Int. J. Sci. R. Tech., 2025 2(4)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Formulation and Evaluation of Fast Dissolving Film of Lisinopril

Siddhesh Gawari*, S. R. Ghodake

Loknete Shri Dada patil pharate College of pharmacy

ABSTRACT

"An ultra-thin film containing an active ingredient that dissolves or disintegrates in the saliva at aremarkably fast rate, within few seconds without the aid of water or chewing," is the definition ofa fast-dissolving oral film (FDOF). The most up-to-date oral solid dosage form is fast-dissolving oral films (FDOFs), which provide more comfort and flexibility. It improves the absorption of active pharmaceutical ingredients (APIs) by dissolving them in saliva and allowing them to be swallowed without chewing or water. The oral mucosa is four to a thousand times more permeable than the epidermis, allowing for rapid drug absorption and rapid bioavailability. Formulated drug- opening foams (FDOFs) are made from hydrophilic polymers that dissolve rapidly in the mouth and release the medication into the bloodstream via the buccal mucosa. [1] A fast-dissolving drug delivery method is developed to enhance bioavailability of drugs with modest dosages and significant first-pass metabolism.

Keywords: Fast Dissolving Film, Lisinopril, FDOF, APIs

INTRODUCTION

1.2 Oral Dissolving Film Theory:

In this setup, a thin film is present. Sublingual administration improves bioavailability because the drug dissolves faster and bypasses first-pass metabolism. Because SA is more easily absorbed, it breaks down and dissolves rapidly in the mouth. The following are the three main types of oral films:

1.Films have a rapid dissolving or releasing time (when held to the mouth).

2.Mucoadhesive films that dissolve (for use in the buccal or gingival area). The third option is buccal mucosa-adhering sustained-release films. [3]

1.3 Mechanism of oral mouth dissolving film theory:

Figure 1: Mechanism of oral mouth dissolving film theory

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Figure 2: Mouth-dissolving film

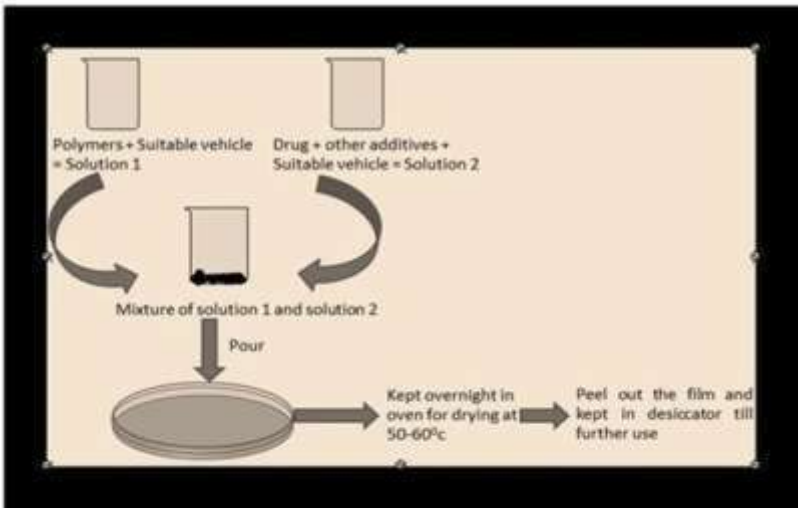
1.4 Need for fast-dissolving drug delivery systems: [4]

Patients with dysphasia may find it easier to take their medication as prescribed when it dissolves quickly. If a medicine is subject to patent protection, the marketing department will find that FDDS is a useful tool for managing the medical life cycle.

METHODS

1 Solvent casting method [81]

Fast dissolving films were prepared by solvent casting method as per the composition shown in table 1.In this method, the required quantity of water soluble polymer Sodium carboxymethyl cellulose was dissolved in distilled water in a beaker (covered with aluminium foil) with continuous stirring on magnetic stirrer to make required percentage of polymer solution and then the weighed quantity of ingredients like lisinopril as drug , glycerol as plasticizer, and menthol a flavor, Saccharin sodium as Sweetening agent was dissolved in distilled water in another beaker and then this mixture was added to the polymer solution. After continuous stirring for 2 hours the solution was left undisturbed for 12 – 16 hours to remove all the air bubbles. This polymeric – drug solution was then poured on to the moulds, allowed to air dry , packed in aluminum foil and then stored in desiccators until use.



Advantages

•Film has a fine gloss and is devoid of flaws like die lines, and it has superior uniformity of thickness and clarity to extrusion.

•The recommended finished film thickness is typically 12-100 m; however different
thicknesses are available to fulfill API loading and dissolving needs. The film has better physical qualitiesand is more flexible.

Disadvantages:

1.The polymer needs to be soluble in water or a volatile solvent.
2.It is ideal to generate a stable solution with a reasonable minimum solid content and viscosity.
3.It must be feasible to create a homogeneous film and be released from the casting support.

6.2.2 Experimental Design [82]

Box–Behnken design was employed to studythe effect of each independent variable on dependent variables Disintegration time (sec), Drug content (%) and Drug release (%) Lisinopril film formulation were prepared by solvent casting method.The Lisinopril film were optimized by using Box-Behnken Experimental Design (3 Factor, 2 Level, and DesignExpert Version 13). The independent variables selected were Sodium carboxymethyl cellulose(mg) (X1), Sodium starch glycolate(mg) (X2) and Glycerol(ml) (X3) with their low and high levels for preparing 13 run of formulations and dependent variable selected were Disintegration time(sec) ,(wetting time (sec)and Drug release (%). Finally optimized was selected for further characterization.

Table 14: DOE suggested and experimental batches

Formulation code	Lisinopril (mg)	Sodium carboxymethyl cellulose (mg)	Sodium starch glycolate(mg)	Glycerol (ml)	Sacchari n sodium (mg)	Menthol (ml)	Distilled water(ml)
L1	158.96	450	10	0.5	10	Q. S	Q. S
L2	158.96	450	11	0.75	10	Q. S	Q. S
L3	158.96	650	10	0.75	10	Q. S	Q. S
L4	158.96	650	12	0.75	10	Q. S	Q. S
L5	158.96	250	11	1	10	Q. S	Q. S
L6	158.96	250	11	0.5	10	Q. S	Q. S
L7	158.96	250	10	0.75	10	Q. S	Q. S
L8	158.96	450	10	1	10	Q. S	Q. S
L9	158.96	650	11	1	10	Q. S	Q. S
L10	158.96	450	12	1	10	Q. S	Q. S
L11	158.96	250	12	0.75	10	Q. S	Q. S
L12	158.96	450	12	0.5	10	Q. S	Q. S
L13	158.96	650	11	0.5	**10**	Q. S	Q. S

Calculation for Petri Dish

Diameter of Petri dish = 9cm Area of circle =
= 3.14 × 4.5 × 4.5
=63.585 cm2
Area of Single patch = L × W Area of Single patch =2×2
= 4 cm2
So, Total no of films = 63.585 / 4
=15.89
Total amount of drug requires = i.e. (Total no of films × Dose of drug) = 15.896×10 Total amount of drug require =158.96 mg

Table 15: List of independent variable and dependent variable on box Behnken design

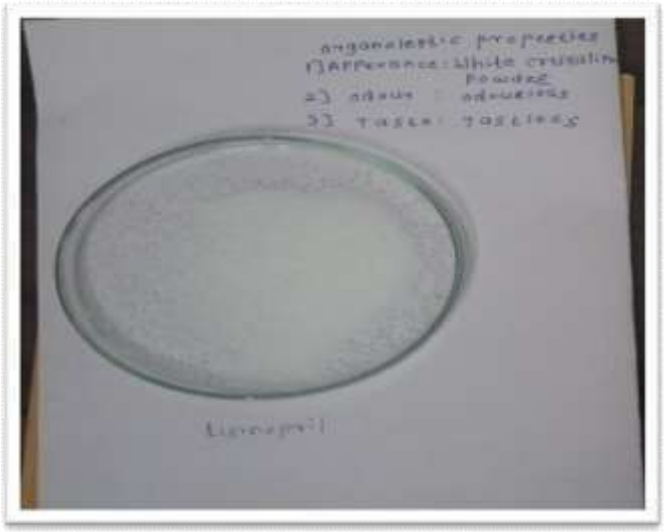
Independent Variable	Low (-1)	High (+)
Sodium carboxymethyl cellulose(mg)	250	450
Sodium starch glycolate(mg)	10	12
Glycerol(ml)	0.5	1
Dependent Variable	**Constraint**	
Disintegration time(sec)	Maximize	
Drug content (%)	Maximize	
Drug release (%)	Maximize	

RESULT AND DISCUSSION

7.1 PREFORMULATION STUDY

7.1.1 Identification of drug

1.1.1.1 Appearance



7.1.1.2 Active pharmaceutical ingredient: Lisinopril

7.1.2 Melting point

The capillary tube method was used to determine the melting point. The melting point of Lisinopril was found to be 164 and recorded melting point of Lisinopril 162-165 °C.

Table 16: Observation of melting point

Drug name	Observed value	Reported value
Lisinopril	164	162-165

Figure 10: Melting point of Lisinopril

7.1.3 Solubility study of lisinopril

The solubility study of lisinopril across various mediums reveals that methanol provides the highest solubility at 48.16 mg/mL, making it the most effective solvent for dissolving lisinopril. Ethanol (30.14 mg/mL) and distilled water (29.14 mg/mL) also demonstrate good solubility, suggesting they are suitable alternatives for formulation purposes.

Table 17: Solubility in different Medium

Medium	Solubility(mg/ml)
Distilled water	29.14
Methanol	48.16
Ethanol	30.14
Phosphate buffer ph 6.8	28.46
Phosphate buffer ph 7.4	26.54
Acidic buffer	21.46

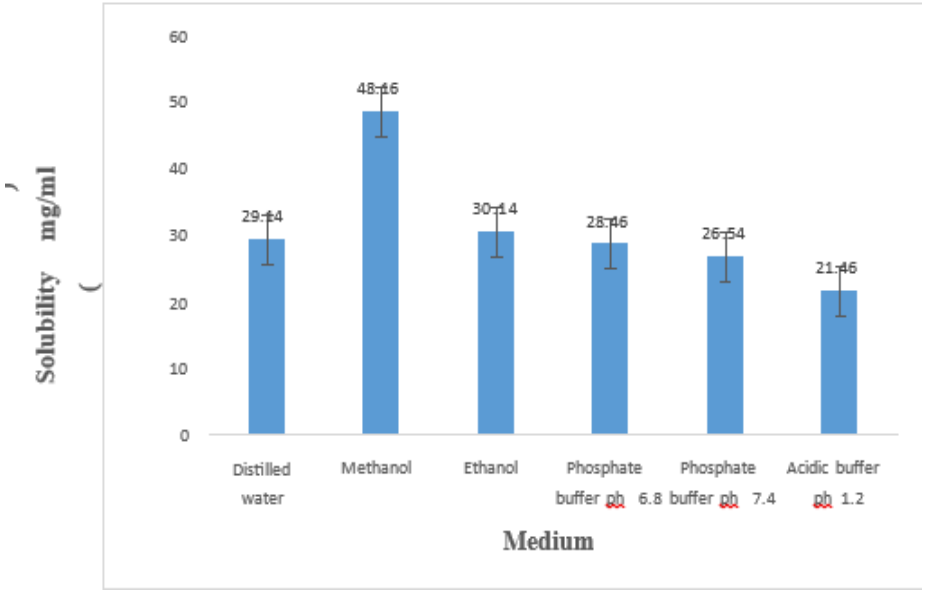


Figure 11: Solubility in different Medium

7.1.2 Spectrophotometric characterization of Lisinopril in UV Spectroscopy

7.1.2.1 Detection of Absorption Maxima (λ max)

Table 18: Observation of λmax

Drug name	Observed value(nm)	Reported value(nm)
Cilnidipine	210	210-220

7.1.2.2 Calibration curve

Table 19: Calibration curve in Distilled water

Concentration (µg/ml)	Absorbance
0	0
2	0.015
4	0.021
6	0.035
8	0.052
10	0.062
12	0.071

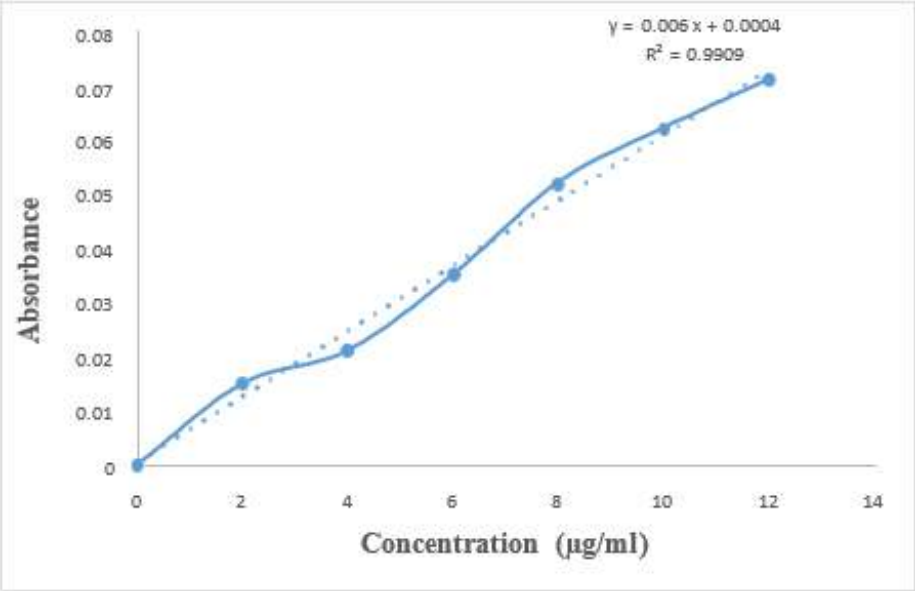


Figure 12: Calibration curve in Distilled water

Equation	y = 0.006x + 0.0004
Correlation coefficient	0.9909

7.1.2.2.2 Calibration curve in Methanol

Table 20: Calibration curve in Methanol

Concentration (µg/ml)	Absorbance
0	0
2	0.125
4	0.235
6	0.354
8	0.487
10	0.587
12	0.747

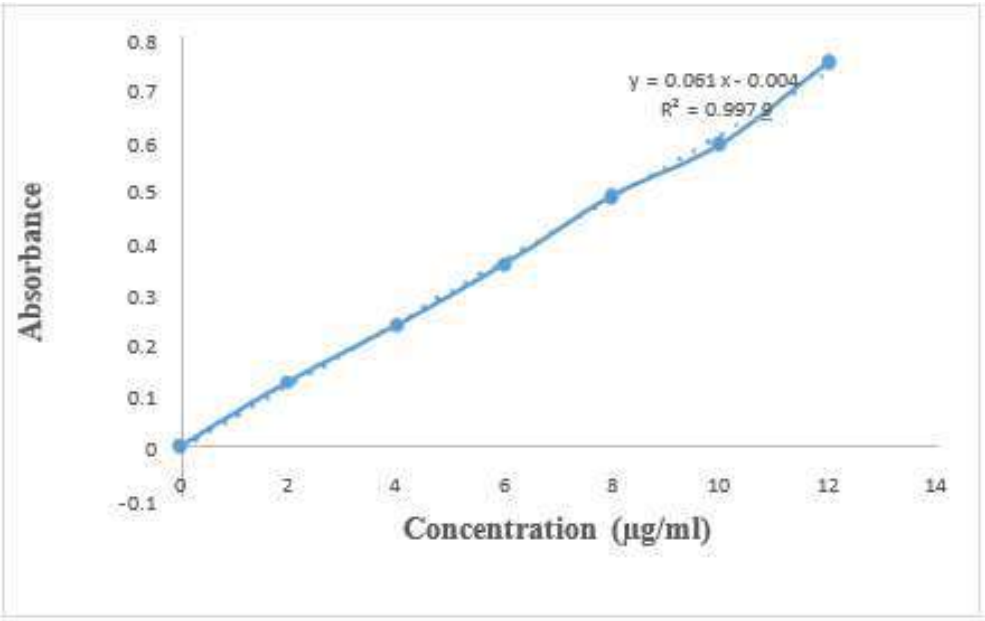


Figure 13: Calibration curve in Methanol

Equation	y = 0.061x - 0.004
Correlation coefficient	0.9979

7.1.2.2.3 Calibration curve in Ethanol

Table 21: Calibration curve in Ethanol

Concentration (µg/ml)	**Absorbance**
0	0
2	0.125
4	0.185
6	0.350
8	0.427
10	0.589
12	0.647

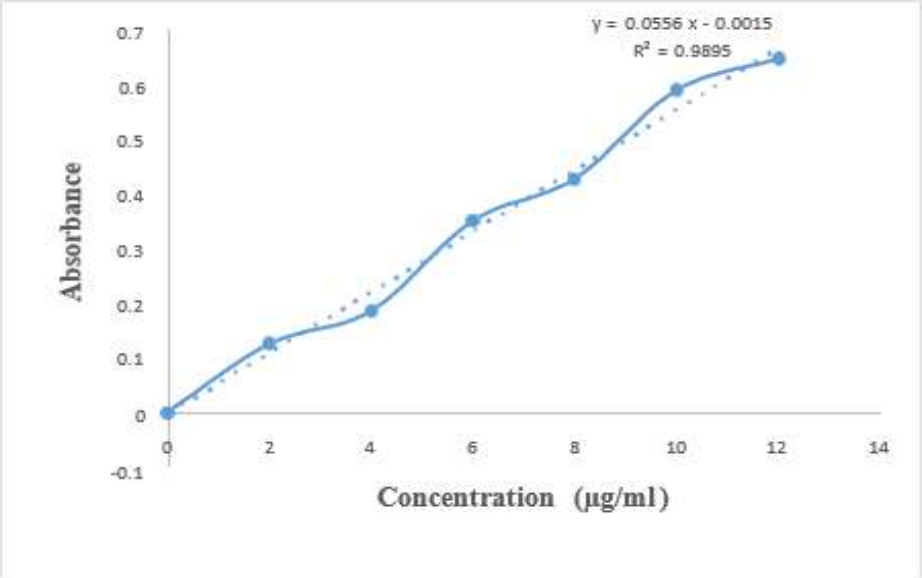


Figure 14: Calibration curve in ethanol

Equation	y = 0.0556x - 0.0015
Correlation coefficient	0.9895

7.1.2.2.4 Calibration curve in Phosphate buffer pH 6.8

Table 22: Calibration curve in Phosphate buffer pH 6.8

Concentration (µg/ml)	**Absorbance**
0	0
2	0.012
4	0.125
6	0.251
8	0.416
10	0.520
12	0.640

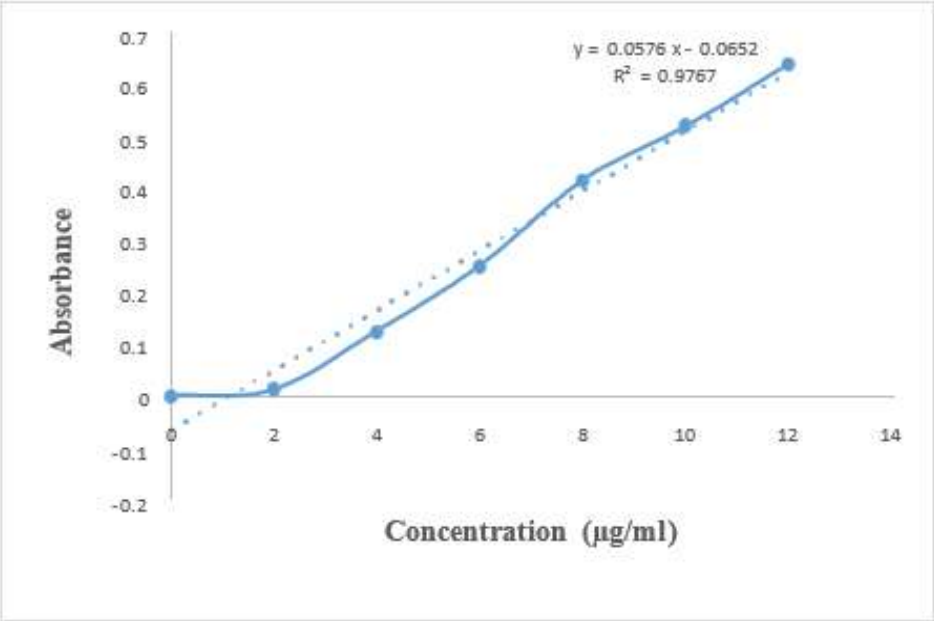


Figure 15: Calibration curve in Phosphate buffer pH 6.8

Equation	y = 0.0576x - 0.0652
Correlation coefficient	0.9767

7.1.2.2.5 Calibration curve in Phosphate buffer pH 7.4

Table 23: Calibration curve in Phosphate buffer pH 7.4

Concentration (µg/ml)	Absorbance
0	0
2	0.125
4	0.198
6	0.224
8	0.314
10	0.456
12	0.489

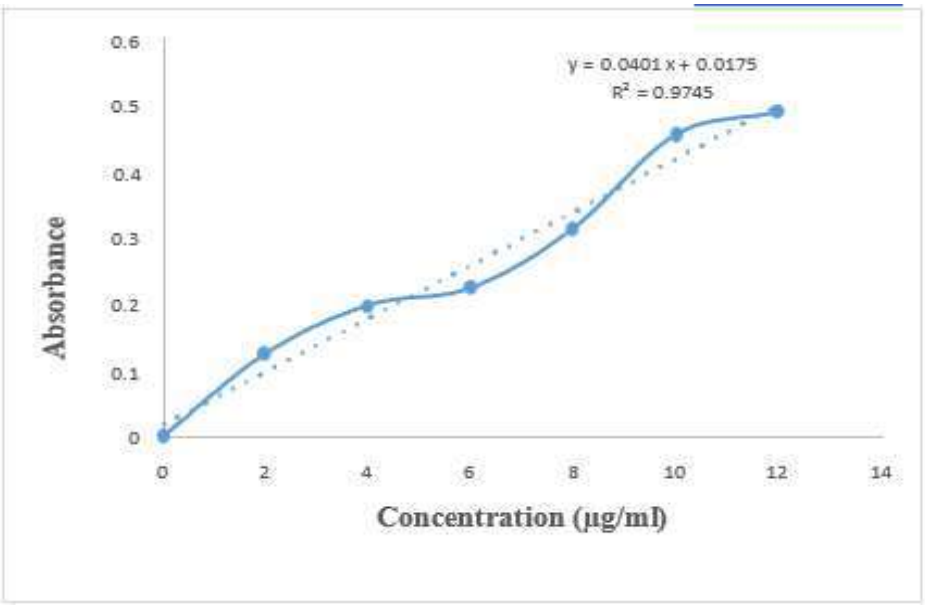


Figure 16: Calibration curve in Phosphate buffer pH 7.4

Equation	y = 0.0401x + 0.0175
Correlation coefficient	0.9745

7.1.2.2.6 Calibration curve in Acidic buffer pH 1.2

Concentration (µg/ml)	Absorbance
0	0
2	0.122
4	0.132
6	0.169
8	0.241
10	0.3997
12	0.487

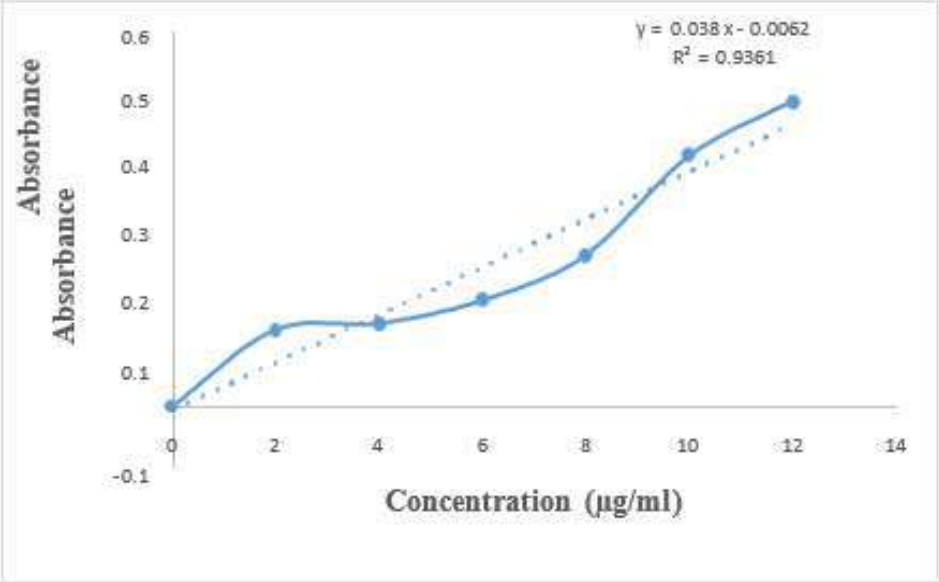


Figure 17: Calibration curve in Acidic buffer pH 1.2

7.2 Post Formulation Study

7.2.1 Transparency

Physical appearance of the formulations. The clear transparency indicates that there are no visible particles or impurities present in any of the formulations. Additionally, the optimization of batch L8 suggests that it meets the desired criteria for clarity and uniformity, making it the preferred choice for further development or use in applications requiring clear formulations.

Table 25: Transparency of L1to L13

Formulation code	Transparency
L1	Clear
L2	Clear
L3	Clear
L4	Clear
L5	Clear
L6	Clear
L7	Clear
L8	Clear
L9	Clear
L10	Clear

L11	Clear
L12	Clear
L13	Clear

7.2.2Weight Variation

The optimized batch (L8) of the fast dissolving film formulation exhibited a weight variation of 46.4 ± 0.24. This result indicates a consistent weight among different units of the film, ensuring uniformity in dosage. A low variation in weight is crucial for maintaining the quality and efficacy of the pharmaceutical product. Therefore, batch L8 meets the desired standards for weight uniformity in the formulation.

26: Weight Variation L1to L13

Formulation code	Weight Variation (mg)
L1	54.6±0.01
L2	62.56±0.02
L3	58.46±0.03
L4	89.1±0.01
L5	79.9±0..05
L6	87.3±0.12
L7	91.46±0.03
L8	46.4±0.24
L9	79±0.03
L10	47±0.15
L11	49±0.02
L12	36.56±0.06
L13	62.3±0.005

7.2.3 Moisture content

Moisture content data, formulation L8 emerges as the optimized choice due to its comparatively low moisture content of 2.7% ± 0.546.

27: Moisture content L1to L13

Formulation code	Moisture content (%)
L1	4 ± 0.879
L2	5 ± 0.546
L3	4.5 ± 0.442
L4	6± 0.534
L5	5.2 ± 0.945
L6	6.2± 0.764
L7	7 .1± 0.345
L8	2.7± 0.546
L9	5.4± 0.142
L10	4.6± 0.503
L11	3±0.511
L12	2.9±0.234
L13	3.5±0.141

7.2.4 Thickness (mm)

The optimized batch (L8) of the fast dissolving film formulation exhibited a thickness of 0.14 ± 0.010 mm.

28: Thickness (mm) L1to L13

Formulation code	Thickness(mm)
L1	0.11 ± 0.0.1
L2	0.13 ± 0.0.2
L3	0.10 ± 0.01
L4	0.16 ± 0.005
L5	0.15 ± 0.03
L6	0.14 ± 0.04
L7	0.9 ± 0.005
L8	0.14 ± 0.010
L9	0.16 ± 0.005
L10	0.11 ± 0.05
L11	0.9±0.01
L12	0.17±0.02
L13	0.15±0.04

7.2.5 Folding endurance study

29: Folding endurance L1to L13

The optimized batch (l8) of the fast dissolving film formulation demonstrated excellent folding endurance, with a value exceeding 300.

Formulation code	Folding endurance
L1	> 300
L2	> 300
L3	> 300
L4	150
L5	209
L6	> 300
L7	124
L8	> 300
L9	130
L10	> 300
L11	> 300
L12	> 300
L13	> 300

7.2.6 Surface pH

The optimized fast dissolving film formulation (l8) exhibited a pH of 6.1.

Table 30: PH of L1to L13

Formulation code	ph
L1	6.3±0.002
L2	6.40. ±003
L3	6.13±0.06
L4	6.7±0.07
L5	6.5±0.07
L6	6.83±0.06
L7	7.13±0.05
L8	6.1±0.06
L9	6.94±0.03
L10	6.67±0.04

L11	6.70±0.06
L12	6.56±0.05
L13	6.59±0.012

7.2.7 Drug Content (%)

Formulation L8 exhibits the highest drug content among the tested formulations, with a percentage of 96.48%.

Table 31: Drug Content (%) of L1to L13

Formulation code	Drug Content (%)
L1	87.89
L2	90.16
L3	89.98
L4	93
L5	86.65
L6	73.56
L7	89.13
L8	96.48
L9	88.36
L10	94.56
L11	79
L12	78.46
L13	88.49

ANOVA for Linear model Response 2: Drug content

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	343.74	3	114.58	5.62	0.0189	significant
A-Sodium carboxymethyl cellulose	123.95	1	123.95	6.08	0.0358	
B-Sodium starch glycolate	42.60	1	42.60	2.09	0.1823	
C-glycerol	177.19	1	177.19	8.69	0.0163	
Residual	183.52	9	20.39			
Cor Total	527.26	12				

Factor coding is coded.

Sum of squares is Type III - Partial

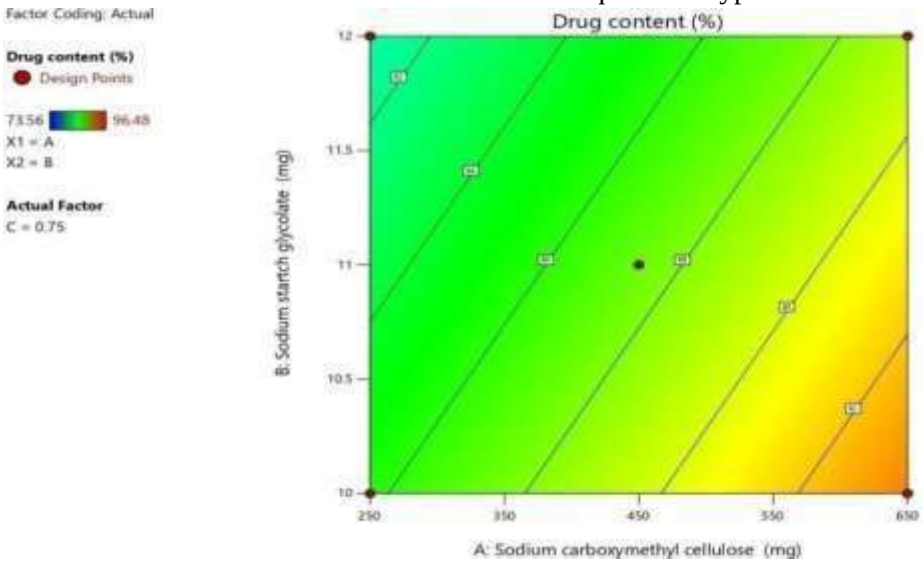


Figure 18: Counter plot

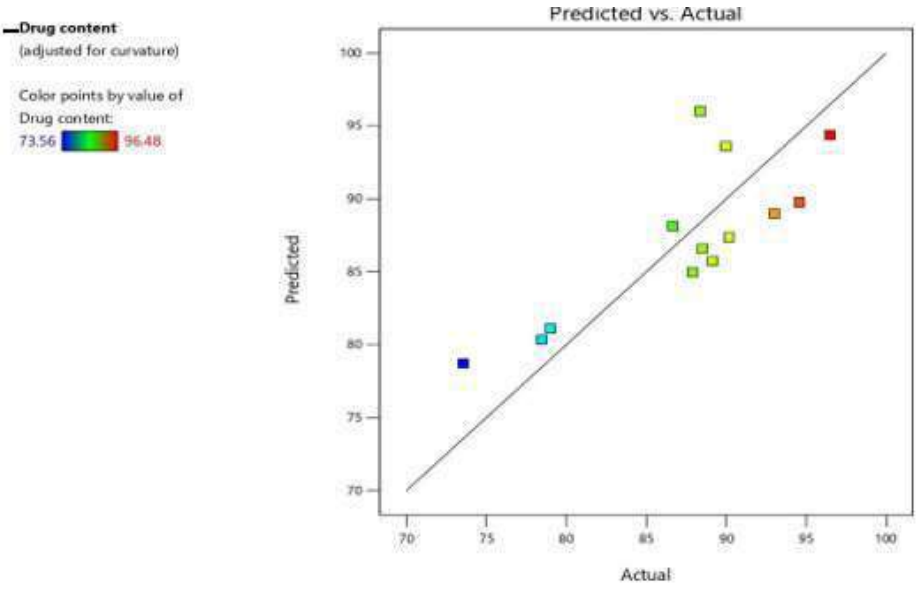


Figure 19: Predicted vs Actual plot

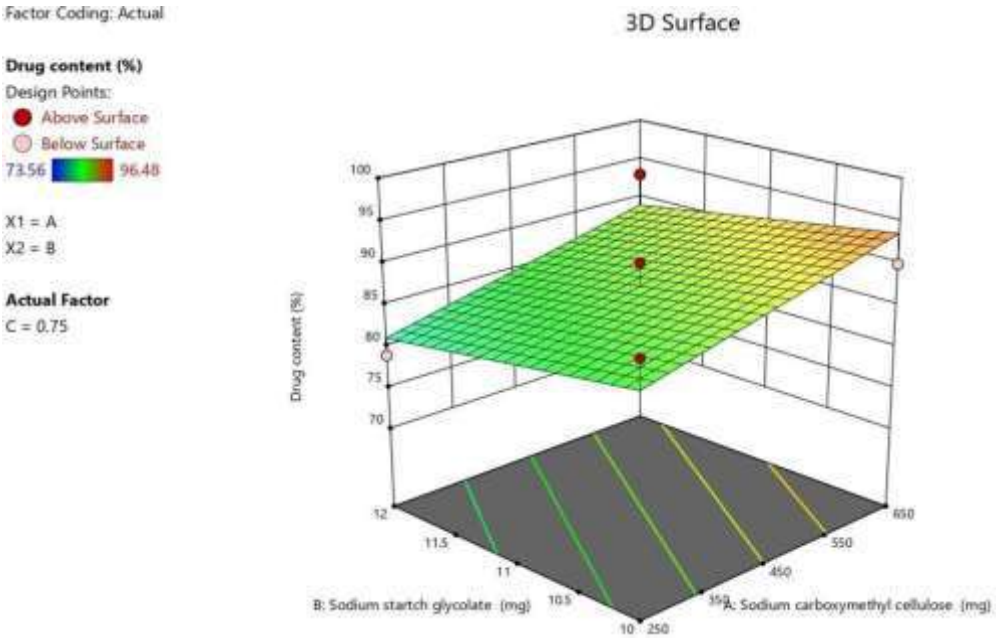


Figure 20: 3D Surface plot

7.2.8 Tensile strength (N/mm²)

The tensile strength of formulation L8 is determined to be 3.4 ± 0.14 N/mm², positioning it as the optimized batch among the formulations tested. This suggests that formulation L8 possesses favorable mechanical characteristics, which are crucial for the integrity and performance of the product.

Table 32: Tensile strength (N/mm²) of L1to L13

Formulation code	Tensile strength((N/mm²))
L1	5.3 ± 0.01
L2	6.9 ± 0.02
L3	6.8 ± 0.04
L4	4.3 ± 0.02
L5	3.9 ± 0.03
L6	9.5 ± 0.02
L7	4.1 ± 0.23
L8	3.4 ± 0.14

L9	4.8 ± 0.05
L10	7.6 ± 0.04
L11	5.4 ± 0.03
L12	6.7 ± 0.13
L13	7.4 ± 0.5

7.2.9 Percentage elongation (%)

Percentage elongation for various formulations ranges from 13.6% to 45.26%.

Table 33: Percentage elongation (%) of L1to L13

Formulation code	Percentage elongation (%)
L1	27.4 ± 0.12
L2	33.2 ± 0.07
L3	34.2 ± 0.01
L4	17.0 ± 0.14
L5	16.8 ± 0.34
L6	45.26 ± 0.010
L7	13.6± 0.05
L8	39.3 ± 0.12
L9	22.1 ± 0.30
L10	37.0 ± 0.15
L11	26.5 ± 0.10
L12	30.3 ± 0.07
L13	38.0 ± 0.14

7.2.10. in Vitro Disintegration Time

The disintegration time for various formulations of fast-dissolving oral films (batch L8) ranges from 22 to 62 seconds.

Table 34: Disintegration Time of L1to L13

Formulation code	Disintegration Time(sec)
L1	35
L2	38
L3	53
L4	62
L5	29
L6	28
L7	32
L8	22
L9	53
L10	27
L11	30
L12	43
L13	37

ANOVA for Linear model Response 1: disintegration time

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	992.50	3	330.83	4.11	0.0431	significant
A-Sodium carboxymethyl cellulose	924.50	1	924.50	11.48	0.0080	

B-Sodium starch glycolate	50.00	1	50.00	0.6211	0.4509	
C-glycerol	18.00	1	18.00	0.2236	0.6476	
Residual	724.58	9	80.51			
Cor Total	1717.08	2				

Factor coding is coded.
Sum of squares is Type III - Partial

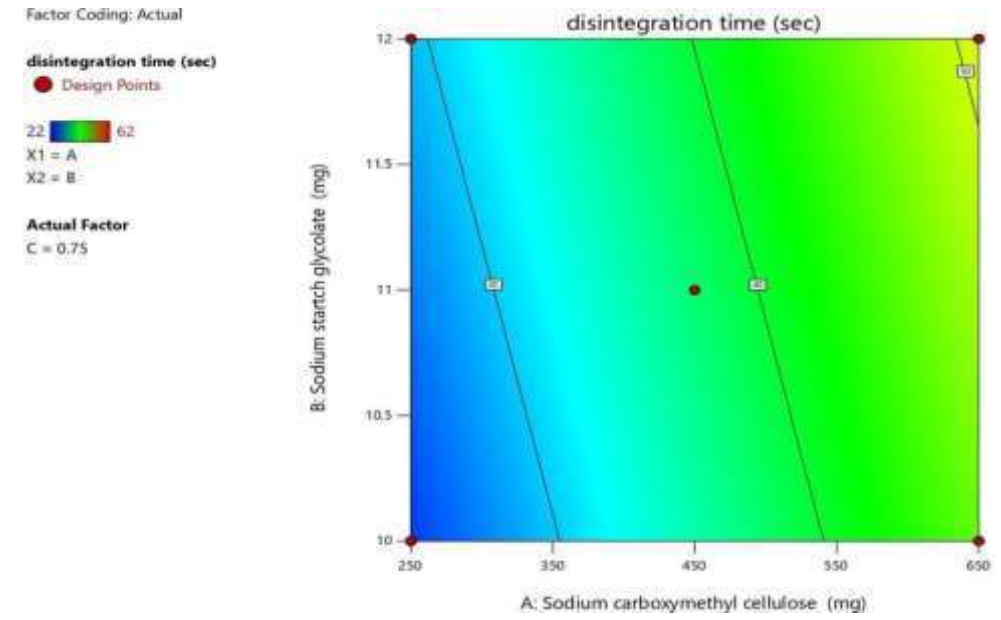


Figure 21: Counter plot

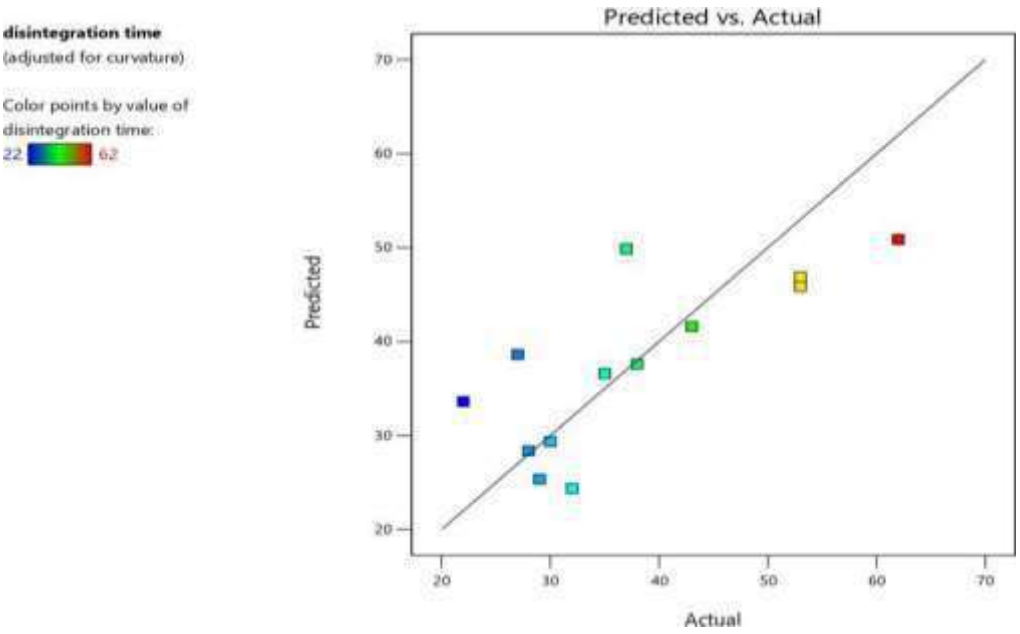


Figure 22: Predicted vs Actual plot

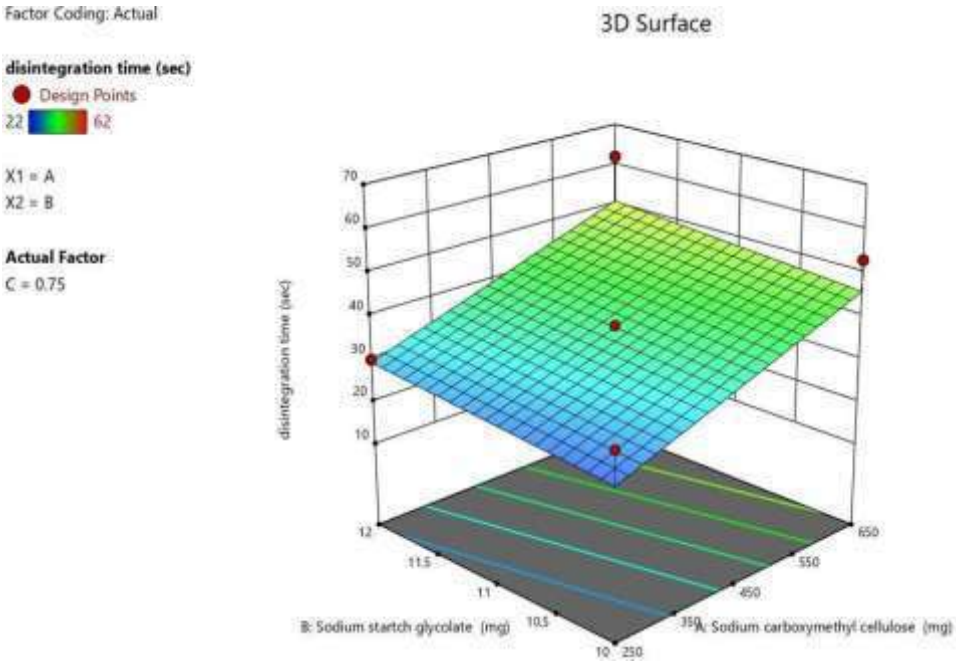


Figure 23: 3D Surface plot

7.2.11 In Vitro drug release study

The in-vitro diffusion study for the L8 optimized batch shows exceptional performance, with an initial drug release of 20.56% ± 0.04 at 1 minute and reaching a near-complete release of 98.99% ± 0.687 at 10 minutes.

Table 35: Drug release of L1-L6

Time (min)	L1	L2	L3	L4	L5	L6
0	0	0	0	0	0	0
1	23.56±0.01	19.46±0.03	15.46±0.03	20.46±0.03	17.89±0.005	17.89±0.05
2	35.56±0.02	32.56±0.06	30.12±0.01	30.44±0.05	29.45±0.156	28.79±0.01
3	45.63±0.123	44.78±0.05	41.35±0.156	43.56±0.06	38.89±0.05	35.44±0.02
4	52.64±0.05	50.16±0.04	50.66±0.04	53.49±0.08	49.89±0.063	49.76±0.05
5	62.49±0.03	64.64±0.346	58.79±0.04	61.44±0.07	57.89±0.741	53.66±0.06
6	69.25±0.01	69.77±0.254	63.55±0.632	73.89±0.05	68.79±0.523	69.88±0.05
7	73.44±0.06	74.56±0.03	71.46±0.542	77.46±0.04	74.56±0.03	79.98±.01
8	78.36±0.314	81.66±0.02	79.86±0.31	84.53±0.01	80.16±0.04	86.56±0.03
9	84.56±0.03	88.66±0.467	86.56±0.04	89.65±0.02	85.66±0.345	90.16±0.04
10	86±0.146	90.13±0.05	89.46±0.03	91±0.01	89.87±0.01	94.58±0.01

All values expressed as mean ± SD (n=3)

Table 36: Drug release of L7-L13

Time (min)	L7	L8	L9	L10	L11	L12	L13
0	0	0	0	0	0	0	0
1	16.56±0.04	20.56±0.04	18.46±0.05	13.56±0.05	12.55±0.01	9.56±0.05	8.56±0.425
2	26.55±0.05	29.65±0.05	25.46±0.146	24.63±0.03	20.33±0.05	19.87±0.01	15.65±0.347
3	38.79±0.01	38.46±0.02	34.56±0.364	36.87±0.01	32.46±0.031	21.59±0.324	23.49±0.387
4	47.36±0.05	46.78±0.451	40.13±0.87	43.56±0.06	41.38±0.415	35.49±0.631	30.44±0.14
5	54.65±0.03	53.25±0.01	49.65±0.125	54.68±0.04	49.50.056 ±	43.99±0.956	39.76±0.462

6	67.89±0.136	63.54±0.02	51.32±0.236	61.65±0.03	53.66±0.03	54.87±0.843	43.56±0.25
7	76.56±0.05	72.46±0.05	60.15±0.123	78.36±0.01	69.78±0.01	61.47±0.14	51.36±0.12
8	83.56±0.06	88.13±0.136	79.56±0.654	82.56±0.364	72.35±0.54	67.84±01	59.34±0.05
9	89.46±0.05	84.56±0.122	87.65±0.321	88.46±0.325	79.88±0.12	70.16±0.2	67.23±0.631
10	92.46±0.01	98.99±0.687	93±0.487	92±0.02	83±0.51	73±0.514	71±0.47

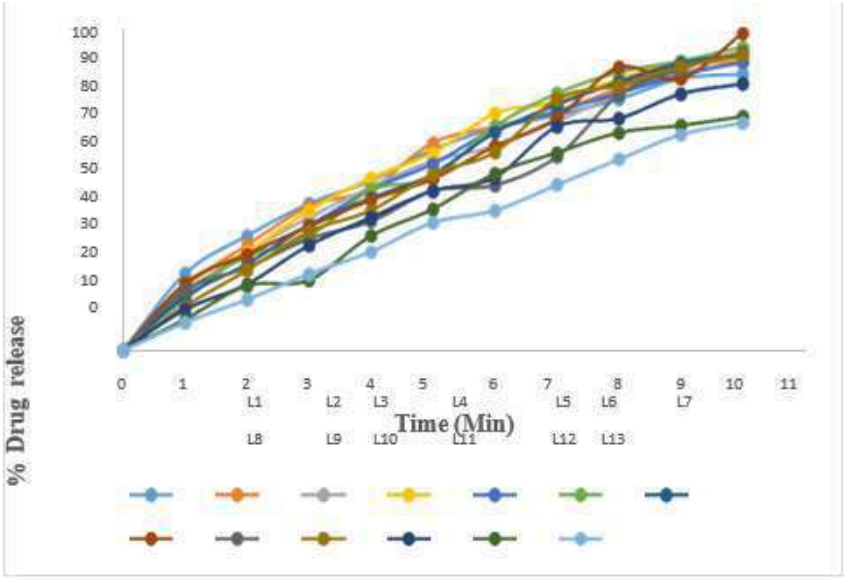


Figure 24: Drug Release of L1-L13

Kinetic analysis of drug release-

In order to define the release mechanism that gives the best description of the release pattern; the in vitro release data for all optimized batches were fitted to kinetic equations models. The kinetic equations were used i.e., zero, first-order and Higuchi model. Both the kinetic rate constant (k) and the determination coefficient (R2) were calculated and presented in below graphs. The best fit model with the highest determination coefficient (R2) value for optimized batch was Zero order model.

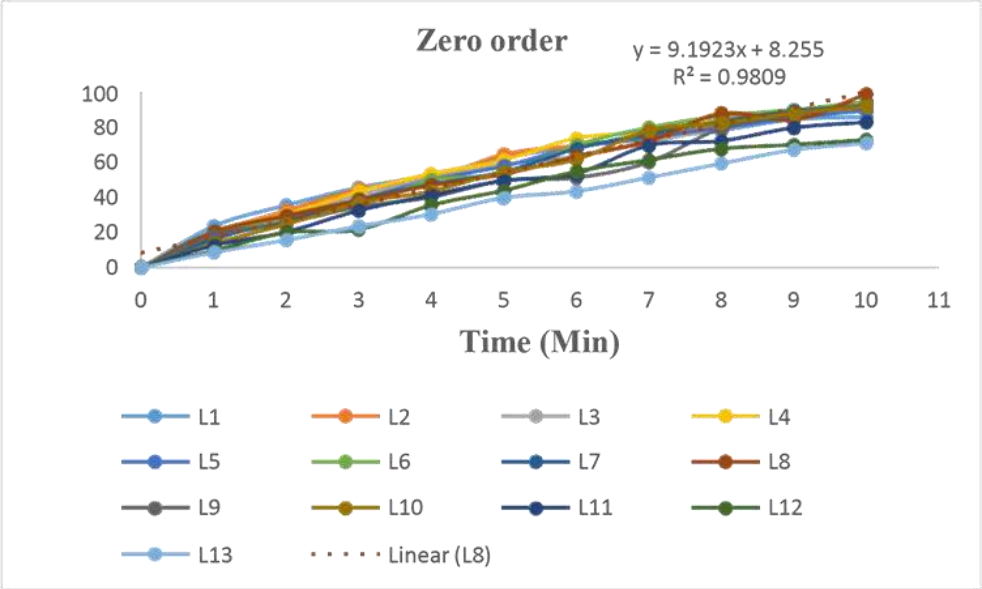


Figure 25: Zero order model of L1-L13

Table 37: Zero Order Model (L8)

Zero Order Model	
Formulation Code	**R2 Value**
L8	0.9809

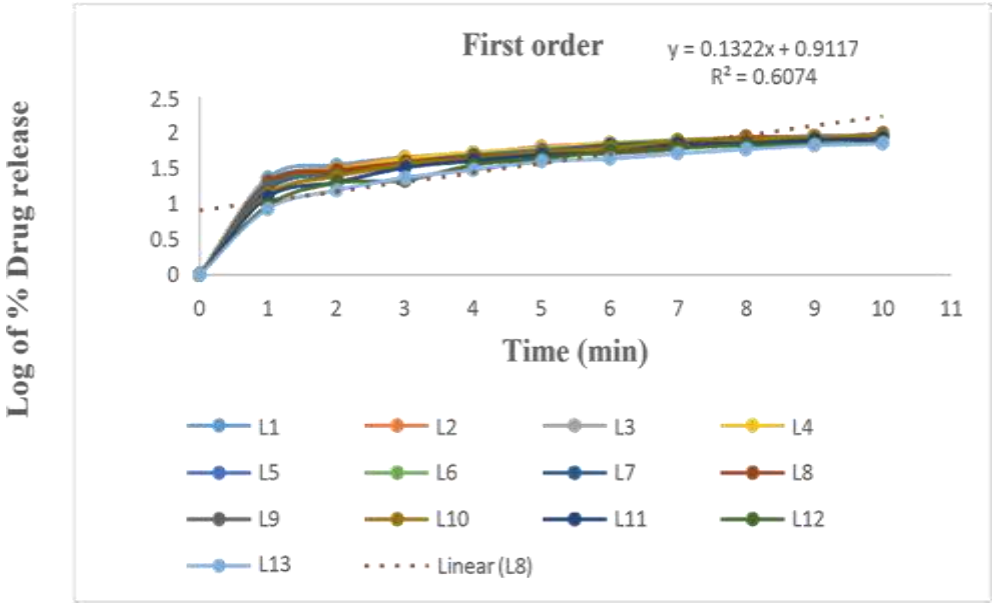


Figure 26: First order model of L1-L13

Table 38: First Order Model (L8)

First Order Model	
Formulation Code	**R2 Value**
L8	0.6074

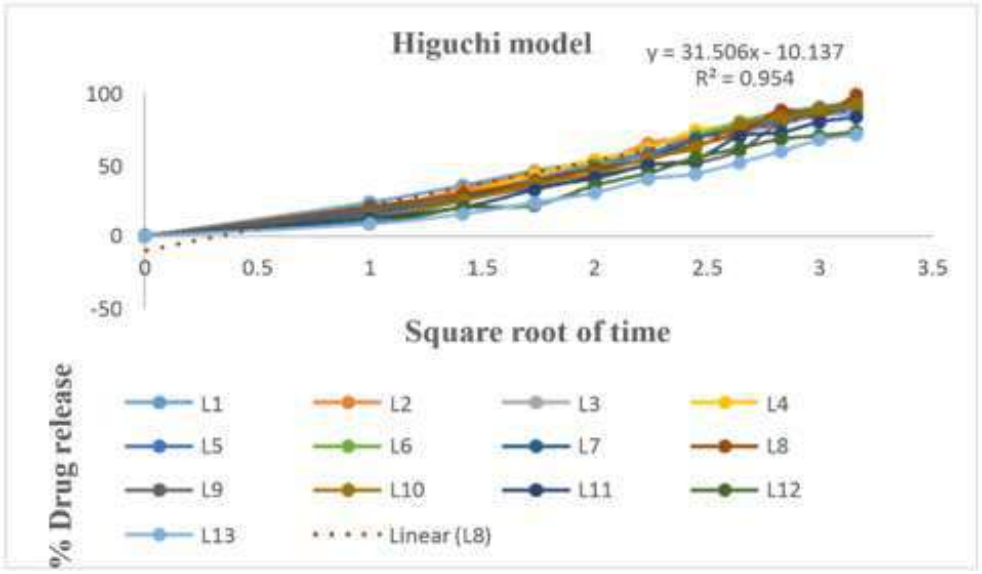


Figure 27: Higuchi Model of L1-L13

Table 39: Higuchi Model (L8)

Higuchi Model	
Formulation Code	**R2 Value**
L8	0.954

ANOVA for 2FI model Response 3: Drug release

Source	Sum Squares of	df	Mean Square	F-value	p-value	
Model	648.41	6	108.07	4.67	0.0413	significant
A-Sodium carboxymethyl cellulose	29.84	1	29.84	1.29	0.2993	
B-Sodium glycolate starch	97.37	1	97.37	4.21	0.0860	
C-glycerol	303.56	1	303.56	13.13	0.0110	
AB	30.25	1	30.25	1.31	0.2962	
AC	178.36	1	178.36	7.72	0.0321	
BC	9.03	1	9.03	0.3906	0.5550	
Residual	138.71	6	23.12			
Cor Total	787.12	12				

Final Equation in Terms of Actual Factors

Drug release	=
+274.99738	
-0.261069	Sodium carboxymethyl cellulose
-14.18375	Sodium starch glycolate
-101.56750	glycerol
+0.013750	Sodium carboxymethyl cellulose * Sodium starch glycolate
+0.133550	Sodium carboxymethyl cellulose * glycerol
+6.01000	Sodium starch glycolate * glycerol

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor and the intercept is not at the center of the design space.

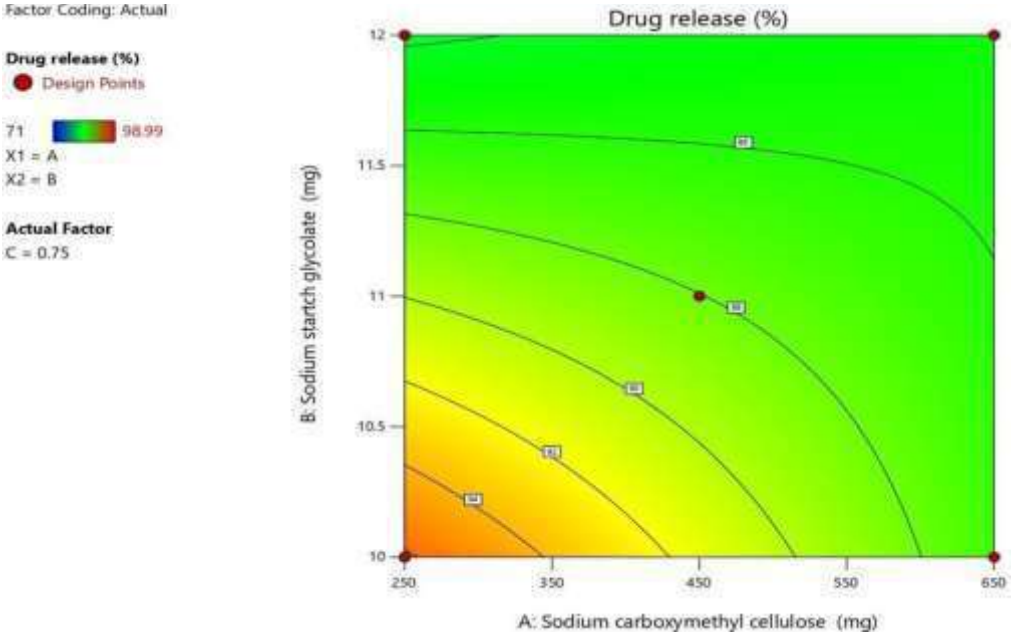


Figure 28: Counter plot

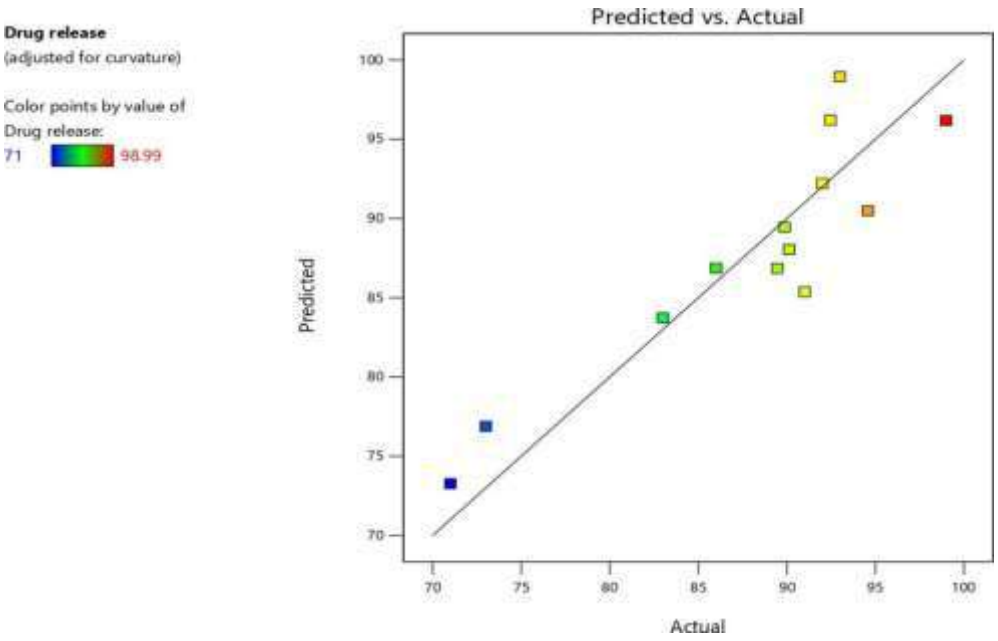


Figure 29: Predicted vs Actual plot

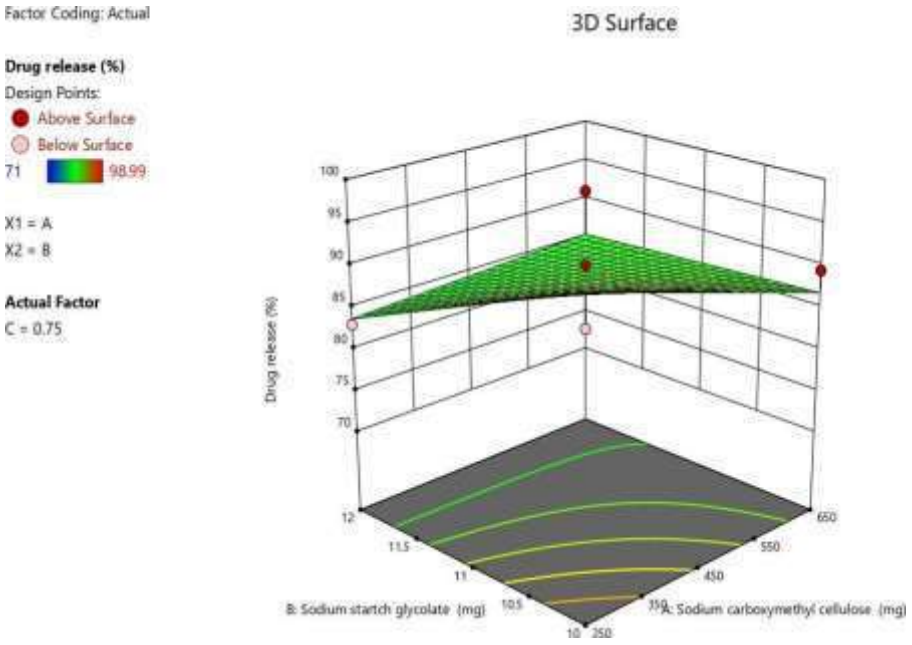


Figure: 30 3D Surface plot

7.2.12 Ex- vivo diffusion study

The ex-vivo diffusion study demonstrates that L8 is the optimized batch, showing superior performance among formulations L1-L13. L8 exhibits rapid initial drug permeation at 1 minute (19.63% ± 0.03), maintains high permeation at 5 minutes (54.18% ± 0.03), and achieves near- complete permeation at 10 minutes (97.89% ± 0.51).

Table 40: Drug permeation of L1-L7

Time (min)	L1	L2	L3	L4	L5	L6	L7
0	0	0	0	0	0	0	0
1	12.56±0.12	13.46±0.05	15.60±0.02	14.32±0.054	18.97±0.06	14.56±00.03	14.35±0.06
2	24.53±0.02	38.79±0.31	29.87±0.01	26.54±0.036	28.46±0.01	23.55±0.01	25.46±0.02
3	39.87±0	39.74±0.	34.12±0.	38.78±0.74	37.40.056±0	32.45±0.	35.46±0

	.05	01	146	3	.453	06	.03
4	49.46±0.06	47.13±0.02	45.66±0.036	40.12±0.324	42.33±0.221	40.18±0.01	45.56±0.01
5	57.32±0.01	57.88±0.03	56.49±0.045	51.46±0.347	54.79±0.654	50.16±0.05	53.65±0.05
6	68.74±0.05	67.36±0.354	68.47±0.01	63.48±0.51113	62.15±0.716	64.53±0.01	66.49±0.01
8	79.85±0.06	80.16±0.345	78.46±0.02	67.16±0.02	65.49±0.02	72.13±0.05	73.56±0.06
9	82.46±0.05	80.46±0.06	86.45±0.04	78.45±0.01	76.88±0.01	84.56±0.06	86.65±0.01
10	89.12±0.01	90.12±0.04	89.71±0.123	87.89±0.003	91.11±0.05	93.56±0.01	90.12±0.01

All values expressed as mean ±STD

Table 41: Drug permeation of L8-L13

Time (min)	L8	L9	L10	L11	L12	L13
0	0	0	0	0	0	0
1	19.63±0.03	15.32±0.01	13.46±0.18	12.01±0.01	11.87±0.87	14.56±0.06
2	38.79±0.01	26.53±0.35	20.46±0.97	21.35±0.02	18.96±0.364	21.56±0.07
3	38.79±0.04	37.89±0.14	37.46±0.87	34.55±0.79	29.56±0.254	30.16±0.05
4	49.78±0.14	43.56±0.34	48.32±0.78	49.97±0.87	37.13±0.387	40.13±0.03
5	54.18±0.03	53.14±0.65	58.94±0.65	52.36±0.54	46.25±0.964	51.36±0.54
6	65.87±0.05	65.44±0.33	69.88±0.34	67.46±0.94	53.44±0.03	61.45±0.63
8	75.59±0.04	78.93±0.62	77.65±0.34	78.98 ±0.1	64.31±0.04	72.36±0.74
9	87.89±0.01	86.54±0.87	89.13±0.12	80.16±0.02	75.66±0.05	81.13±0.34
10	97.89±0.51	94.56±0.961	91.23±0.47	88.87±0.01	80.13±0.03	89.56±0.01

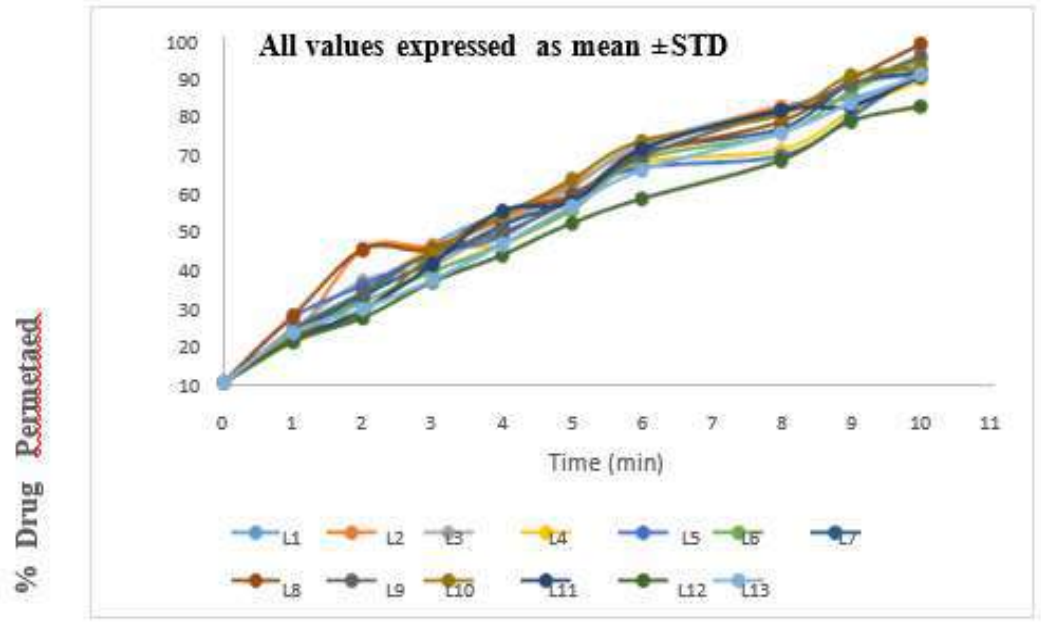


Figure 31: % Drug Permeation of L1-L13

7.2.13 Stability study

The stability studies of the L8 optimized batch indicate excellent stability over a 90-day period. The drug content remains consistent at 96.48% throughout the study, demonstrating that the active ingredient's concentration does not degrade over time.

Table 41: Stability studies data of L8 optimized batch

Sr.no	Time in days	Drug Content (%)	Disintegration time (sec)	*In –vitro* drug release (%)
1.	Initial (0 days)	96.48	22	98.99
2.	1 month (30 days)	96.48	22	98.99
3.	3 months(90days)	96.48	21	98.78

CONCLUSION

The formulation study of Lisinopril tablets identified Batch L8 as the most promising candidate due to its superior physical and chemical properties. It displayed consistent weight, ideal pH, appropriate viscosity, high drug content, and an excellent in vitro release profile, with 98.67% of the drug released over 12 hours. The stability of Batch L8 was confirmed through zeta potential measurements and long-term stability testing, making it a suitable candidate for further development and potential clinical application

REFERENCE

1. Mahajan A, Chhabra N, Aggarwal G. Formulation and characterization of fast dissolving buccal films: A review. Der Pharm Lett. 2011;3(1):152-65.
2. Suresh B, Halloran D, James L. Quick dissolving films: A novel approach to drug delivery. Drug Development Technology. 2006:1-7.
3. Patel AR, Prajapati DS, Raval JA. Fast dissolving films (FDFs) as a newer venture in fast dissolving dosage forms. Int. J. Drug Dev. Res. 2010 Apr;2(2):232-4.
4. Keshavarao KP, Mudit D, Gunashekara K, Anis S, Singh Mangla N, Ajay K. Formulation and evaluation of mouth dissolving film containing Rofecoxib. IRJP. 2011;2(3):273-8.
5. Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics. 2008 Nov 1;70(3):895-900.
6. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. Journal of controlled release. 2009 Oct 15;139(2):94-107.
7. Radhakisan UR, Chavan V, Tribhuvan N. Mouth dissolving film and their patent: An overview. International Research Journal of Pharmacy. 2012;3(9):39-42.
8. Lodhi DS, Panwar AS, Golani P, Verma M. A Review Of The Combination Of Xanthine And Bronchodilator Drug In Mouth-Dissolving Film For Asthma Treatment". Structure. 2021; 4:5.
9. Eixarch H, Haltner-Ukomadu E, Beisswenger C, Bock U. Drug delivery to the lung: permeability and physicochemical characteristics of drugs as the basis for a pulmonary biopharmaceutical classification system (pBCS). Journal of Epithelial Biology & Pharmacology. 2010 Jan 13;3(1).
10. Sheoran R. Fast dissolving oral films: a review with future prospects. International journal of pharmaceutical education and research. 2018 May;12(2):15-32.
11. Goa KL, Balfour JA, Zuanetti G. Lisinopril: a review of its pharmacology and clinical efficacy in the early management of acute myocardial infarction. Drugs. 1996 Oct;52(4):564-88.
12. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi pharmaceutical journal. 2016 Sep 1;24(5):537-46.
13. Sharma D, Kaur D, Verma S, Singh D, Singh M, Singh G, Garg R. Fast dissolving oral films technology: A recent trend for an innovative oral drug delivery system. International Journal of Drug Delivery. 2015 Oct 12;7(2):60-75.
14. Arunachalam A, Karthikeyan M, Kumar SA, Konam K, Prasad PH, Sethuraman S, Manidipa S. Fast dissolving drug delivery system: A review. Journal of global trends in pharmaceutical sciences. 2010 Oct;1(1):92-110.
15. Sakellariou P, Rowe RC. Interactions in cellulose derivative films for oral drug delivery. Progress in polymer science. 1995 Jan 1;20(5):889-942.
16. Banker GS. Film coating theory and practice. Journal of pharmaceutical sciences. 1966 Jan;55(1):81-9.
17. Juluru NS. Fast dissolving oral films: A review. IJAPBC. 2013 Jan;2(1):108-12.
18. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. International Journal of ChemTech Research. 2010 Jan 1;2(1):576-83.

19. Chonkar AD, Bhagawati ST, Udupa N. An overview on fast dissolving oral films. Asian Journal of Pharmacy and Technology. 2015;5(3):129-37.
20. Prakash I, DuBois GE, Clos JF, Wilkens KL, Fosdick LE. Development of rebiana, a natural, non-caloric sweetener. Food and Chemical Toxicology. 2008 Jul 1;46(7):S75- 82.
21. Panda BP, Dey NS, Rao ME. Development of innovative orally fast disintegrating film dosage forms: a review. International Journal of Pharmaceutical Sciences and Nanotechnology. 2012 Jul;5(2):1666-74.
22. Dave RH, Shah DA, Patel PG. Development and evaluation of high loading oral dissolving film of aspirin and acetaminophen. Journal of pharmaceutical sciences and pharmacology. 2014 Jun 1;1(2):112-22.
23. Salawi A. An insight into preparatory methods and characterization of orodispersible film—A review. Pharmaceuticals. 2022 Jul 9;15(7):844.
24. Patel DM, Patel DJ, Darji PJ. Formulation and evaluation of fast dissolving film of cetirizine & Dextromethorphan. Int Jr Ph Sci &Nanotech. 2016;9(3):3305-11.
25. Kshirsagar T, Jaiswal N, Chavan G, Zambre K, Ramkrushna S, Dinesh D. Formulation & evaluation of fast dissolving oral film. World J. Pharm. Res. 2021 Jul;10(9):503-61.
26. Gholve S, Savalsure S, Bhusnure O, Suryavanshi S, Birajdar M. Formulation and evaluation of oral fast dissolving sublingual film of propranolol HCl. International Journal of Pharma Research and Health Sciences. 2018;6(2):65-72.
27. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films: innovations in formulation and technology. Int J Pharm Sci Rev Res. 2011 Jul;9(2):9-15.
28. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. Journal of controlled release. 2009 Oct 15;139(2):94-107.
29. Deshmane S, Joshi UM, Channawar MA, Biyani KR, Chandewar A. Design and characterization of carbopol-HPMC-ethyl cellulose based buccal compact containing propranolol HCl. Indian Journal of Pharmaceutical Education and Research. 2010 Jul 1;44(3):253-8.
30. Khairnar A, Jain P, Baviskar D, Jain D. Development of mucoadhesive buccal patch containing aceclofenac: in vitro evaluations. Int J PharmTech Res. 2009 Oct;1(4):978- 81.
31. Han JH, Floros JD. Casting antimicrobial packaging films and measuring their physical properties and antimicrobial activity. Journal of Plastic Film & Sheeting. 1997 Oct;13(4):287-98.
32. Chana-Thaworn J, Chanthachum S, Wittaya T. Properties and antimicrobial activity of edible films incorporated with kiam wood (Cotyleobium lanceotatum) extract. LWT- Food Science and Technology. 2011 Jan 1;44(1):284-92.
33. Hoque N, Alam F, Sarkar D, Yakin J, Ahmed SA, Pathak BJ, Judder MI, Dash B, Panigrahy UP, Alam F, Sarkar D. Formulation And Evaluation Of Fast- Dissolving Oral Disintegrated Film Of Valdecoxib.
34. Baranauskaite J, Ockun MA, Uner B, Gungor B, Duman G, Tas C, Yesilada E. Development and In vitro characterization of pullulan fast dissolving films loaded with Panax ginseng extract, antioxidant properties and cytotoxic efficiency on lung and breast cancer cell lines. Journal of Drug Delivery Science and Technology. 2022 Oct 1; 76:103701.
35. Lynthong B, Bhavya Shree T, Kamath K, Shabaraya AR. Oro-Dispersible Film: An Effective Approach for the Quick Drug Release.
36. Kheawfu K, Kaewpinta A, Chanmahasathien W, Rachtanapun P, Jantrawut P. Extraction of nicotine from tobacco leaves and development of fast dissolving nicotine extract film. Membranes. 2021 May 28;11(6):403.
37. Sharma A, Agarwal D. Formulation and Evaluation of Montelukast Sodium Oral Dissolving Film. Asian Journal of Pharmaceutical Research and Development. 2021 Feb 15;9(1):130-40.
38. Kshitija P. Deshmukh, Sayyad Sohail. Formulation and Evaluation Of Fast Dissolving Oral Films.wjpps.20211 (1).396-406.
39. Patil SS, Patil SJ, Vakhariya RR, Chopade AR, Mohite SK. Formulation and Evaluation of Fast Dissolving Buccal Film of Curcumin as Promising Route of Buccal Delivery.
40. Bilal Q, Unhale S, Shelke S, Kale P, Sarode P, Biyani D. A review on mouth dissolving films. Eur. J. Pharm. Med. Res. 2020; 7:232-8.
41. Shendge RS, Salunkhe KS, Girish K. Formulation And Evaluation Of Fast Dissolving Sublingual

Film Of Antihistamine Drug. European Journal of Molecular & Clinical Medicine.;7(4):2020.
42. Tizkam HH, Fadhil OQ, Ghazy E. Formulation and Evaluation of Metoclopramide Fast Dissolving Film (FDF). Syst. Rev. Pharm. 2020 Dec 1; 11:1641-6.
43. Qin ZY, Jia XW, Liu Q, Kong BH, Wang H. Fast dissolving oral films for drug delivery prepared from chitosan/pullulan electrospinning nanofibers. International journal of biological macromolecules. 2019 Sep 15; 137:224-31.
44. Raza SN, Kar AH, Wani TU, Khan NA. Formulation and evaluation of mouth dissolving films of losartan potassium using 32 factorial design. Int. J. Pharm. Sci. Res. 2019;10(3):1402-11.
45. Palepu S. Preparation and evaluation of fast dissolving sublingual film of lisinopril. Journal of Drug Delivery and Therapeutics. 2019 Feb 15;9(1-s):101-6.
46. Gupta P, Bisht A, Rao DN. Fast dissolving oral films: a comprehensive review. World Journal of Pharmaceutical and Medical Research, Wjpmr. 2019;5(7):116-27.
47. Bala R, Sharma S. Formulation optimization and evaluation of fast dissolving film of aprepitant by using design of experiment. Bulletin of Faculty of Pharmacy, Cairo University. 2018 Dec 1;56(2):159-68.
48. Harshitha KN, Shruthi BN, ST B. Design and Characterization of Fast Dissolving Films of Cilnidipine Solid Dispersions.
49. Gholve S, Savalsure S, Bhusnure O, Suryavanshi S, Birajdar M. Formulation and evaluation of oral fast dissolving sublingual film of propranolol HCl. International Journal of Pharma Research and Health Sciences. 2018;6(2):65-72.
50. Thonte SS, Pentewar RS, Bhusnure OG, Gholve SB, Gaikwad VM, Pujdekar AA. Formulation and evaluation of oral fast dissolving film of glipizide. W Jr Ph Res. 2017 May 10;6(7):1279-97.
51. Rajeswari D, Babu BN, Desu PK, Rao PV, Anitha B. Formulation and Evaluation of fast dissolving films of Telmisartan. World Journal of Pharmacy and Pharmaceutical Sciences. 2017 Sep 11;6(11):1038-47.
52. Kathpalia H, Patil A. Formulation and Evaluation of Orally Disintegrating Films of Levocetirizine Dihydrochloride. Indian Journal of Pharmaceutical Sciences. 2017 Mar 1;79(2).
53. Mor J, Dubey V, Jalwal P. Formulation and evaluation of oral dissolving films of lisinopril. IntJResPharmSci2016.;1:34-8.
54. Ali MS, Vijendar C, Kumar SD, Krishnaveni J. Formulation and evaluation of fast dissolving oral films of diazepam. Journal of pharmacovigilance. 2016 May 28; 4(3):1- 5.
55. Kothapuvari PK, Rawat S, Kadimpati KK. Preparation of fast dissolving oral films of new generation anti migraine drugs by solvent casting method. Int J Current Res. 2016;8(5):30704-10.
56. Ayorinde JO, Odeniyi MA, Balogun-Agbaje O. Formulation and Evaluation of Oral Dissolving Films of Amlodipine Besylate Using Blends of Starches With Hydroxypropyl Methyl Cellulose. Polimery w Medycynie. 2016 Jan 1;46(1).
57. Soni MM, Patel KR. Formulation and evaluation of fast dissolving film of lurasidone Hcl. Int. J. Pharm. Res. Bio. Sci. 2016;5(2):101-23.
58. Jani R, Patel R, Shah P. Formulation and evaluation of orodispersible film of hydroxyzine hydrochloride. World J Pharm Res. 2015 Jul 4; 4:754-0.
59. Hanif M, Zaman M, Chaurasiya V. Polymers used in buccal film: a review. Designed Monomers and Polymers. 2015 Feb 17;18(2):105-11.
60. Rajashekar. M, Rashmi. B, Sravanthi. Ch, Nagaraju.T, Shravan Kumar. Y, Madhusudhan Rao. Y.Formulation and Evaluation of Lisinopril Fast Disintegrating Films and Tablets. J.PHARM.SCI. TECH. MGMT. (2015);1 (1) ,48-71.
61. Sharma D, Kaur D, Verma S, Singh D, Singh M, Singh G, Garg R. Fast dissolving oral films technology: A recent trend for an innovative oral drug delivery system. International Journal of Drug Delivery. 2015 Oct 12;7(2):60-75.
62. Kurmi R, Ganju K, Lodhi DS, Chouksey K. Formulation, development and evaluation of fast dissolving oral film of anti-migraine drug. World Journal of Pharmaceutical and Medical Research. 2015;8.
63. Maheswari KM, Devineni PK, Deekonda S, Shaik S, Uppala NP, Nalluri BN. Development and evaluation of mouth dissolving films of amlodipine besylate for enhanced therapeutic efficacy. Journal of pharmaceutics. 2014;2014.

64. Deepthi A, Reddy BV, Navaneetha K. Formulation and evaluation of fast dissolving oral films of zolmitriptan. American journal of advanced drug delivery. 2014;2(2):153- 63.
65. Deepthi A, Reddy BV, Navaneetha K. Formulation and evaluation of fast dissolving oral films of zolmitriptan. American journal of advanced drug delivery. 2014;2(2):153- 63.
66. Parhi R. Improvement Of Dissolution Rate Of Indomethacin From Fast Dissolving Tablets. Indonesian Journal of Pharmacy. 2014 Jul 1;25(3):198.
67. Kurra N, Baru CR, Vidyadhara KP. Vanitha. Formulation and evaluation of fast dissolving sublingual lisinopril tablets. Indo American Journal of Pharmaceutical Sciences. 2014;1(6):378-91.
68. Bansal S, Bansal M, Garg G. Formulation and evaluation of fast dissolving film of an antihypertensive drug. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2013 Oct 1;3(4).
69. Bhagwat DA. Formulation and evaluation of fast dissolving buccal patch of olmesartan medoxomil. Asian Journal of Biomedical and Pharmaceutical Sciences. 2013 Jun 1;3(21):51.
70. Raju PN, Kumar MS, Reddy CM, Ravishankar K. Formulation and evaluation of fast dissolving films of loratidine by solvent casting method. The pharma innovation. 2013 Apr 1; 2(2).
71. Kumria R, Gupta V, Bansal S, Wadhwa J, Nair AB. Oral buccoadhesive films of ondansetron: development and evaluation. International journal of pharmaceutical investigation. 2013 Apr;3(2):112.
72. Mandeep K, Rana AC, Nimrata S. Fast Dissolving Films: An Innovative Drug Delivery System. International Journal of Pharmaceutical Research & Allied Sciences. 2013 Jan 1;2(1).
73. Thonte, S. S., et al. Pandey GS, Kumar R, Sharma R, Singh Y, Teotia UV. Development and optimization of oral fast dissolving film of salbutamol sulphate by design of experiment. Am. J. PharmTech Res. 2013;3(4):407-23.
74. Londhe VY, Umalkar KB. Formulation development and evaluation of fast dissolving film of telmisartan. Indian Journal of Pharmaceutical Sciences. 2012 Mar;74(2):122.
75. Lisinopril: Uses, Interactions, Mechanism of Action | DrugBank Online (Access date 2024)
76. Sodium carboxymethyl cellulose | C8H15NaO8 | CID 23706213 - PubChem (nih.gov)
77. Sodium glycolate | C2H3NaO3 | CID 517347 - PubChem (nih.gov)
78. Glycerin | C3H8O3 | CID 753 - PubChem (nih.gov)
79. Saccharin sodium | C7H4NNaO3S | CID 656582 - PubChem (nih.gov)
80. Menthol | C10H20O | CID 1254 - PubChem (nih.gov)
81. Pawar R, Sharma R, Darwhekar G. Formulation and evaluation of mouth dissolving film of prochlorperazine maleate. Journal of Drug Delivery and Therapeutics. 2019 Nov 15;9(6):110-5.
82. Shah KA, Gao B, Kamal R, Razzaq A, Qi S, Zhu QN, Lina S, Huang L, Cremin G, Iqbal H, Menaa F. Development and characterizations of pullulan and maltodextrin-based oral fast-dissolving films employing a box–behnken experimental design. Materials. 2022 May 18;15(10):3591.
83. Mokhtar M, Sammour OA, Hammad MA, Megrab NA. Effect of some formulation parameters on flurbiprofen encapsulation and release rates of niosomes prepared from proniosomes. International journal of pharmaceutics. 2008 Sep 1;361(1-2):104-11.
84. Rokade PS, Patil PM. Development and validation of analytical method for estimation of 5-Fluorouracil in bulk and marketed formulation by UV- spectrophotometer. J Pharm Sci Rev Res. 2017; 42:8-11.
85. Wade A, Weller PJ. Benzalkonium Chloride. Benzethonium Chloride,"" Cetrimide," in: Handbook of Pharmaceutical Excipients, American Pharmaceutical Association, Washington, DC. 1994:27-31.
86. Paolino D, Cosco D, Muzzalupo R, Trapasso E, Picci N, Fresta M. Innovative bolasurfactant niosomes as topical delivery systems of 5-fluorouracil for the treatment of skin cancer. International journal of Pharmaceutics. 2008 Apr 2;353(1-2):233-42.
87. Pathan A, Gupta MK, Jain NK, Dubey A, Agrawal A. Formulation and evaluation of fast dissolving oral film of promethazine

hydrochloride using different surfactant. J. Innov. Pharm. Bio. Sci. 2016;3(1):74-84.

88. Chavan DU, Marques SM, Bhide PJ, Kumar L, Shirodkar RK. Rapidly dissolving felodipine nanoparticle strips-formulation using design of experiment and characterisation. Journal of Drug Delivery Science and Technology. 2020 Dec 1; 60:102053.
89. Pathan A, Gupta MK, Jain NK, Dubey A, Agrawal A. Formulation and evaluation of fast dissolving oral film of promethazine hydrochloride using different surfactant. J. Innov. Pharm. Bio. Sci. 2016;3(1):74-84.
90. Nalluri BN, Sravani B, Anusha VS, Sribramhini R, Maheswari KM. Development and evaluation of mouth dissolving films of sumatriptan succinate for better therapeutic efficacy. Journal of applied pharmaceutical science. 2013 Aug 30;3(8):161-6.
91. Bharti K, Mittal P, Mishra B. Formulation and characterization of fast dissolving oral films containing buspirone hydrochloride nanoparticles using design of experiment. Journal of Drug Delivery Science and Technology. 2019 Feb 1; 49:420-32.
92. Chougule PC. Design and evaluation of formulated mouth dissolving film of domperidone and study the effect of concentration of polymers on drug release. Asian Journal of Pharmaceutics (AJP). 2017;11(04).
93. Ramzan M, Gourion-Arsiquaud S, Hussain A, Gulati JS, Zhang Q, Trehan S, Puri V, Michniak-Kohn B, Kaur IP. In vitro release, ex vivo penetration, and in vivo dermatokinetics of ketoconazole-loaded solid lipid nanoparticles for topical delivery. Drug Delivery and Translational Research. 2022 Jul 1:1-25.
94. Patel DM, Patel DJ, Darji PJ. Formulation and evaluation of fast dissolving film of cetirizine & Dextromethorphan. Int Jr Ph Sci &Nanotech. 2016;9(3):3305-11.

HOW TO CITE: Siddhesh Gawari*, S. R. Ghodake, Formulation and Evaluation of Fast Dissolving Film of Lisinopril, Int. J. Sci. R. Tech., 2025, 2 (4), 664-689. https://doi.org/10.5281/zenodo.15304422