: T1, which shows 93.45±1.27%, T2, which shows 95.24±1.18%, T3, which shows 96.24±1.08%, T4, which shows 97.48±1.24%, and T5, which shows 98.45±1.16%.
Films containing Lamivudine and polyvinylidene fluoride (PVP) were tested for their ability to release the medication in vitro. By the conclusion of 12 minutes, the following values are shown by the Trail T6: 94.26±1.18%, 96.24±1.69%, 97.35±1.09%, 98.68±1.26%, and 98.86±1.20%.

Various ratios of Lamivudine Mouth Dissolving Films using Gelatin as the polymer were studied for their in-vitro drug release. At the conclusion of 12 minutes, the values for Trail T11 are 95.65±1.08%, T12 is 95.59±1.20%, T13 is 96.37±1.36%, T14 is 97.85±1.35%, and T15 is 99.25±1.20%.
T15 has the highest rate of medication release across all Trials after 10 minutes. Consequently, it was selected as the optimal route.

Comparison of optimized trail with marketed trail:

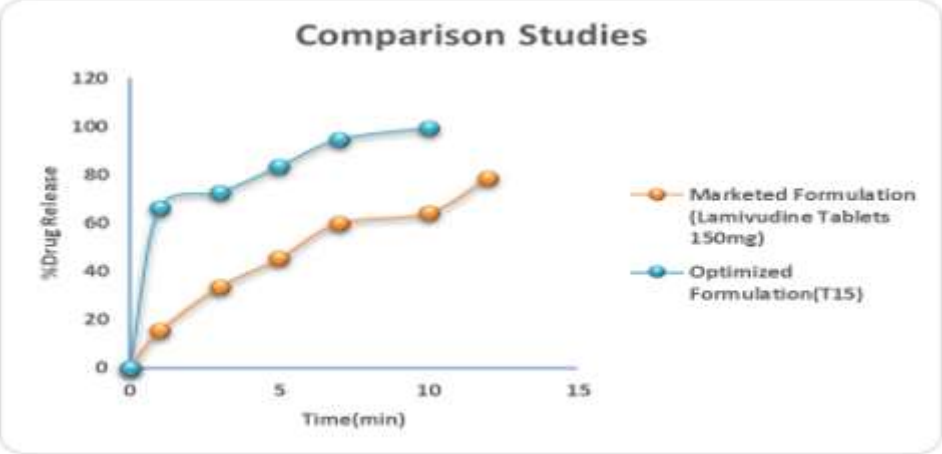

Figure No.18 In vitro Comparison studies of Optimized trail with Marketed Trails

Discussion: In vitro drug release studies comparing Optimised Trails to Marketed Trails. The results of the comparison experiments reveal that after 10 minutes, the Optimised trail demonstrated a drug release of 99.25±1.20%, whereas the marketed trail showed a drug release of 78.54±1.05% after 12 minutes. When compared to the marketed trail, the Optimised Trail T15 had the best release.

Drug release kinetics studies

Zero order

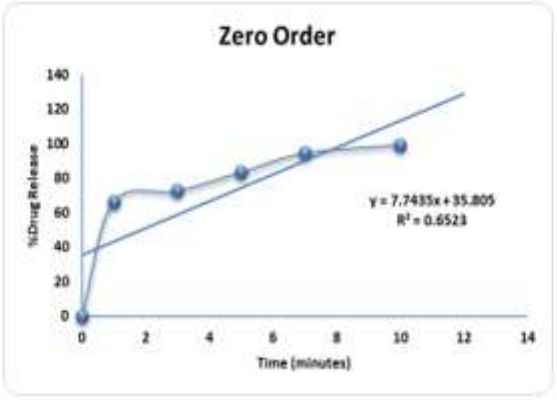

Figure No.19 Zero order plot of Lamivudine T15 Trail (Time Vs % Drug Release)

First order

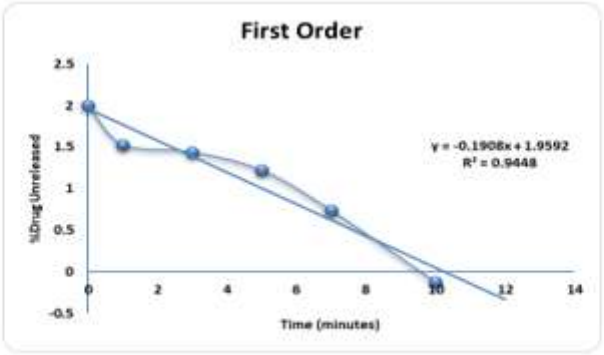

Figure No.20 First order plot of Lamivudine T15 Trail (Time Vs Log% ARA)

Higuchi plot

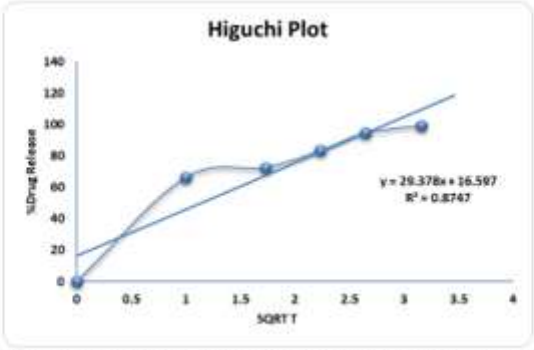

Figure No.21 Higuchi plot of Lamivudine T15 Trail (%Drug Release vs Root Time)

Korsmeyer -peppas plot

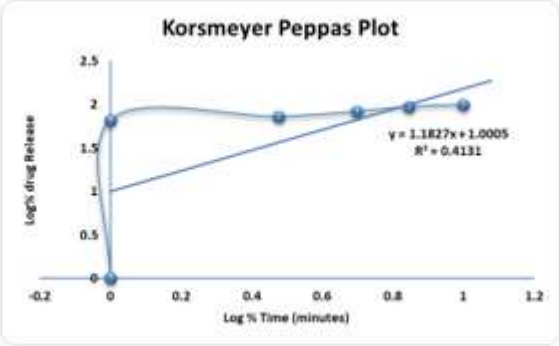

Figure No.22 Korsmeyer -Peppas plot of Lamivudine T15 Trail (Log%Drug Release vs Log % Time

Discussion: Mathematical model equations, such as first-order and zero-order techniques, were used to describe the drug release from the mouth dissolving films. Optimised trail T15 adheres to first-order drug release with a super case-II transport mechanism, according to the regression results.

Stability Studies

The optimised trail (TF15) was the subject of a stability analysis. After being sealed in an airtight container, the trails were kept in a stability chamber for the first and third months

at a temperature of 40 ± 2°C and relative humidity of 75 ± 5%. After that, at 30, and 60-day intervals, the samples were taken out and examined for things like surface pH, tensile strength, in-vitro dissolution tests, visual appearance, and drug content homogeneity.

Discussion: T For the stability tests, we used the optimised trail, or T15. After being sealed in an airtight container, the trails were kept in a controlled environment at a temperature of 40 ± 2°C and a relative humidity of 75 ± 5% for the first two months. Visual appearance, drug content uniformity, surface pH, tensile strength, and in-vitro dissolution studies were performed. The samples were subsequently withdrawn at 30, 90, and 36-hour intervals. Stability studies found that the optimised mouth dissolving films were stable for up to three months.

Summary and Conclusion:

Lamivudine oral drug delivery films were produced in this work. These films provide a practical and acceptable way to administer the medication orally, with the desired properties of quicker disintegration and dissolution and increased bioavailability. Lamivudine mouth dissolving films were made utilising the solvent casting process, Lycoat as super disintegrants, gelatin as film forming agent, and propylene glycol as plasticiser. Research such as FTIR, DSC, and XRD were conducted as part of the pre-formulation studies to characterise the API and determine if the medication and the excipient were compatible. The drug's properties were confirmed by the API characterisation. The final formulation's polymers, plasticisers, and disintegrant were chosen after drug-excipient compatibility experiments yielded satisfactory results. Physical appearance, weight uniformity, drug content uniformity, thickness, folding endurance, surface pH, in vitro disintegration time, tensile strength, percent elongation, scanning electron microscopy, in vitro dissolution, stability, stability, taste evaluation by spitting, evaluation of optimised formulation compared to marketed formulation, drug release kinetics, and stability studies are some of the evaluation parameters that the trials undergo. The solvent casting process was used to successfully create the final formulation (T15) utilising Gelatin as the polymer and Lycoat as the disintegrant. The result was a drug release of 99.25±1.20% after 10 minutes and a quick disintegration time of 16±1 sec. best trail T15's in vitro dissolution data was fitted using a variety of kinetic models, including zero-order, first-order, Higuchi, and the korsemeyer-peppas equation. The R2 score for optimised trail T15 is 0.944. It confirms the first-order release as its value approaches 1. The korsmeyer and peppas plot provides more evidence of the drug release mechanism; for the optimised trail (T15), the 'n' value is 1.183, meaning that the n value was greater than 0.89, indicating the Super case-II transport mechanism. An airtight container was used to hold the Optimised Trail for Stability Studies. The chamber was kept at 40 ± 2°C and 75 ± 5% RH during the first and third months. After that, at 30, and 60-day intervals, the samples were taken out and examined for things like surface pH, tensile strength, in-vitro dissolution tests, visual appearance, and drug content homogeneity. Considering the findings of the trials that included 125 mg of Lycoat as the disintegrant, 400 mg of Gelatin as the film-forming agent, and 25 ml of Propylene Glycol as the plasticiser. Compared to other trails, Trail T15 was able to achieve better in-vitro correlation limits in a shorter amount of time. Further research confirmed that the solvent casting approach provided the most effective means of rapid medication release.

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