RESEARCH ARTICLE

Design of Fast Dissolving Oral Film of Lamivudine using Ion Exchange Resins Indion 204, Tulsion 335 and Doshion P551

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ABSTRACT

Ion exchange resigns are suitable for usage as flavor masking agents and sustained pharmaceutical release due to their inherent properties such as high ion exchangeability, modified administration capacity, physiochemical stability, and non-solubility in any solvent. Ion-exchange resins (IERs) are macromolecular polymers with differing cationic and anionic functional groups qualitatively as well as quantitatively. The polymer chain is fabricated in such a way that it consists of different salt-forming groups in repeating mode. In this study, we have tried to create a rapid dissolving oro-film of lamivudine using the ion exchange resins indion 204, tulsion 335, and doshion P551. FDOFs attempt to boost patient compliance by shortening the time it takes for the treatment to take effect, in addition to having a quick onset of action and higher bioavailability and also it's a conventional dosage form. Out of three different resins, indion 204 gives a very excellent result with 1:1.5 ratio, where the maximum amount of complexation is within 4 hours of stirring. Their resinate are converted into granules and exhibit satisfactory value of angle of repose, bulk density, and flow property. Drug loading with indion 204 resin showed above 94%."

Keywords: Doshion P551, Fast dissolving films, Ion exchange resigns, Indion 204, Tulsion 335.

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INTRODUCTION

The medication is taken orally, which is thought to be the most effective method of drug administration. The taste of any oral formulation given to a pediatric or geriatric patient, particularly the bitter component, substantially impacts the patient's ability to adhere to pharmaceutical therapy.[1] Masking flavor is a major challenge in any medication delivery system; as a result, drugs gets released in the patient's oral cavity, which is proximal to the taste-sensing organelles, improving patient compliance and compliance rates.[2] Taste masking techniques, include microencapsulation, different polymers, encapsulated with polymer lipids, flavoring and sweetening chemicals, and others. Lipophilic carriers are frequently used in pharmaceuticals to mask a drug's harsh taste or block taste buds. These measures are utilized to avoid fast drug release when the flavor masking approach comes into touch with the quick drug release method. Ion exchange resin (IER) is a non-complex, cheaper complexation method that does not require extra chemicals or organic solvents to achieve the desired outcome. Interpenetrating polymer network (IPN) beads were used as a tool for sustained-release pharmaceutical carrier by many scientists for many years due to its multiple advantageous properties. This technique was stable, nontoxic, biocompatible, and biodegradable, which drew the pharmaceutical industry's attention, leading to its widespread use.[3]

Because of their desired optimum ion exchangeability, effective administration capacity, physiochemical efficiency, and non-solubility in any solvent, they are proven excellent alternatives for taste masking and prolonged drug release. A drug-resinate complex is generated when an ion-reacting pharmaceutical deals with an appropriate ion exchange resin, resulting in the taste masking of the drug and resin combination. IERs are macromolecular polymers containing a mixture of cationic and anionic functional groups and the basic group. The polymer chain is fabricated in such a way that it consists of different salt-forming groups in repeating mode. The drug-resin combination remains unaffected at the pH values present in salivary fluid due to the weak ionic

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Table 1: Formulation ingredients

Ingredient (%)	*Drug: resin (1:1)*	*Drug: Resin (1:1.5)*	*Drug: resin (1:2)*
	F1	*F2*	*F3*
Lamivudine (%)	30	30	30
Glycerine (%)	15	15	15
Pectin (%)	40	40	40
Citric Acid (%)	4	4	4
Sodium Saccharide (%)	4	4	4
Cross Carmi lose Sodium (CCS) (%)	3	3	3
Peppermint oil	Q.S.	Q.S.	Q.S.
Water (mL)	5	5	5

Table 2: Effect of Lamivudine: Resin ratio on % drug Content

Resin	*Drug: Resin Complex Ratio*	*% Drug Content*
Indion 204	1:1	61.07
	1:1.5	65.07
	1:2	63.48
	1:2.5	62.23
	1:3	63.83
Tulsion 335	1:1	60.23
	1:1.5	61.22
	1:2	59.99
	1:2.5	62.56
	1:3	62.53
Doshion P551	1:1	62.66
	1:1.5	63.08
	1:2	63.57
	1:2.5	64.56
	1:3	62.29

contact between the medicament and the resin substrate.[3] When device-related complications (DRCs) come into contact with gastrointestinal (GI) fluids such as stomach acid, they are freed from their drug bindings and absorbed. On the other hand, the resin does not exchange with counter ions and goes unaltered through the GI tract.[4]

Lamivudine is a drug used in the protocol for treating hepatitis B infection. Lamivudine is a medication that heads from the class of nucleoside reverse transcriptase inhibitors (NRTIs). It mediates by, among other things, minimizing the amount of hepatitis B and human immunodeficiency virus (HIV) in the bloodstream. The mechanism for lamivudine as potent antiviral candidature involves conversion to its triphosphate at the intracellular level, which competes with cytosine triphosphate for inclusion in the viral DNA strand during virus formation and concludes in the chain's termination and the cessation of viral DNA replication.[5]

Anatomy of the Taste Buds

Taste buds, which are taste receptor cells, are used by humans to detect taste. The human tongue includes around

Table 3: Effect of stirring time on percentage drug loading

Stirring time (hours)	*Percentage loading (%)*
1	78.92
2	83.55
3	88.72
4	94.96
5	95.07

Table 4: The cumulative percentage of drug release

Sr. no	*Resin*	*Drug: Resin Ratio*	*Cumulative % drug release from DRC (%)*
1	Indion	1:1	81.23
2		1:1.5	82.96
3		1:2	81.50
4		1:2.5	81.09
5		1:3	85.03
6	Tulsion	1:1	77.53
7		1:1.5	76.07
8		1:2	78.05
9		1:2.5	80.06
10		1:3	80.96
11	Doshion	1:1	78.03
12		1:1.5	79.63
13		1:2	76.23
14		1:2.5	80.08
15		1:3	81.91

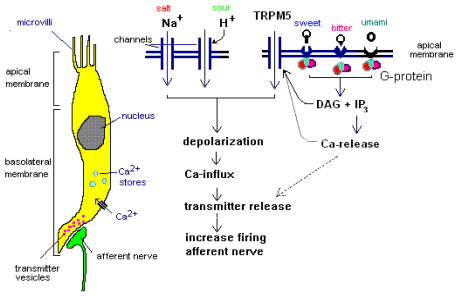

Figure 1: Taste signalling pathways

10000 taste buds, which emerge around 3 months before childbirth. Primarily taste bud has 50–100 taste cells, which are recognized as trans-membrane proteins that get attached to molecules and ions to create sour, sweet, bitter, salty, and umami taste sensations. Microvillus processes protruding from the uppermost point of taste buds into the oral environment *via* the small aperture known as a taste pore. The structure of taste papillae can be visualized as small red dots on the tongue.[6] These dots or flavor papillae, which are placed on the taste papillae, are known as fungi form papillae since they are situated at the front of the tongue. Taste receptors or taste hair are held by the microvilli of taste cells. Food and chemicals that dissolve in saliva both excite the taste receptor. The taste receptor is triggered, which causes a nerve impulse to be sent to the brain, which then identifies the taste Figure 1.[7]

Table 5: Determination of threshold concentration

No of Candidates	*Concentration of drug (µm/mL)*					
	5 ppm	*10 ppm*	*15 ppm*	*20 ppm*	*25 ppm*	*30 ppm*
1	0	0	1	1	2	3
2	0	0	1	1	2	3
3	0	0	1	1	2	3
4	0	0	1	1	2	3
5	0	0	1	1	2	3

Table 6: Evaluation of taste masked resinate

No. of Candidates	*Mark rating to preparation*	
	Drug Substances	*Taste masked Complex*
1	4	0
2	4	0
3	4	0
4	4	0
5	4	1

0: Good, 1: tasteless 2: Slightly bitter,
3: Bitter, 4: Very bitter

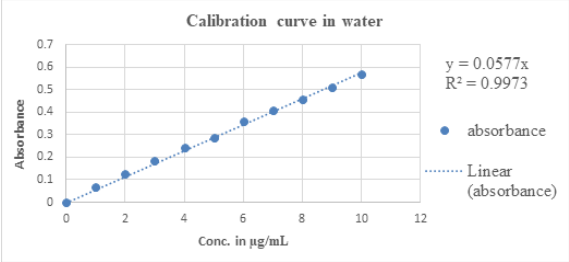

Figure 2: Calibration plot for lamivudine with water

Taste Signalling Pathway

Taste transduction is initiated when a tastant is introduced with cells with taste receptors. The binding of the tastant to the G-protein linked receptor associated cells triggers gustducin (G-protein). The taste sensation process starts when gustducin triggers effector enzymes like phosphodiesterase IA (PDE)[8] or phospholipase C beta 2. The effector enzyme then alters the intracellular levels of second messengers, primarily cAMP (cyclic adenosine monophosphate, inositol, IP3 (1,4,5-triphosphate), and DAG (diacylglycerol). The second messenger was activated ion channels within the cell, including potassium, sodium, and calcium channels on the extracellular membrane. Cell depolarization caused by ionization and neurotransmitters gets released, which direct nerve impulses to the brain carrying the bitter taste signal, and taste blockers function by interfering with taste transduction.

Ion Exchange Complexation

A drug resinate complex is formed when a drug in its ionic form interacts with an adequate ion exchange resin, which can be utilized to mask the taste of the medication. IERs are polymers with a high molecular weight that contain both anionic and cationic functional groups. IER possesses exceptional characteristics such as strong ion exchange capacity, physicochemical stability, good absorbability,

Table 7: Micromeritic properties of DRC

Properties	*Indion 204*				
	1:1	*1:1.5*	*1:2*	*1:2.5*	*1:3*
Angle of repose(°)	30.12	29.40	29.23	30.56	31.84
Housner's ratio	1.19	1.09	1.15	1.06	1.10
Carr's index(%)	15.09	15.23	10.07	12.08	9..23
Tulsion 335					
Angle of repose(°)	30.69	23.15	26.59	22.63	24.80
Housner's ratio	1.16	1.07	1.18	1.20	1.18
Carr's index(%)	16.38	8.19	9.72	14.91	15
Doshion p551					
Angle of repose(°)	26.46	28.30	30.86	31.59	31.08
Housner's ratio	1.12	1.18	1.16	1.19	1.08
Carr's index(%)	15.43	12.10	7.89	11.28	14.61

Table 8: Film thickness and folding endurance

Sr. no.	*Formulation code*	*Mean of thickness (mm)*	*Folding Endurance*
1	F1	0.26 ± 0.02	111 ± 5
2	F2	0.28 ± 0.01	123 ± 2
3	F3	± 0.01	129 ± 4

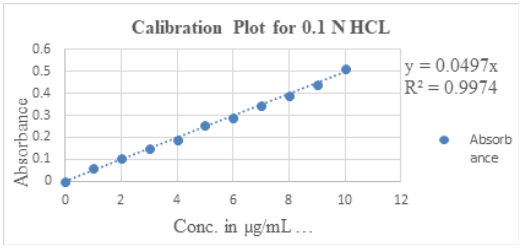

Figure 3: Calibration plot for Lamivudine with 0.1 N HCl

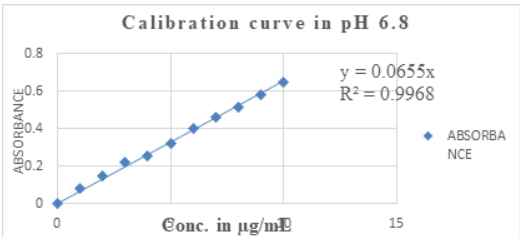

Figure 4: Calibration Plot for Lamivudine with pH 6.8 Phosphate Buffer

and non-solvency in any solvent, making them a potential alternative for usage as a flavor masking agent and to prolong medication release.[8] IER are high-molecular-weight insoluble polymers that include weakly bonded ions that can be easily exchanged with other ions in solution when interacting. IERs are typically classified into cationic exchangers and ionic exchangers, which differ in the type of ions transported between them.[9] Cationic exchangers contain positively charged mobile ions, whereas anion exchangers have negatively charged

Table 9: Drug contents of formulations

Sr. no	*Formulation code*	*Drug Content (%)*	*Uniformity weight (mg)*	*Surface pH*
1	F1	91.23	97.63 ± 0.5	6.7 ± 0.1
2	F2	92.98	94.12 ± 0.5	6.3 ± 0.3
3	F3	92.53	95.49 ± 0.5	6.2 ± 0.2

Table 10: Moisture uptake& loss, disintegration time profile

Sr. no.	*Formulation code*	*% Moisture uptake*	*Moisture loss study*	*Disintegration time(sec.)*
1	F1	1.49 ± 0.25	2.10 ± 0.09	26
2	F2	1.51 ± 0.05	1.25 ± 0.19	29
3	F3	1.53 ± 0.13	1.18 ± 0.12	35

exchangeable ions. As a result, the ion reactive capacity group attached to the resin structure's hydrocarbon network drives the chemical behavior of the resins.[10] The most common resin classifications accepted is based on combinations of strong and weak acid-base cationic and anionic exchangers.[11]

Preparation of Resinate by Batch Method

In this process, an IER is mixed with water to form slurry that may be used to remove ions from water. To make the complex, the correctly weighted quantity of medicine is added to the slurry and stirred to combine the ingredients. Immediately following the preparation of the complex, it is cleaned with water and dried. The amount of time it takes to mix the medicine and the resin, the pH, the temperature, and the swelling of the resin and the drug There are various parameters that can influence the complexation of a medication with a resin, including the resin ratio. When it comes to the manufacturing of taste-masked ion exchange resinates, the batch approach is always preferred over the column method. The important reason for this may be the small particle size of the IERs, which prevents them from being utilized in columnar processes due to the possibility of their washout during operation. The increase in swelling efficiency in the batch process results in a rise in the surface area available for ion exchange.[11,12]

EXPERIMENTAL WORK

Preparation of Calibration Curve of Lamivudine

Spectrophotometry is broadly employed for routine drug analysis. Lamivudine was estimated by spectrophotometry at

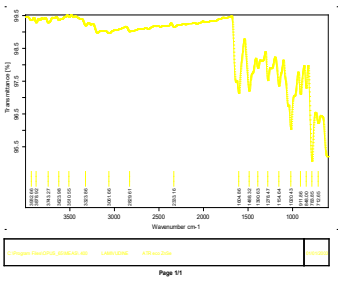

Figure 5: FTIR Spectra for Lamivudine drug

Table 11: Dissolution study

Time (min)	*Percentage dissolution in different time*		
	F1	*F2*	*F3*
0	0	0	0
15	37.26	42.6	35.29
30	45.63	48.43	43.23
45	62.13	66.23	59.79
60	72.53	78.29	69.89
90	80.26	85.19	78.41
120	92.8	95.8	90.22

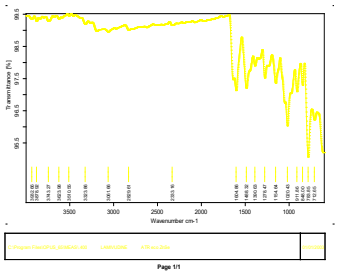

Figure 6: FTIR Spectra for Lamivudine: Indion 204

272 nm using JASCO-V520-UV-vis spectrophotometer. Exact quantity of lamivudine drug (10 mg)was taken and dissolved in 10 mL distilled water, the strength of the solution became 1000 µg/mL and then 1-mL of above solution diluted with 10 mL of distilled water to become 100 µg/mL. Then a series of dilutions are made from stock solution with a concentration range 1–10 ppm[13] from above stock solution. This procedure is reproduced in pH 6.8 phosphate buffer and HCl solution 0.1N.

Preparation of Taste Modified Drug Resin Complexes using IER

Batch preparation of the drug-resin combination is required. Add a correctly weighted lamivudine drug (100 mg) to the foresaid resin-containing solution and stir for 30 minutes on a magnetic stirrer. After that, add correctly weighted resin (150 mg) to the foresaid resin-containing solution and mix for another 30 minutes on a magnetic stirrer. Testing distilled water on a regular basis determined how long it took for the system to attain equilibrium. To eliminate any leftover contaminants, the resins were filtered and washed with 15 mL distilled water. UV-spectroscopy was used to determine drug concentration in the filtrate solution. The lamivudine absorbed was subjected for mathematical treatment for the amount of drug in the stock solution and amount of drug remaining in the filtrate at the conclusion of the equilibrium.[14] Resinates were subjected for 12 hours in a laboratory oven at 50°C before being stored in a desiccator with a tight-fitting lid. The four batches of drug-resin were made, with the drug-resin ratios being 1:1, 1:1.5, 1:2, 1:2.5, and 1:3. The slurry was continuously churned for 4 hours. Before measuring the drug content of the resins produced by filtering, they had to be separated and washed with a substantial amount of deionized water (Table 1).[15]

Table 12: Stability Study Parameter

Parameter	*F1*			*F2*			*F3*		
Days	10	20	30	10	20	30	10	20	30
Appearance	No Change	No Change	No Change	No Change	No Change	No Change	No Change	No Change	No Change
Drug Content (%)	91.23	91.22	91.19	92.38	92.36	92.35	95.53	95.53	95.51
Disintegration time (sec)	26	26	24	29	28	26	25	23	22
Folding endurance	195	192	190	203	200	199	198	196	194
Weight Uniformity	97.63	97.52	97.09	94.12	94.01	93.92	95.49	95.00	94.89

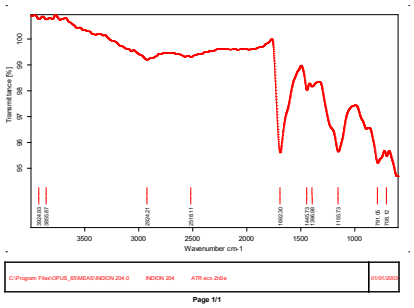

Figure 7: FTIR Spectra for Indion 204

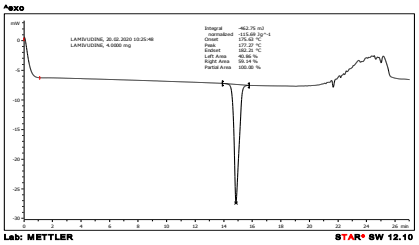

Figure 8: DSC Spectra for lamivudine

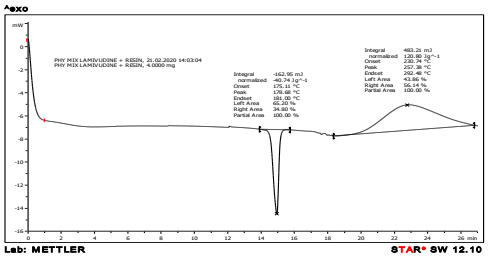

Figure 9: DSC spectra for Lamivudine: Indion 204 (Physical Mixture)

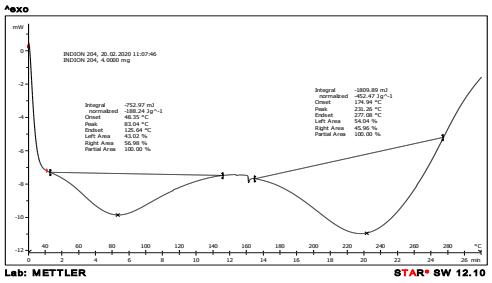

Figure 10: DSC spectra for Indion 204

Evaluation of Taste Masked Products

Determination of Drug Content

We utilized 100 mg of the taste-masked complex and shook it for an hour at 100 rpm to conceal the flavor of the HCL 0.1 N. The resultant solution was then filtered and analyzed for presence of lamivudine drug using a UV-spectrophotometer.[16,17]

Determination of Threshold Bitterness Concentration

Many drug concentrations ranging from 10 to 50 mg/mL were prepared using pH 6.8 phosphate buffer. Following that, 10 mL of the diluted solution was analyzed for taste by swirling in the oral cavity for 30 seconds, concentrating on the base of the tongue, followed by a solution rinse. If the bitter taste in the mouth was no longer noticed after 30 seconds, the solution was spat out and let to sit for at least 1 minute to check if this was due to delayed sensitivity. To prevent infection, the mouth was next washed with safe drinking water. You should wait at least 10 minutes after the first maximum concentration to taste the next. After each testing, the oral cavity was carefully cleaned with safe drinking water until no bitter taste remained.[18,19]

In-vitro Evaluation of Bitter Taste of Resonates

The precisely weighted taste masked complex was combined with 10 mL of pH 6.8 phosphate buffer in a volumetric flask and swirled at 50 rpm. The stirring was halted at various time points at 0, 10, 30, 60, 120 seconds. The dispersion was filtered, and the lamivudine concentration from the filtered resinate was calculated. In 10 mL of phosphate buffer, the time it took for resinate to reach the drug concentration equivalent to the threshold bitterness was recorded.[20,28]

Micromeritic Properties of Taste Masked Products

Angle of Repose

The funnel method was adopted to calculate the plane angle of repose for each formulation's granules. The granules were poured through a funnel opening on a piece of plane paper placed on a horizontal surface. These results in a granule pile of varying angles on the paper are plotted.[29]

Bulk and Tapped Density

Tapped bulk density along with loose bulk density were calculated. From each formula, 20 gm of powder was moderately shaken to deconstruct any agglomerates that may have formed before being placed into a 50 mL measuring cylinder. At 2 second intervals, it was permitted to fall under its own gravity onto a hard surface from a 1-inch height. The tapping was continued until there was no further deviation in volume.[310]

The following formulas are used to compute tapped bulk density (TBD) and loose bulk density (LBD)

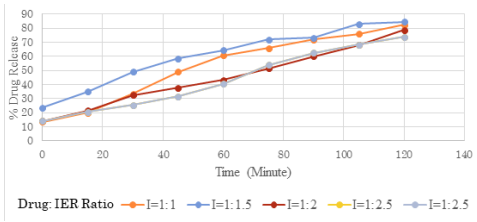

Figure 11: Cumulative drug release of Lamivudine and Indion 204 DRC

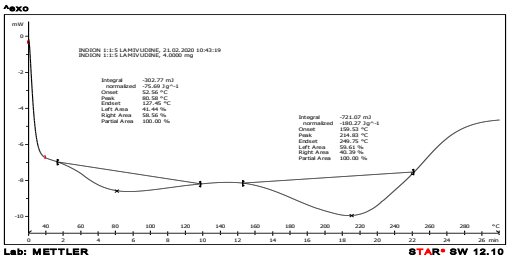

Figure 12: Indion 1:1.5 DSC Spectra

LBD: Weight of powder/volume of the packing
TBD: Weight of powder/tapped volume of the packing

Compressibility Index

Carr's compressibility index was calculated to determine the compressibility index of the formulation blends:

$$\text{Carr's Compressibility Index:} \frac{(\text{TBD}-\text{LBD})}{\text{TBN}} \times 100$$

Formulation of FDOFs of Taste-masked DRC of Lamivudine

The selection of taste of resin for taste masking required consideration of a number of features. For an acidic drug anion exchange resins are used for a basic drug cationic exchange resin are used. In the present work a weak cation exchange resin, i.e., indion 204, tulsion 335, doshion P551 was used for the taste masking of lamivudine. Weak cationic exchange resin are used here because of their weak binding capacity and the basic nature drug, therefore, they were selected for the immediate release taste masking formulation. It was observed that stirring for 4 hours is required to achieve drug loading equilibrium, so all the samples are stirred for 4 hours.[31]

RESULT AND DISCUSSION

Calibration Plot for Lamivudine with Water, HCL 0.1N and Phosphate Buffer pH 6.8

As reported, the solution of lamivudine in water obeyed Beer's Law between concentration ranges 1–10 µg/mL at 272 nm. The equation obtained as y= 0.0577x0 and R^2=0.9973. In 0.1N HCL the linearity was obtained between concentration ranges 1–10 µg/mL. the equation and R^2 obtained are y= 0.0497x and R^2= 0.9974. pH 6.8 Phosphate buffer was obtained between concentration ranges 1–10 ug/mL. the equation R^2 obtained are y= 0.0655x and R^2=0.9968. (refer Figure 2-4)

Film Thickness

Films were yellowish brown colored and smooth in appearance. The values are almost uniforms in all formulations. Film thickness is determined using vernier calliper. All film are measured at five positions, one at the center and four corners of the film and then calculated by mean of the thickness. The thickness of film varies between 0.26 ± 0.02 to 0.29 ± 0.01 mm.

Folding Endurance

A film's folding strength or durability can be decided by repeatedly folding it at the same site unless it loses its integrity. The folding strength of a 2x2 cm diameter strip was tested by folding the film at the same location multiple times until a visible break was noticed, and the average value was calculated and indicated folding endurance more than 100, suggesting that the formulation is resistant and flexible. The films are cut with a sharp scalpel (4 cm^2). And then this film was repeatedly folding about 30–35 folds per minute are continued till it was broken. The folding endurance is found to be between 111 to 129 fold after the film was break (refer Table 8).

Uniformity Weight

The five films were chosen at random and weighted individually, after which the mean weight and standard deviation were computed.

Surface pH Measurement

The film's surface pH may impact positive or negative effects *in-vivo*. The oral mucosa may be irritated by an acidic or alkaline pH. As a result, it is kept as close to neutral as possible. The film is exposed to 1-mL of filtered water. pH was calculated by exposing closely combined glass electrodes to film's surface upto equilibrium for 1 minute Five films were given each film are 4 cm^2 are cut at five different places from casted films and weight individually and calculated variations are various between 94.12 ± 97.63. Surface pH is determined using a digital pH meter (refer Table 9).

Impact of Stirring Time on Percentage Drug Loading

The resins are soaked in water for 30 minutes with continue stirring. Then add a specific amount of drug to the slurry. And continue stirring for 1, 2, 3, 4, 5 hours. The percentage of drug loading can be calculated by taking the absorbance of the filtrate (refer Table 3).

Drug Content

UV-spectrophotometer is used to evaluate the films for drug content. Films are 4 cm^2 in size and come from three separate casted film locations. Each patch was dissolved in pH 6.8 phosphate buffer in a volumetric flask of 50 mL. The solution's absorbance was determined at 272 nm using a UV-visible spectrophotometer.[4] The standard graph was used to calculate the percentage of drug content, and the same technique was done for all formulations. The drug content of DRC with indion 204 shows better result than tulsion and doshion. The drug content of drug: Indion 1:1.5 ratio showed 65.07% (Figure 5 to 11).

Effect of Lamivudine: Resin Ratio on % Drug Content

Different Drug

Resin ratios are prepared such as 1:1, 1:1.5, 1:2, 1:2.5, 1:3 are studied. The lamivudine: indion 204 in 1:1.5 ratio give best

drug loading about 94.51% and drug content 65.07% as the resin ratio increased but drug content gave variation some time (refer Table 2).The prepared film formulations are analyzed for determination of drug content under UVspectroscopy in reported wavelength (272 nm). The all formulation found the drug content in between 91–93% (refer Table 9).

Percentage Moisture Absorption

The PMA test was carried out to calculate the physical stability of the mouth-dissolving film under high humidity conditions. The 5 films are taken, weights are noted and kept in a desiccators with three saturated solutions of aluminum chloride, with the humidity inside the desiccator maintained at 79.5%. After 72 hours, the film is removed, weighed, and the % moisture absorption away is computed using the formula below.

$$\% \text{ Moisture Absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

The PMA is important to check the physical stability in different humidity condition. Take 5 film to check PMA the film was initially weighted and then taken into the desiccators. Desiccators contain saturated sodium chloride solution. After 3 days film was removed and again weight to that 5 films. As are varies between 1.49 ± 0.25 to 1.53 ± 0.13. (refer Table 9)

Moisture Loss Study

To assess the integrity and physical stability of the films, a percent moisture loss analysis was performed. The moisture loss capacity of the film was measured by placing a known weight and predetermined size of the film on a desiccator containing anhydrous calcium chloride for 3 days.[32] The film was removed and re-weighed, and the % moisture loss of the film was calculated using the formula,

$$\% \text{ Moisture Loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

The %moisture loss of the films was discovered to be in the range of 1.180.12 to 2.100.09. The standard deviation values are quite low, indicating that the medication lost very little moisture.

***In-vitro* Disintegration Time**

The disintegration time can be determined in such a way that it is the point at which film loses its integrity. The *in vitro* disintegration time was measured visually in a petri dish containing 20 mL of phosphate buffer pH 6.8 and spun every 10 seconds. All of the films had disintegration times ranging from 26 to 32 seconds. The FDA[33] recommends a disintegration time of 5 to 30 seconds (refer Table 10).

***In-vitro* Dissolution Time**

The usual basket or paddle apparatus can be used for dissolution testing. The test is performed in 900 mL of pH 6.8 phosphate buffer. Place the strip in the basket and collect the sample at the intervals suggested. The batch-prepared drug resin complex was subjected to dissolution tests in 0.1N HCL using a USP type 2 equipment at 100 rpm and 37°C, which revealed that drug release, took 120 minutes.[31] The cumulative drug release and cumulative percentage of drug retained are computed using this method. The type 2 apparatus was used for the *in-vitro* drug dissolving investigation. The experiments are carried out at 37°C in 900 mL of pH 6.8 phosphate buffer with a stirring speed of 50 rpm. A total 5 samples are collected and analyzed using UV spectroscopy. (refer Table 11)

Stability Study

Accelerated (40ºC/75% RH) and real time (30ºC/65% RH) stability study was carried out as per ICH guideline at tile of interval 10, 20, 30, 40, 50, 60 days. Films are evaluated for change in physical parameter, drug release and drug content. From the two months stability data it can be concluded that in F5 formulation there is no any substantial difference in the disintegration time, drug release, drug concentration, and physical appearance. The stability study was carried out as per ICH guidelines at the time interval of 0, 10, 20, 30 days. Film are evaluated for such physical parameter, drug release, drug content, disintegration time, folding endurance, weight uniformity, etc. There are no major changes to that formulation. (Refer Table 12)

Determination of Threshold Bitterness Concentration

The bitterness potential of lamivudine was assessed by a group of 5 volunteers with healthy status and was found to be 15 m/mL. The threshold bitterness concentration was not attained upto 120 seconds.[5] (refer Table 5)

Sensory Evaluation of Taste Masked Resinates

When the flavor-masked resinate was examined for its taste by examining candidates, the candidates did not experience characteristic lamivudine taste after holding resinate in their oral cavity for 30 seconds, indicating that the characteristic taste of the lamivudine was effectively disguised.[7] The 5 volunteers are asked to rate the food on a scale of 0 to 1, with 0 being the best and 1 being the worst.[34]

1: slightly bitter, 2: bitter, 3: extremely bitter (refer Table 6).

DISCUSSION

When trying to manufacture a product that is free of unpleasant active pharmaceutical ingredients (APIs), scientists have run into some obstacles.[35] There are a few different approaches that, when combined, can effectively hide the disagreeable flavour of the medication; however, it is important to utilise these strategies with caution so as not to limit the body's ability to absorb them.[36] According to the findings of the research, the use of ion exchange resin technology is a method that is both reasonably easy and successful in masking the bitter taste of a variety of pharmaceuticals that have a bitter flavour, hence boosting patient compliance.[37] Every single pharmaceutical formulation should be designed with the intention of providing a superior patient-compliant system that delivers the ideal therapeutic dose. Innovative FDOF strategies require prompt action on the part of the user. Patients report feeling satisfied with their treatment after using this tried-and-true dose form, which features improved absorption.[38-39] It was observed that,

out of the three resins that were put to the test, Indion 204 had the best results when combined with a ratio of 1:1.5, which made it possible for the most complexation to take place after only four hours of stirring. The resinate is processed into granules, which are characterised by adequate levels of angle of repose, bulk density, and flow property respectively. More than 94% of the medication was loaded into the Indion 204 resin, according to the findings.[40]

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