FORMULATION AND EVALUATION OF MOUTH DISSOLVING FILM OF DESLORATADINE 3^2 BY FACTORIAL DESIGN

Rajat Pawar[1*], Chanchal Navin Raj[2]

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Abstract: In the current investigation, the Antihistaminic drug desloratadine is formulated into a mouth dissolving film (MDF) for immediate drug release, enhanced therapeutic efficacy, and enhanced patient compliance. Batch processing with resins indion-204 was used to taste masking; complexes with processing duration, pH, temperature, and drug-resin ratio. Resins indion-234 effectively covered the taste. and determined that a drug-resin ratio of 1:1, a pH of 7, and a temperature of 30°C within 3 hours resulted in the most effective drug loading. MDF and then prepared using the optimized resinate. The rapid medication delivery achieved by combining the medicine with polymers like HPMC E-5 and HPMC E-15 in the mouth dissolving film. The plasticizer PEG 400 was used in a solvent casting process to create a film that dissolves in the mouth. Disintegration time, film thickness, and folding endurance investigated as response variables; a 3^2-level complete factorial design used to optimize the influence of independent factors such as HPMC E-5 and HPMC E-15. Using design of expert software, we examined the answers and discovered that HPMC E-5 and HPMC E-15 concentrations had large effects on the dependent variables. Maximum dissolving rate (99.02 0.284%) and minimal disintegration time 10 second were observed for the developed optimized formulation & FTIR spectrophotometry used to identify drug excipient interaction. All response values are determined to be statistically significant. Physical appearance, disintegration time, thickness, drug content, and in vitro drug release all remained stable during the stability trial. A film that dissolves in the mouth is a novel idea for the rapid administration of the medicine. This mixture, then, may be used to immediately alleviate allergic reactions.

Keywords: Desloratadine, Mouth Dissolving Film, HPMC E-5, HPMC E-15, Antihistaminic Drug

[1 *]Research Scholar, Sunrise University, Bagad Rajput, Alwar, Rajasthan, 301028, India
Email: [1*]rajatpawar74@gmail.com
[2 *] Sunrise University, Bagad Rajput, Alwar, Rajasthan, 301028, India

[*]Corresponding Author
Rajat Pawar[1*]
[1*]Research Scholar, Sunrise University, Bagad Rajput, Alwar, Rajasthan, 301028, India
Email: [1*]rajatpawar74@gmail.com

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1. INTRODUCTION :

Administering a medicine via the mouth is the most common and practical option. At least 85 percent of the medications used for systemic impact are likely taken orally. When a new medicine is developed, the pharmaceutical firm puts in a lot of work to make sure it can be prepared to be used orally. If the medicine cannot be given orally and a more complicated parental route is necessary, then the most common site for its delivery and subsequent successful treatment is a hospital or doctor's office. If patients are unable to effectively self-administer their medication, the market for the treatment might be much less than otherwise anticipated.[1]

Tablets and capsules, both solid oral dose forms, are widely used now days. This comprises both hard and soft gelatin capsules, as well as regular and controlled-release tablets. By contrast, liquid oral dosage forms, such as syrups, suspensions, solutions, and elixirs, are typically designed to contain one dose of medication in 5 to 30 ml. Tablet formulation and design can be thought of as the process by which the formulator ensures that the correct amount of the active drug in the correct form is delivered at or over the proper time at the proper rate and in the desired location while protecting its chemical integrity. When a patient is responsible for dosing themselves, the inaccuracy caused by such measures is estimated to be between 20 and 50 percent. The benefit of tablets and capsules is that they are unit dosage forms, thus they contain exactly one normal dose of the medicine. Pharmaceutical technologists have created a unique oral dose form called Orodispersible Tablets to meet the demands of patients who are traveling or who have limited access to water. [2,3]

Traditional tablets and hard gelatin capsules might be difficult for certain people to swallow,including the elderly, young children, and those with dysphasia.[4]
Patients hospitalized for acute neuromuscular problems and head traumas account for 30-50% of those diagnosed with dysphasia, whereas 45% of the general population has it.**:** limitations of traditional fast-dissolving intraoral tablets are circumvented by fast-dissolving films for oral mucosal administration.[5]

These films that dissolve in the mouth like breath mints have become more popular in recent years. When put in the mouth, these films immediately disintegrate to release the taste.

The development of a fast-dissolving drug delivery system has as one of its main goals the improvement of patient compliance and dosing convenience, as well as the identification and satisfaction of an unmet need among both general and specialized patient populations (such as children and the elderly). This method is a mouth-dissolving dosage form that may be used by people of all ages to take their prescriptions without drawing attention to them[6,7]

2. MATERIALS AND METHOD:

Materials:
Desloratadine was obtained as Zydus Cadila Health Care Pvt. Ltd. HPMC E-5, HPMC E-15, PVA, Sodium CMC, PEG-400, and Sodium saccharin, Citric acid, Raspberry, Amaranth; Indion 204 Indion 234 was obtained from loba chemicals.

Preparation of Mouth dissolving film:
Solvent casting is the preferred process for preparation of mouth dissolving films because it allows for the dissolution of water-soluble components into a clear, viscous solution. A suitable solvent is used to dissolve the medication and any excipients. The two solutions are combined, agitated, and then cast onto the prepared Petri dish, which is then dried.[8]

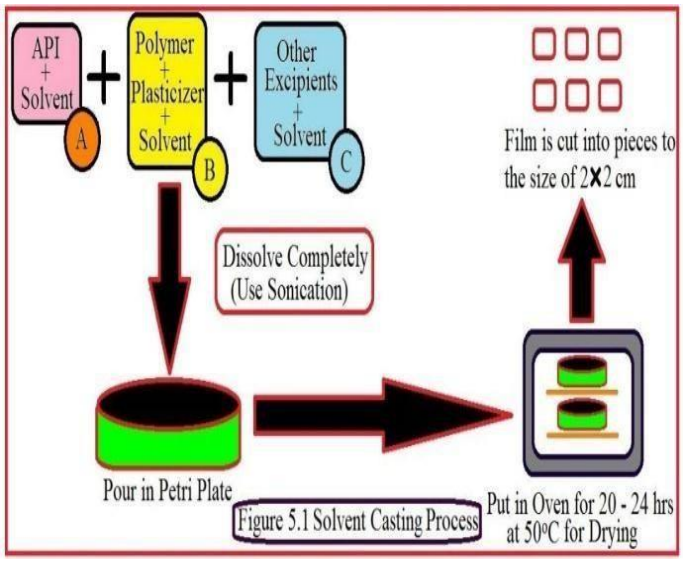


Figure : 1 Method of Preparation of MDF

Trial Batches of Mouth dissolving film of Desloratadine:

Desloratadine mouth dissolving films were made using the formulas in the tables below. The excipients were dissolved in distilled water and then put into the Petri dish after being well mixed.

Table: 1 Formula of Mouth dissolving film Using HPMC E5

Ingredients	Formulation code			
	A1	**A2**	**A3**	**A4**
Drug: resin complex Desloratadine:Indion-204 (Equivalent to 5 mg Desloratadine) (gm)	0.960	0.960	0.960	0.960
HPMC E-5 (%)	1	2	3	4
PEG-400 (ml)	0.12	0.24	0.36	0.48
Citric acid (gm)	0.31	0.31	0.31	0.31
Sodium saccharin (gm)	0.11	0.11	0.11	0.11
Amaranth	q.s	q.s	q.s	q.s
Raspberry	q.s	q.s	q.s	q.s
Water (ml)	45	45	45	45

Table:2 Formula of Mouth dissolving film using HPMC E15

Ingredients	Formulation code			
	B1	**B2**	**B3**	**B4**
Drug: resin complex Desloratadine:Indion-204 (Equivalent to 5 mg Desloratadine) (gm)	0.960	0.960	0.960	0.960
HPMC E-15 (%)	1	2	3	4
PEG-400 (ml)	0.12	0.24	0.36	0.48
Citric acid (gm)	0.31	0.31	0.31	0.31

Sodium saccharin (gm)	0.11	0.11	0.11	0.11
Amaranth	q.s	q.s	q.s	q.s
Raspberry	q.s	q.s	q.s	q.s
Water (ml)	45	45	45	45

Table: 3 Formula of Mouth dissolving film using PVA

Ingredients	**Formulation code**			
	C1	**C2**	**C3**	**C4**
Drug: resin complex Desloratadine:Indion-204 (Equivalent to 5 mg Desloratadine) (gm)	0.960	0.960	0.960	0.960
PVA (%)	1	2	3	4
PEG-400 (ml)	0.12	0.24	0.36	0.48
Citric acid (gm)	0.31	0.31	0.31	0.31
Sodium saccharin (gm)	0.11	0.11	0.11	0.11
Amaranth	q.s	q.s	q.s	q.s
Raspberry	q.s	q.s	q.s	q.s
Water (ml)	45	45	45	45

Table:4 Formula of Mouth dissolving film using Na CMC

Ingredients	**Formulation code**			
	D1	**D2**	**D3**	**D4**
Drug: resin complex Desloratadine:Indion-204 (Equivalent to 5 mg Desloratadine) (gm)	0.960	0.960	0.960	0.960
Na CMC (%)	1	2	3	4
PEG-400 (ml)	0.12	0.24	0.36	0.48
Citric acid (gm)	0.31	0.31	0.31	0.31
Sodium saccharin (gm)	0.11	0.11	0.11	0.11
Amaranth	q.s	q.s	q.s	q.s
Raspberry	q.s	q.s	q.s	q.s
Water (ml)	45	45	45	45

Evaluation of Trial Batches of Mouth dissolving film of Desloratadine:

Disintegration Time: Film measuring 2x2 cm^2 was placed in a beaker containing 50 ml of saliva and the time it took to dissolve was recorded.[9]

Thickness: A micrometer screw gauge may be used to precisely measure it at several predetermined points. This is crucial for ensuring consistent dosing in the strip by measuring film thickness uniformly.[10]

Folding Endurance: To test the strip's folding durability, fold it over and over again at the same spot until it snaps. The folding endurance of a film is measured by counting the number of folds it can withstand before tearing.[11]

Optimization of Mouth dissolving film:
In this experiment, we employed a 3^2-level complete factorial design to find the optimal formulation. Two components were considered at three different levels, and nine different permutations were tested. Independent variables were polymer concentration (X1), HPMC E-5, and HPMC E-15 (X2). We chose to measure the disintegration time (Y1), thickness (Y2), and folding endurance (Y3). In Tables 4 and 5 displayed the batch and level formulation variables from the experimental factorial design used to create the mouth dissolving dosage form of desloratadine.

This experimental setup yields the following polynomial equation:

$$Y = B_0 + B_1X_1 + B_2X_2 + B_{12}X_1X_2 + B_{11}X_1^2 + B_{22}X_2^2$$

Where, **B** = Intercept / arithmetic mean

X_1 and X_2 = Variables

B_1 and B_2 = Co-efficient of X_1 and X_2 variable

B12 = Co-efficient of interaction

B_{11} and B_{22} = Co-efficient of quadratic terms

Table: 5 Factorial design batches for Mouth dissolving film of Desloratadine

Run	Coded value		Responses		
Batch code	**HPMC E-5 (X_1)**	**HPMC E-15 (X_2)**	**Disintegration time (Y_1)**	**Thickness (Y_2)**	**Folding Endurance (Y_3)**
F1	-1	-1	-	-	-
F2	-1	0	-	-	-
F3	-1	+1	-	-	-
F4	0	-1	-	-	-
F5	0	0	-	-	-
F6	0	+1	-	-	-
F7	1	-1	-	-	-
F8	1	0	-	-	-
F9	1	+1	-	-	-

Table: 6 Level of formulation variables for Mouth Dissolving Dosage Form of Desloratadine

Independent variables	Levels (%)		
	-1	***0***	***+1***

HPMC E-5 (X_1)	1	1.3	1.6
HPMC E-15 (X_2)	0.5	0.7	0.9

Optimization of Mouth Dissolving Dosage Form of Desloratadine: Solvent casting was used to create the optimal mouth dissolving dosage form of desloratadine (Table 6) the excipients were dissolved in distilled water and then put into the Petri dish after being well mixed.

Table:7Optimized formulations of Mouth dissolving film of Desloratadine

Ingredients	**Formulation code**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Drug: resin complex Desloratadine:Indion 204 (Equivalent to 5 mg Desloratadine) (gm)	0.960	0.960	0.960	0.960	0.960	0.960	0.960	0.960	0.960
HPMC E- 5 (%)	1	1	1	1.3	1.3	1.3	1.6	1.6	1.6
HPMC E-15 (%)	0.5	0.7	0.9	0.5	0.7	0.9	0.5	0.7	0.9
PEG 400 (ml)	0.18	0.2	0.23	0.21	0.24	0.26	0.25	0.27	0.3
Citric acid(gm)	0.31	0.31	0.31	0.31	0.31	0.31	0.31	0.31	0.31
Sodium saccharin (gm)	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
Amaranth	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Raspberry	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Water (ml)	45	45	45	45	45	45	45	45	45

Evaluation of Optimized Formulation of Mouth dissolving film of Desloratadine

Physical Appearance/Texture:
The film's physical characteristics were evaluated by looking at it and touching it with two fingers.

Determination of Thickness: A micrometer was used to determine film thickness. Each sample was measured three times to get an average thickness. Air bubbled, nicked, or torn samples, as well as those with mean thickness variations over 5%, were not included in the study.[12]

Determination of Folding Endurance: The precise value of folding endurance (a measure of fragility) is determined by counting the Number of times the film may be folded at the same area before breaking. The prepared films were physically tested for their folding durability. A square of film (2x2 cm^2) was cut precisely and then folded over and over again until it snapped.[13]

Determination of Weight Variation: The films were measured and sliced into (2x2 cm^2) Electronic balance was used to figure out the difference in weight.

***In-vitro* Disintegration Studies:**
The film's disintegration and dissolution properties might be inferred from its disintegration time. The film used in this experiment measured exactly (2x2 cm^2) and was put in a beaker containing 10 milliliters of artificial saliva. The in vitro disintegration time was recorded as the amount of time the film took to shatter.[14]

Measurement of Tensile Strength:
The literature-referenced method of measuring tensile strength was used to fast-dissolving oral film. Two-by-two centimeter strips of film were produced. Each strip was put in the tensile grips of the testing machine in a longitudinal orientation. The strips were dragged by the top clamp at a speed of 60

mm/min across the head, with an initial grip separation of 10 mm. After the credits rolled, the test was judged complete. Each film's measurements were taken three times. The film's quality was determined by calculating three mechanical properties: tensile strength, elastic modulus, and percent elongation. The tensile strength of a material may be determined by applying a load until the film specimen ruptures; this is done by taking the average of three measurements and using the following equation to describe the cross sectional area of the broken film.[15]

$$Tensile\ Strength = \frac{Load\ at\ failure}{Strip\ Thickness \times Strip\ Width} \times 100$$

Measurement of Percentage elongation:
The following formula was used to calculate the elongation in percentage terms:

$$\%\ Elongation = \frac{Increase\ in\ length\ of\ strip}{Initial\ length\ of\ strip} \times 100$$

Determination of Drug Content:
Desloratadine concentration was calculated by dissolving sheets of known area (2x2 cm2) in 0.1 N HCl. Absorbance at 241 nm (using a UV-VIS double beam spectro-photometer) was used to quantify the concentration of desloratadine in the sample. An R2 = 0.997 standard calibration curve of 0.1N HCl was used to calculate the drug concentration. [16]

***In-vitro* Dissolution Studies:**
0.1N HCl was also used in the dissolving test. After that, we put each film sample (equal to 5mg of medication) into the dissolving medium. At 37o 0.5oC, 50 rpm, and with 900 ml of each dissolving media, a dissolution study was conducted using a Tablet dissolution USP (XXI)/(XXII)(Electrolab). Using a spectrophotometer set at 241 nm (UV-VIS double beam spectrophotometer), 5 ml samples were taken at 2, 4, 6, 8, 10, 15, 20, 25, and 30-minute intervals. Using a calibrated standard curve, the concentration was calculated.[17]

Surface pH:
The potential for adverse consequences in vivo was studied by measuring the surface pH of rapidly dissolving films. The oral mucosa may be irritated by a surface pH that is too acidic or alkaline; hence it was decided to maintain a pH value as near to neutral as feasible. After soaking the films in distilled water for 30 minutes at room temperature, they were placed in a closed Petri dish. The pH of the solution at the surface was measured using a digital pH meter (Elico, India). Research on Stability According to the ICH recommendation, the oral films were stable for 1 month when kept at 40 degrees Celsius and 75% humidity. The film's morphological features, disintegration time, drug content, and in vitro dissolution studies should be monitored during storage.[18]

3. RESULTS AND DISCUSSION:

Characterization of Mouth dissolving film
Fourier Transform Infra-Red (FTIR)
The FTIR analysis was conducted as described in Table 8 and Figure 2 show the FTIR spectra of Desloratadine, HPMC E-5, HPMC E-15, and the physical combination, respectively. The physical mixture's signature peaks followed a path only slightly different from that of the pure drug. So, no interactions between drugs and their excipients were identified.

Table: 8 FTIR spectra of Desloratadine, Indion-204 and Desloratadine: Indion204 Complex

Drug /polymer	N-H Stretch -1 cm	C- Stretch(aliphatic) -1 cm	Aromatic C=Cstretchcm-1	C-H bend -1 cm	C-O-C Stretch (ether) -1 cm

Desloratadine Resinate	3302.87	2939.16	1636.12	1479.31	-
HPMC E 5	-	2980.77	1650.20	1456.20	1052.77
HPMC E 15	-	2928.11	1612.00	1474.25	1050.98
Physical Mixture	3344.87	2969.65	1664.14	1464.59	1006.74

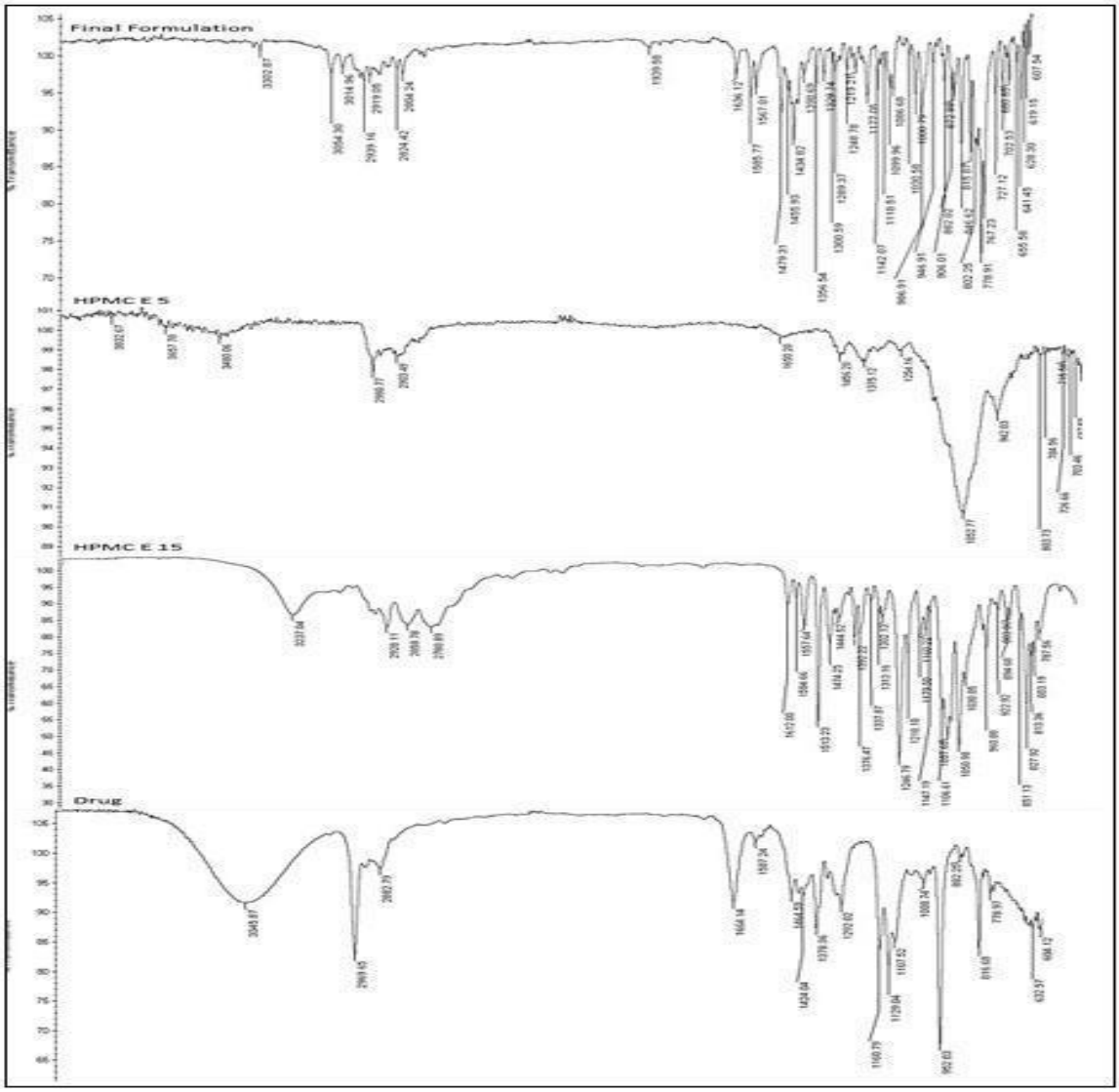
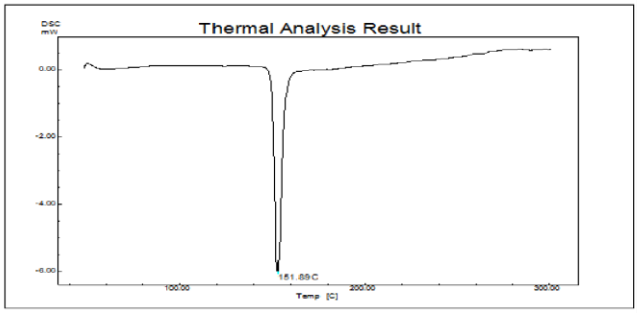
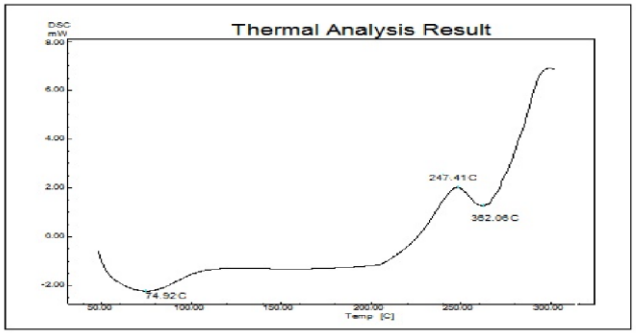


Figure : 2 FTIR spectra of Drug, HPMC E15, HPMC E5 and mixture of Resinate, HPMC E15 and HPMC E5

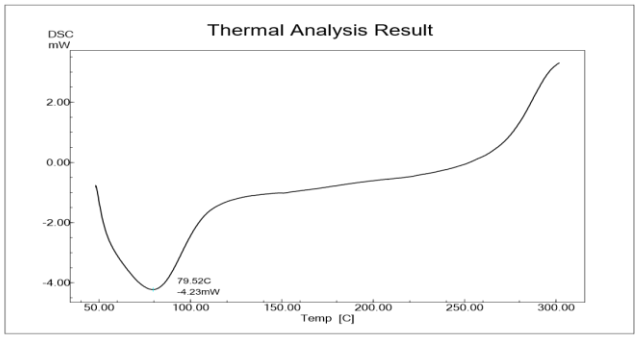
Differential Scanning Calorimetry (DSC)



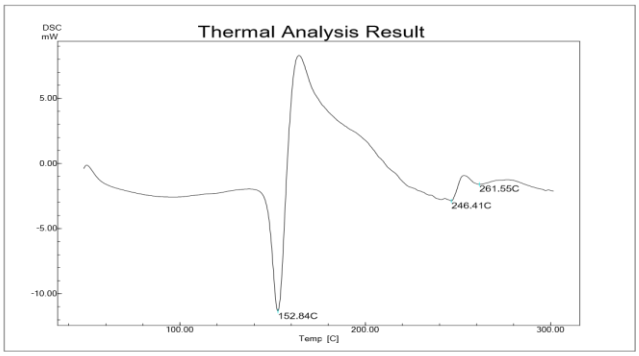
(A)



(B)



(C)



(D)

Figure :3 Thermogram of (A) Drug, (B) HPMC E15, (C) HPMC E5 and (D) mixture of Drug, HPMC E15 and HPMC E5

Selecting chemically compatible excipients is facilitated by differential scanning calorimetry (DSC), which may be used to probe and predict the physicochemical interaction between components in a formulation. The thermogram of a combination would change if there were any interaction between the components, either via the formation of new peaks or the elimination of existing ones. The drug's melting point, bioavailability, and release

kinetics will all shift if it undergoes a polymorphic mutation.
Figure no. 3 shows a DSC thermo gram of desloratadine in its final state. The melting point of the pure substance, as seen on a thermogram, is 151.89°C , where there is an endothermic peak. There is no drug-excipient interaction, as shown by the DSC thermo gram for the drug-loaded film, which exhibits a peak at roughly 152.84 °C.

Evaluation of Trial Batches of Mouth dissolving film of Desloratadine
Disintegration Time:

Table: 9 Disintegration time of Mouth dissolving film of Desloratadine in HPMCE5

HPMC E- 5 (sec)	Formulation code			
	A1	A2	A3	A4
	4.33 ± 0.47	13.5 ± 1.22	17.33 ± 0.33	50.33 ± 1.19

Table: 10 Disintegration time of Mouth dissolving film of Desloratadine

HPMC E- 15 (sec)	Formulation code			
	B1	B2	B3	B4
	9.83 ± 0.62	16.33 ± 1.25	32.33 ± 0.39	66.50 ± 1.08

Table: 11 Disintegration time of Mouth dissolving film of Desloratadine

PVA (Sec)	Formulation code			
	C1	C2	C3	C4
	208.16 ± 1.03	258.33 ± 0.85	363.50 ± 1.47	508.33 ± 0.85

Table: 12 Disintegration time of Mouth dissolving film of Desloratadine

Sodium CMC (sec)	Formulation code			
	D1	D2	D3	D4
	143.33 ± 0.62	187.83 ± 0.24	317.16 ± 0.51	388.50 ± 0.71

It was discovered that the disintegration period lengthened with increasing polymer content. The polymers HPMC E-5 and HPMC E-15 disintegrated the film more quickly than other formulations.
That's why we went with a 32-full factorial design using HPMC E-5 and E-15 (a combined 1.5%).

Thickness:

Table: 13 Thickness of Mouth dissolving film of Desloratadine (HPMC E5)

HPMC E5 (mm)	Formulation code			
	A1	A2	A3	A4
	0.031 ± 0.002	0.073 ± 0.005	0.110 ± 0.012	0.126 ± 0.012

Table: 14 Thickness of Mouth dissolving film of Desloratadine (HPMC E15)

HPMC E15 (mm)	Formulation code			
	B1	B2	B3	B4
	0.031 ± 0.002	0.083 ± 0.017	0.116 ± 0.029	0.120 ± 0.008

Table: 15 Thickness of Mouth dissolving film of Desloratadine (PVA)

PVA (mm)	Formulation code			
	C1	C2	C3	C4
	0.079 ± 0.004	0.126 ± 0.012	0.146 ± 0.011	0.175 ± 0.004

Table: 16 Thickness of Mouth dissolving film of Desloratadine (Na CMC)

Sodium CMC (mm)	Formulation code			
	D1	D2	D3	D4
	0.076 ± 0.003	0.110 ± 0.034	0.123 ± 0.023	0.136 ± 0.027

Since HPMC E-5 and HPMC E-15 had a more manageable thickness at lower polymer concentrations they were chosen for the 3^2level complete factorial design. :

Folding Endurance:

Table: 17 Folding endurance of Mouth dissolving film of Desloratadine (HPMC E5)

HPMC E5	Formulation code			
	A1	A2	A3	A4
	380.66 ± 3.09	450.33 ± 4.92	524.00 ± 2.83	577.66 ± 2.05

Table: 18 Folding endurance of Mouth dissolving film of Desloratadine (HPMC E15)

HPMC 15	Formulation code			
	B1	B2	B3	B4
	404.00 ± 3.27	481.66 ± 2.49	513.66 ± 3.68	624.33 ± 2.87

Table: 19 Folding endurance of Mouth dissolving film of Desloratadine (PVA)

PVA	Formulation code			
	C1	C2	C3	C4
	178.00 ± 2.160	204.00 ± 2.94	226.66 ± 1.69	254.33 ± 3.35

Table: 20 Folding endurance of Mouth dissolving film of Desloratadine (Na CMC)

Sodium CMC	Formulation code			
	D1	D2	D3	D4
	148.66 ± 2.62	181.00 ± 4.55	204.33 ± 4.11	228.66 ± 3.28

Since HPMC E-5 and HPMC E-15 were found to have more folding endurance than the other formulations, they were chosen for the 3^2-factorial design.

Evaluation of Optimized Formulation of Mouth dissolving film of Desloratadine

Physical Appearance/Texture :

The films are sleek and sophisticated in their transparency, pink hue, and silky smooth feel.

Determination of Thickness:

The mouth dissolving dosage form thickness was determined using the procedure described in Section determined that the thickness of the mouth dissolving dosage form should be between 0.052 and 0.005 and 0.082 and 0.014 millimeters.

*All the readings are expressed as mean ± standard deviation (n=3)

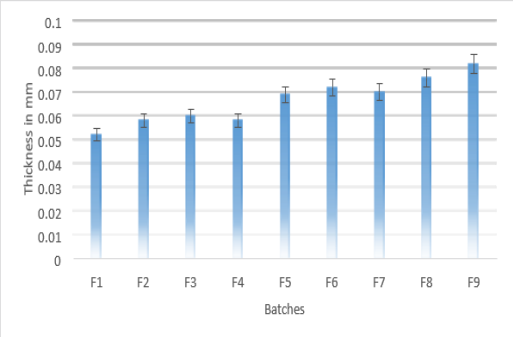


Figure: 4 Thickness of Mouth dissolving film of Desloratadine in optimized formula

The film's thickness grows in proportion to the polymer's concentration. The homogeneity of medication distribution may be seen in the film's thickness.

Determination of Folding Endurance :

The technique described in Section was used to evaluate the folding endurance of the mouth dissolving film. That the folding endurance of the Mouth Dissolving Dosage Form was between 410.00 3.29 and 466.00 4.24.

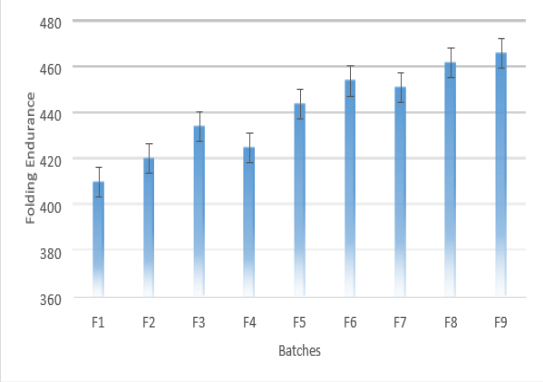


Figure :5 Folding Endurance of Mouth dissolving film of Desloratadine in optimized formula

The polymer's folding durability grows proportionally with its concentration. The film's strength and durability in the face of repeated folding are reflected in the film's folding endurance

Determination of Weight Variation :

The mouth-dissolving dosage form's weight was determined using the procedure described in Section. It was determined that the typical weight of a Mouth Dissolving Dosage Form is between 10.03 and 0.17 and 0.34 grams. *

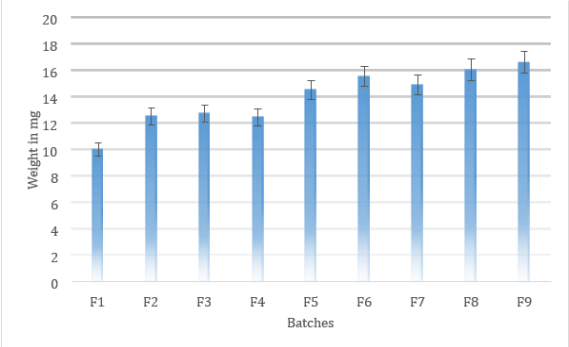


Figure: 6 Weight of Mouth dissolving film of Desloratadine in optimized formula

The polymer's mass grows proportionally with its concentration. The film's consistent weight gains indicate that the components were spread out evenly.

***In-vitro* Disintegration Studies :**

Following the protocol outlined in Section the in vitro disintegration time of the Mouth Dissolving Dosage Form was determined. Researchers determined that the disintegration period of the mouth dissolving film was between 7.61 0.48 to 16.33 0.58 minutes. The disintegration times listed in table 21 are the ones that really occurred.

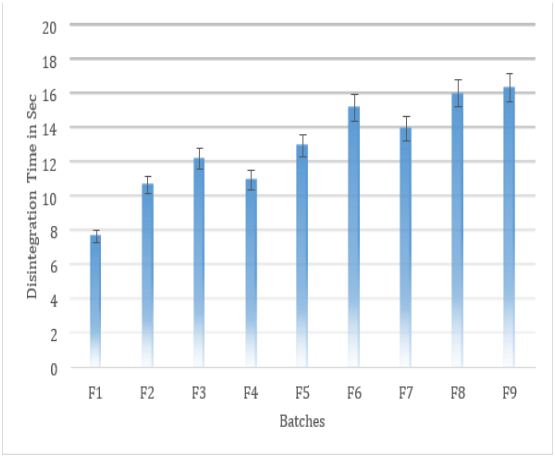


Figure: 7 Disintegration time of Mouth dissolving film of Desloratadine in optimized formula

Disintegration time rises and medication release is slowed with increasing polymer concentration.

Measurement of Tensile Strength :

According to the procedure described in Section the tensile strength of the Mouth Dissolving Dosage Form was determined. Researchers determined that the tensile strength of the mouth dissolving dosage form was between 51.72 1.61 N/m2 to 74.66 0.67 N/m2.

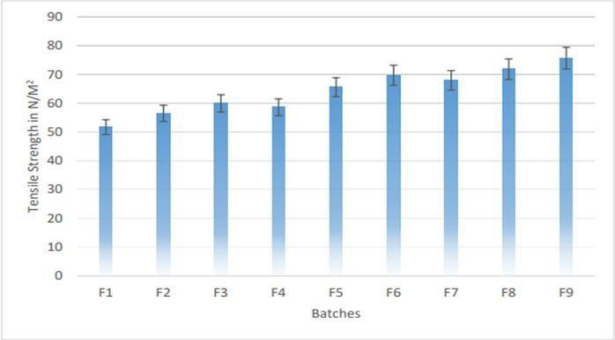


Figure: 8 Tensile strength of Mouth dissolving film of Desloratadine in optimized formula

The tensile strength improves with increasing polymer content. It's what makes the film sturdy and long-lasting.

Measurement of Percentage Elongation:

Following the procedure outlined in Section 4 we determined the percentage elongation of the mouth-dissolving dosage form. Extending the mouth dissolving dosage form by a percentage yielded results between 21.690.64 to34.450.88

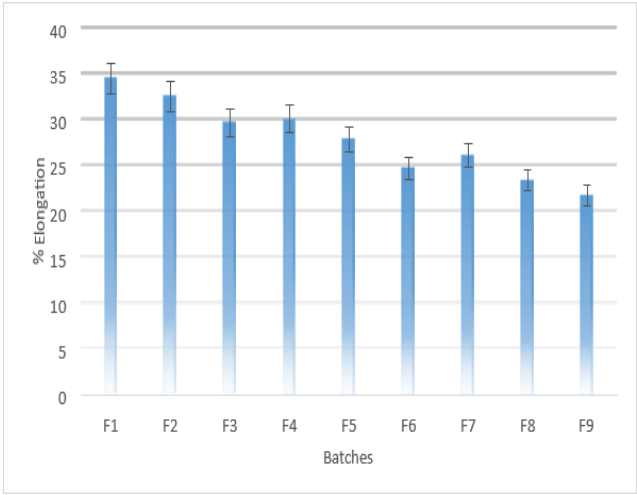


Figure :9 Tensile strength of Mouth dissolving film of Desloratadine in optimized formula

Percentage elongation reduces as polymer concentration rises. The elasticity of a film may be measured in terms of its percentage of elongation.

Determination of Drug Content :

As described in Section the drug content of the Mouth Dissolving Dosage Form was determined. The drug content of the mouth dissolving dosage form was determined to be between 97.73 0.63 and 99.56 0.57, which is within the range of allowable values as defined by IP.

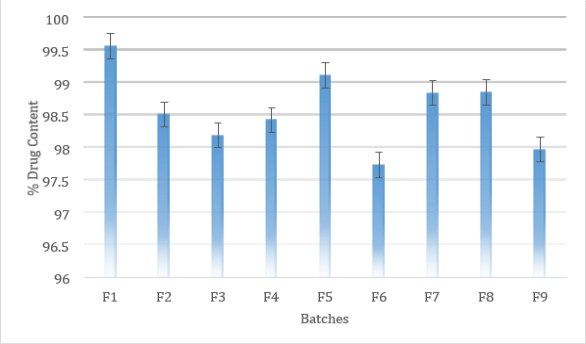


Figure :10 Percentage Drug Content in Mouth dissolving film of Desloratadine in optimized formula

The drug content in the film diminishes with increasing film concentration and prolonged breakdown time. This parameter is useful for determining how much drug is in the movie.

***In-vitro* Dissolution Studies:** The technique for the in-vitro dissolution research of the mouth-dissolving dosage form is described in Section. Figure 11 displays the percent cumulative medication release of all optimized formulations. Disintegration time and drug solubility both increased with higher HPMC E5 and HPMC E15 concentrations..

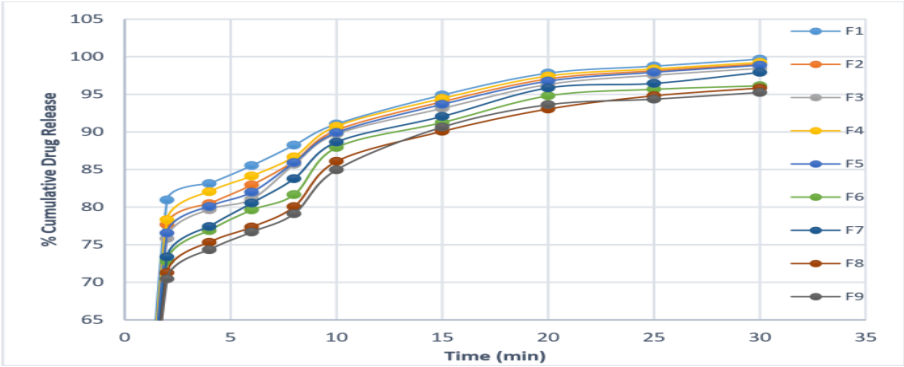


Figure: 11 % Cumulative drug release of formulations F1 to F9

Increases in film concentration result in slower disintegration and hence lower cumulative drug release. This value provides insight into the drug's dissolution kinetics.

Surface pH :

The mouth dissolving dosage form's surface pH was determined using the procedure described in. This dosage form's surface pH was measured to be between 6.97 0.05 to 7.06 0.12.

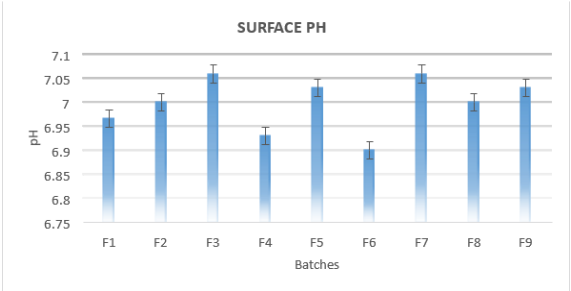


Figure :12 Drug Content in Mouth dissolving film of Desloratadine in optimized formula

Table: 21 Evaluation data of Mouth dissolving film of Desloratadine

Formulation	Weight variation (mg) Mean± SD	Thickness (mm) Mean± SD	Folding endurance (Times) Mean±SD	Drug Content (%) Mean±SD	*% Elongation* Mean±SD	*Tensile Strength N/m2* Mean±SD	Disintegration Time (sec) Mean±SD
F1	10.03 ± 0.17	0.052± 0.005	410.00 ± .29	99.56±0. 57	34.45 ± .88	51.72 ± .61	7.61 ± 0.48
F2	12.18 ± 0.12	.057±0. 016	420.33 ± 2.45	98.51 ± .79	32.52 ± 0.88	56.51 ± 0.46	10.66 ± 0.47
F3	12.76 ± 0.25	0.060±0 .008	434.00 ± .28	98.19 ± .74	29.66 ± 0.92	59.93 ± 1.38	12.22 ± 0.58
F4	12.46 ± 0.11	.058±0. 019	424.00 ± 4.23	98.42 ± .11	30.08 ± 0.30	58.61 ± 1.01	10.93 ± 0.13
F5	14.53 ± 0.31	0.069±0 .021	444.33 ± 2.91	99.11 ± .88	27.84 ± 0.22	64.58 ± 0.97	12.95 ± 0.43
F6	14.46 ± 0.17	0.072± 0.026	454.00 ± 3.79	97.73 ± .63	24.86 ± 0.39	69.70 ± 0.24	14.16 ± 0.54
F7	14.93 ± 0.43	0.070± 0.015	451.33 ± 4.26	98.84 ± .91	26.07 ± 0.38	67.95 ± 0.54	13.90 ± 0.27
F8	16.06 ± 0.18	0.076 ± 0.023	462.33 ± 4.68	98.85 ± .61	23.34 ± 0.53	71.83 ± 0.80	16.19 ± 0.52
F9	16.63 ± 0.34	0.082± 0.015	466.00 ± 4.25	97.97 ± .56	21.69 ± 0.64	74.66 ± 0.67	16.33 ± 0.58

Data Analysis: All of the data was entered into the trial version of DESIGN-EXPERT 8.0.7.1 and analyzed using ANOVA. Table 22 displays the results of a 3^2-way complete factorial design.

Table :22 Summary of 3^2 full factorial Design

Run	Coded value		Responses		
Batch code	**HPMC E 5 (X1)**	**HPMC E 15 (X2)**	**Disintegration time (Y1)**	**Thickness (Y2)**	**Folding Endurance (Y3)**
F1		-1	07.66	0.052	410.00
F4	0	-1	10.96	0.058	424.00
F7	+1	-1	13.96	0.070	451.33
F2	-1	0	10.66	0.058	420.33
F5	0	0	12.95	0.069	444.33
F8	+1	0	16.00	0.076	462.33
F3	-1	+1	12.22	0.060	434.00
F6	0	+1	14.16	0.072	454.00
F9	+1	+1	16.33	0.082	466.00

Response Y1: Disintegration Time Analysis of Variance Table [Partial sum of squares - Type III]

Table 23 displayed the results of the investigation of disintegration time variance.

Table :23 ANOVA for Response Surface Quadratic Model of disintegration time

Source	Sum of squares	Df	Mean square	F value	P-value Prove> F	
Model	63.19	3	21.06	131.06	<0.0001	**Significant**
X1 HPMC E5	41.34	1	41.34	257.26	<0.0001	
X2 HPMC E 15	20.65	1	20.65	128.47	<0.0001	
X1X2	1.20	1	1.20	7.46	0.0293	
$X1^2$	0.022	1	0.022	0.16	0.7096	
$X2^2$	0.33	1	0.33	2.39	0.1825	
Residual	1.12	7	0.16			
Lack of fit	1.12	5	0.22			
Pure error	0.000	2	0.000			
Cor total	64.31	10	-			

An F-value of 131.06 for the model indicates that it is statistically significant. Both X1 and X2 had statistically significant effects on the disintegration time of the formulation, with P values of 0.0001 and 0.0001 (P 0.05) respectively. All the co-efficients had positive values, which meant that the disintegration time of the formulation became longer as the polymer concentration increased. The P > 0.05 result for the b22 nonlinearity co - efficient meant that it was a statistically unimportant factor; hence it was left out of the simplified model equation. The regression analysis equation is shown. Since P 0.05, the Coefficients b1, b2, and b12 were kept in the final model specification.

Analysis of variance (ANOVA) was used to rule out irrelevant variables, and the results are shown in Table 24 High values for Y1 (disintegration time) correlation coefficients suggest a strong match. For = 0.05, the minimum value of F is 2 (df = 1, 3). It can be inferred that the interaction term b11 and b22 does not substantially contribute to the prediction of Y1 (disintegration time) and may be excluded from the entire model since the computed value (F = 1.53) is less than the crucial value (F = 2).

Table: 24 ANOVA for Reduced Model of disintegration time

Source	Sum of squares	Df	Mean square	F value	P-value Prove> F	
Model	63.19	3	21.06	131.06	<0.0001	
X1 HPMC E5	41.34	1	41.34	257.26	<0.0001	**F_{cal}= 1.53**
X2 HPMC E15	20.65	1	20.65	128.47	<0.0001	**F_{tab}= 2**
X1X2	1.20	1	1.20	7.46	0.0293	
Residual	1.12	7	0.16			
Lack of fit	1.12	5	0.22			
Pure error	0.000	2	0.000			

Cor total	64.31	10	-			

Stddev	0.40	**R-Squared**	0.9825
Mean	12.89	**Adj R-Squared**	0.9750
C.V. %	3.11	**Pred R-Squared**	0.9036
PRESS	6.20	**Adeq Precision**	37.064

The "Adeq Precision" parameter evaluates the signal-to-noise ratio. The ideal ratio is larger than 4. Your signal-to-noise ratio of 37.064 is rather good. The design space may be explored with the help of this model.

Final Equation in Terms of Coded Factors: Time to disintegrate = +12.89 + 2.63 X +1.86 X -2.55 X 0.55 X 1 X 2

Disintegration time as a function of HPMC E-5 and HPMC E-15 was shown in Figure 13 and 14 as a Contour plot and a response surface plot (3D), respectively

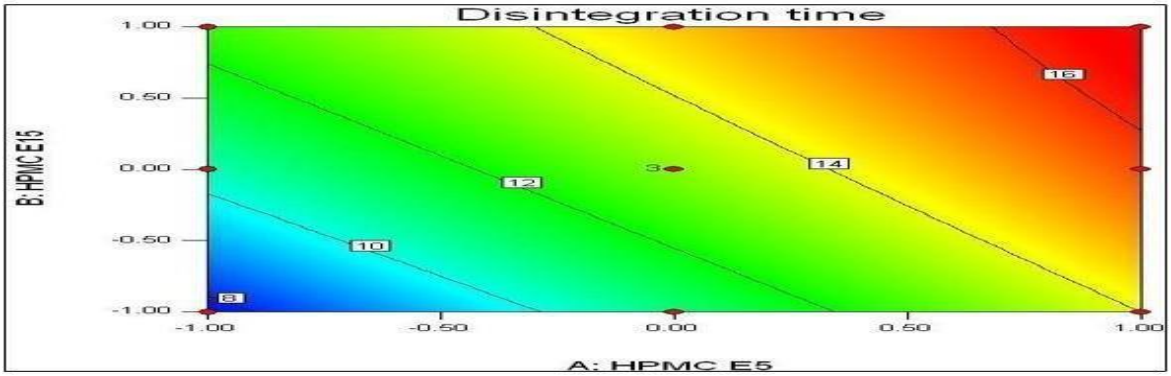


Figure 13 Contour plot showing the effect of HPMC E-5 & HPMC E-15 on disintegration time

Time to disintegrate as seen by a contour plot (Figure 14). Finding the contour plot to be linear. It showed that the disintegration time of Y1 was linearly related to the independent factors. The value of Y1 (disintegration time) increased as the concentration of polymers X1 and X2 rose.

The blue zone and the concentrations of X1 and X2 that produced the required Y1 are easily discernible in the contour map. polymers X1 and X2. The optimal concentrations of X1 and X2 for the intended Y2 may be seen in the blue zone surrounding the contour plot.

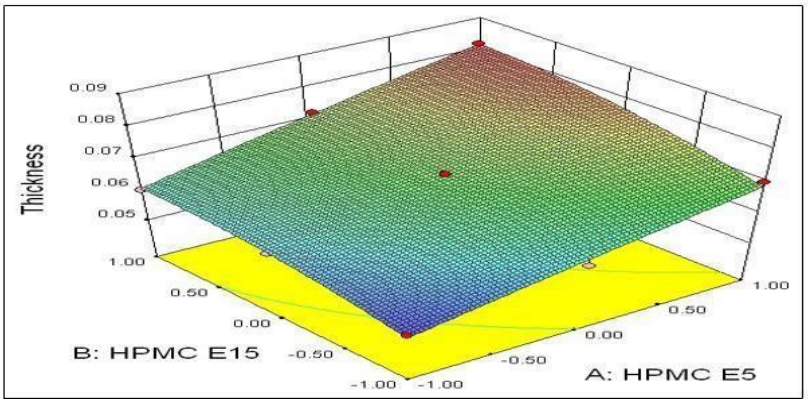


Figure: 14 Response surface plot (3D) showing the effect of HPMC E-5 & HPMC E-15 on thickness

Figure 14 is a visualization of the Y2 (thickness) response surface. According to the surface plot, the disintegration time of the film increased together with the addition of HPMC E -5. To achieve the desired results, however, it is essential to keep the concentration at its optimal level, as shown by the fact that the value of HPMC E -15 climbed steadily from low to high and the thickness of the matrix system did the same. The concentration of polymer that will always provide the desired effects is determined by extrapolating a single point from the region of the surface response plot where those effects are sought.

Response Y3: Folding Endurance
Analysis of Variance Table [Partial sum of squares - Type III]
Table 25 displays the results of an ANOVA on folding endurance.

Table :25 ANOVA for Response Surface Quadratic Model of Folding Endurance

Source	Sum of squares	df	Mean square	F value	P-value Prove> F	
Model	3030.04	5	606.01	60.72	0.0002	Significant
X1 HPMC E5	2216.83	1	2216.83	222.12	<0.0001	-
X2 HPMC E15	763.20	1	763.20	76.47	0.0003	-
X1X2	21.76	1	21.76	2.18	0.1998	
$X1^2$	2.45	1	2.45	0.25	0.6415	
$X2^2$	20.04	1	20.04	2.01	0.2156	
Residual	49.90	8	12.49	-	-	-
Lack of fit	49.90	6	16.65	-	-	-
Pure error	0.000	2	0.000	-	-	-
Cor total	3079.94	10	-	-	-	-

With an F-value of 60.72, the model is statistically significant. Both X1 and X2 had a statistically significant impact on the folding endurance of the formulation, with a P value of less than 0.0001 for X1 and less than 0.0003 for X2. The fact that every co-efficient had a positive value suggested that the formulation's folding endurance improved with increasing polymer concentration.

Since the P values for the nonlinearity co-efficients b12, b11, and b22 were all more than 0.05, they were removed from the complete model equation before producing the reduced model equation. The regression analysis equation is shown. P 0.05 indicated that the coefficients b1 and b2 are significant; hence they were kept in the simplified model.

Analysis of variance (ANOVA) was used to rule out irrelevant variables, and the results are shown in Table 25. Good agreement is shown by high values of the correlation coefficient for Y3 (folding endurance).
For = 0.05, the critical value of F is 1.670 (df = 5, 2). It can be inferred that the interaction term b12, b11, and b22 does not substantially contribute to the prediction of Y3 (folding endurance) and may be excluded from the whole model since the computed value (F = 1.670) is less than the crucial value (F = 3).

Table :26 ANOVA for Reduced Model of Folding Endurance

Source	Sum of squares	df	Mean square	F value	P-value Prove> F	
Model	3030.04	5	606.01	60.72	0.0002	Significant

X1 HPMC E5	2216.83	1	2216.83	222.12	<0.0001	F_{cal}=1.670
X2 HPMC E15	763.20	1	763.20	76.47	0.0003	F_{tab}=3
Residual	49.90	8	12.49	-	-	-
Lack of fit	49.90	6	16.65	-	-	-
Pure error	0.000	2	0.000	-	-	-
Cor total	3079.94	10	-	-	-	-

StdDev	3.53	**R-Squared**	0.9676
Mean	441.45	**Adj R-Squared**	0.9595
C.V. %	0.80	**Pred R-Squared**	0.9303
PRESS	214.72	**Adeq Precision**	33.054

The "Adeq Precision" parameter evaluates the signal-to-noise ratio. The ideal ratio is larger than 4. Your signal-to-noise ratio of 33.054 is satisfactory. The design space may be explored with the help of this model.

Final Equation in Terms of Coded Factors:

Folding Endurance = +441.45 + 19.22X1 + 11.28X2

Figure 4.25 and 4.26 depict the influence of HPMC E-5 and HPMC E-15 on Folding Endurance as a Contour plot and a response surface plot (3D), respectively.

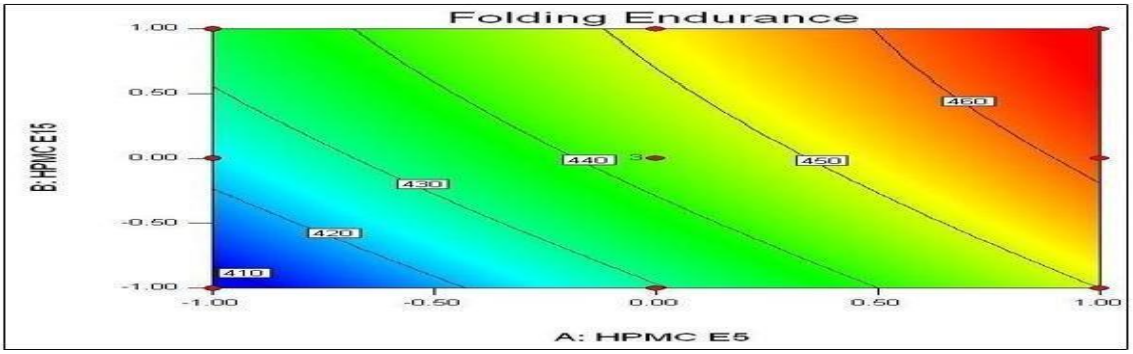


Figure 15 Contour plots showing the effect of HPMC E-5 & HPMC E-15 on folding endurance

The contour plot for folding endurance is shown in Figure 15. Finding the contour plot to be linear. Results showed a linear correlation between the various predictors and Y3 (folding endurance). Folding endurance (Y3) rose as the concentration of polymers X1 and X2 increased. The optimal concentration of X1 and X2 for the intended Y3 may be seen in the blue zone surrounding the contour plot.

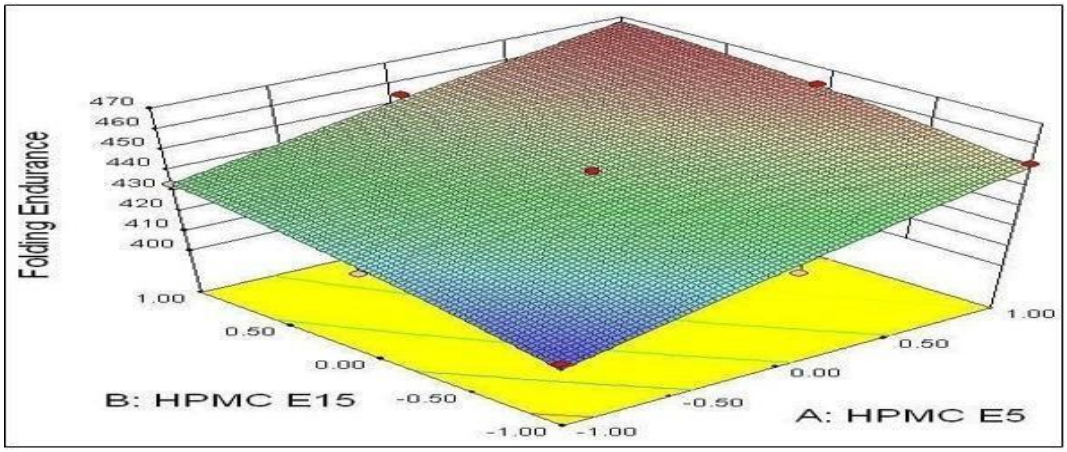


Figure 16 Response surface plot (3D) showing the effect of HPMC E-5 & HPMC E-15 on folding endurance

Folding endurance (Y3) response surface plot is shown in Figure 16. Surface plot analysis revealed that the film's disintegration time increased together with the concentration of HPMC E -5. Value of HPMC E -15, nevertheless, increased from its previous lows. It was inferred from the surface plot that the combination impact of polymer considerably influenced the folding endurance of the system, thus it is required to maintain the optimal concentration to accomplish the desired outcomes while the thickness of the matrix system also continuously grows. The concentration of polymer that will always provide the desired outcomes may be derived from the surface response plot by selecting a single point within the region of interest and extrapolating it along the other two dimensions.

Evaluation of Check Point Batch:

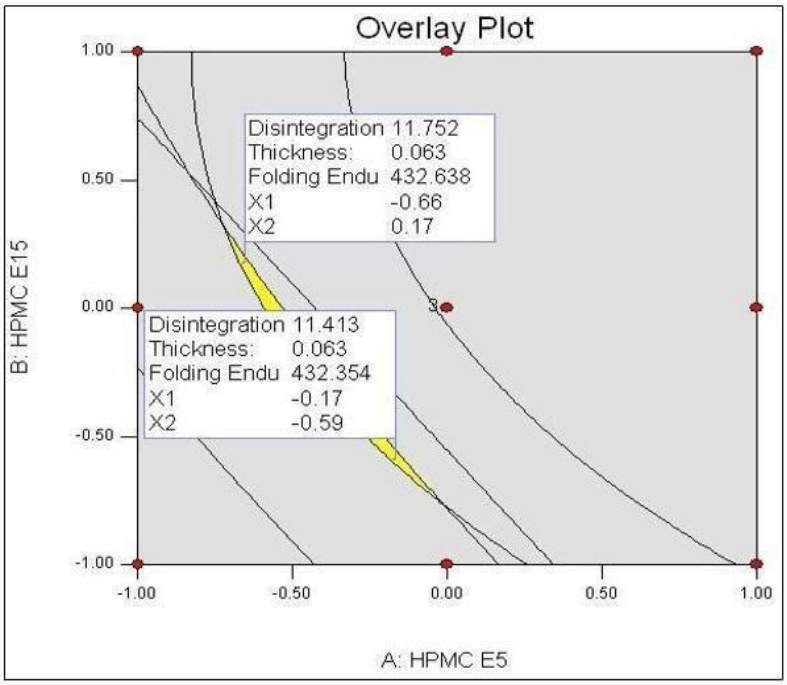


Figure 17 Display an overlay plot for a 3^2-level factorial design.

The disintegration time, thickness, and folding durability of two check point batches were determined using the overlay plot. Following the approach outlined in the

methodology section, we determined the disintegration time, thickness, and folding endurance. Formulation F10 had a disintegration time of 11.25 0.564 sec, whereas F11's was 10.90 0.377 sec. Formulation F10 was determined to have a thickness of 0.065 0.019 mm, whereas F11's thickness was measured at 0.061 0.014 mm. Folding endurance was measured and determined to be 427.25 3.564 for formulation F10 and 434.65 4.347 for formulation F11. Table 26 displayed the disintegration time, thickness, and folding endurance of checkpoint batches.

Table: 27 Formulation of check point batches*

Formulations	Coded value		Actual value	
	X1	X2	Y1	Y2
F10	-0.66	0.17	1.10	1.249
F11	-0.17	0.59	0.734	0.582

Table: 28 Evaluation of check point batches*

Formulations	Disintegration time (sec)	Thickness (mm)	Folding endurance
F10	11.25 ± 0.564	0.065 ± 0.019	427.25 ± 3.564
F11	10.90 ± 0.377	0.061 ± 0.014	434.65 ± 4.347

*All the readings are expressed as mean ± standard deviation (n=3)

Tables 27 and 28 provide the expected and actual values for the two batches of replies from the checkpoints.

Stability study :

Methodology Section details the technique that as used to conduct the stability investigation. Disintegration time, drug content, and in vitro drug release all remained constant throughout the stability testing.

The stability analysis results were shown in Tables 29, 30, and 31. After 15 and 30 days, those at 0 said that their look was refined, translucent, and pink. Therefore, the look of the film remained unchanged.

Table :29 Stability Study data for disintegration time

Stability study at 40°C and 75 % RH	
Test after time (days)	**Disintegration time (Sec.)**
0	7.6
15	8.1
30	8.6

Table :30 Stability Study data for drug content

Stability study at 40°C and 75 % RH	
Test after time (days)	**% drug content**
0	99.56
15	99.14
30	98.63

Table :31 Stability Study data for In-vitro drug release

Stability study at 40°C and 75 % RH	
Test after time (days)	**% Cumulative drug release after 30 min.**
0	99.68
15	98.42
30	97.33

4. CONCLUSION :

The formulation and evaluation of mouth dissolving films (MDFs) of Desloratadine have gained significant attention due to their potential benefits such as improved patient compliance, rapid onset of action, and ease of administration. In this study, various formulations of Desloratadine MDFs were prepared, characterized, and compared to identify the optimal formulation for enhanced therapeutic efficacy.

The study involved the formulation of Desloratadine MDFs using different polymers, plasticizers, and disintegrating agents. The films were prepared by the solvent casting method, and their physicochemical properties, such as thickness, weight variation, folding endurance, surface pH, and drug content uniformity, were evaluated. In addition, various evaluation parameters including disintegration time, drug release profile, and stability studies were conducted.

Desloratadine is a selective, H1 receptor antihistamine drug having bitter in taste. It is the major orally active metabolite of loratadine, approved for allergic rhinitis and/or chronic idiopathic urticaria. Problems like hand tremors, dysphasia and non-cooperative patients, the problems of swallowing is a common phenomenon which leads to poor patient compliance and ineffective therapy.

The study provides a foundation for the development of mouth dissolving films of Desloratadine, but there are several areas that warrant further investigation. These include:

Optimization of formulation: Fine-tuning the composition of formulation A to achieve an ideal balance between disintegration time, drug release profile, and stability.

In vitro-in vivo correlation: Conducting in vivo studies to establish a correlation between the in vitro dissolution profile and the pharmacokinetic behavior of Desloratadine MDFs.

Patient acceptability and preference: Performing user studies to evaluate patient acceptance, taste, ease of administration, and overall preference of the mouth dissolving films.

Scale-up and commercialization: Scaling up the manufacturing process and conducting cost-effectiveness analyses to determine the flexibility of large-scale production and commercialization of Desloratadine MDFs

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