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"DESIGN, OPTIMIZATION AND EVALUATION OF BUCCAL FILMS OF NICORANDIL USING DESIGN OF EXPERIMENTS"

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1. ABSTRACT

In this study aim was to formulate & evaluate fast dissolving buccal films (FDBF's) containing Nicorandil (NIC), a potassium channel activators used in the treatment of angina pectoris & hypertension. fast dissolving buccal films offer several advantages over traditional dosage forms such as improved patient compliance, rapid onset of action & ease of administration without need of water. Nicorandil was incorporated into the films using different polymers, such as HPMC E15 & PVA to optimize the film properties and drug release profile. The films were prepared by solvent casting method. The fast dissolving buccal film of Nicorandil was optimized through a 3- level factorial design and the formulation was optimized on the basis of various evaluation parameters like physicochemical properties, including thickness, weight variation, folding endurance, drug content uniformity & the in-vitro drug release. Among the 13 formulations, F7 formulation shows a rapid drug release 95.3% within 8 minutes. & it has drug content uniformity of 99.26%. The stability studies of the F7 formulation was also assessed under accelerated conditions ensuring their potential long-term storage and the results indicate the fast dissolving buccal films of Nicorandil offer an efficient patient friendly alternative to conventional oral dosage forms with potential for improved therapeutic outcomes in the management of angina pectoris.

KEY WORDS: Fast dissolving buccal films**,** angina pectoris, Nicorandil.

2. INTRODUCTION

Angina pectoris is a medical condition that occurs when your heart receives a decreased amount of oxygenated blood. Often, this occurs due to deposits of cholesterol clogging the blood vessels that carry blood to your heart. Angina pectoris as a substernal chest pain, pressure, or discomfort that is typically exacerbated by exertion and/or anxiety or other emotional or mental stress and is relieved by rest and/or nitroglycerin and Patients who have angina pectoris are at an risk for having a heart attack.[1] Among these advancements, fast dissolving buccal films (FDBF's) have emerged as a promising dosage form due to their numerous advantages such as rapid disintegration, ease of administration, and improved bioavailability.[2]

Nicorandil is a nicotinamide derivative, efficacious in the treatmentof hypertension and angin pectoris. it is a potassium channel pener providing vasodilatation of arterioles and large coronary arteries.[3] Nicorandil is an opener for adenosine triphosphate-sensitive potassium (KATP) channel and a donor for nitric oxide (NO).[4] Nicorandil is rapidly and almost completely absorbed from the gastrointestinal tract, resulting in almost complete bioavailability.[5] Nicorandil may improve the balance between myocardial oxygen supply and demand through a combination of coronary vasodilation as well as a balanced decrease in systemic pre-and afterload.[6] The IUPAC name of N- (2- hydroxyethyl) nicotinamide nitrate (ester) and Nicorandil shows maximum plasma concentration of nicorandil is linearly related to the administered dose.[3] The formulation of Nicorandil FDBFs involves the incorporation of the drug into a thin film matrix composed of biocompatible polymers, plasticizers and other excipients by solvent casting method.[7]

Recent development in novel drug delivery system aims to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration. One such approach is rapidly dissolving Strips. It consists of a very thin oral strip, which releases the active ingredient immediately after uptake into the oral cavity.[8] and film containing active ingredient that dissolves or disintegrates in the saliva remarkably fast, within a few seconds without the need for water or chewing.[9]

In this study, we have developed fast dissolving buccal films of Nicorandil for better treatment of angina pectoris. HPMC E15 and PVA are used as film forming materials. The

optimization of the FDBFs was achieved through the use of the response surface methodology, along with the implementation of a 3-Level factorial design.

3. MATERIALS

Nicorandil was procured from Yarrow chemicals Product Mumbai, India. HPMC E15 was purchased from Yarrow chemicals Mumbai and PVA were purchased from SD fine chemical Laboratories Pvt Ltd. All other chemicals used were of analytical grade.

4. METHODS

4.1. Preparation of standard and stock solutions

About 10mg of Nicorandil was accurately weighed and diluted with phosphate buffer in 100ml volumetric flask of concentration 100µg/ml.

From the above solution 0.5,1,1.5,2,2.5,3,3.5,4,4.5,5 ml was pipette out in a 10 ml volumetric flask and finally diluted up to the mark with simulated saliva buffer which gives required concentration of 5,10,15,20,25,30,35,40,45,50 µg/ml respectively.

4.2. Determination of absorption maxima

Various concentrationed samples were taken one by one and the maximum peak of UV graph was analyzed. From the UV spectrophotometric analysis, it was concluded that the Nicorandil drug showed a λ max at 262 nm. The observed λ max was used for further work to analyze the test samples.

Design of Experiment (DoE)

3-Level Factorial Design was chosen to create the mathematical models that illustrate the relationship between the variables and the responses taken into account during experiment design.

3-Level Factorial Design consisting of 2 factors and 3 levels was performed in order to optimize fast dissolving buccal film is a very important part of preliminary studies. After determining the factors, this design was employed for the statistical investigation of the effects of factors on the selected responses. Design Expert software 12.0.1.0 was used in designing the design. In 3-Level Factorial Design, two factors and three levels were considered for the study. It was used to optimise the independent variables (factors) and to analyze the main effects along with their interaction effects on the dependent variables (responses). The different levels of HPMC E 15 polymer and PVA polymer were taken as

factors and their effects on Disintegration time and cumulative amount of drug release were considered as the responses. The factors with their different levels (high, medium and low) and responses selected are shown in the Table 3. Based on the preliminary studies, the levels of each factor were fixed. In totally, 13 experimental runs were conducted. The mid-point of each edge of the cube represents the 9 out of 13 runs whereas the remaining 5 runs indicates the cube's center point. Analysis of variance (ANOVA) was employed as statistical tool for analysis. Selected independent variables were HPMC E 15 (A) and Poly vinyl Alcohol (PVA) (B) while Disintegration time (X) and percentage cumulative drug release (Y) were considered as dependent responses. Results obtained from 13 formulation.

Table 1: Factors and responses used in the preparation and optimization of Fast dissolving Buccal Film.

Factors	Independent variables	Levels		
		Low	Medium	High
A	Hydroxy Propyl Methyl Cellulose (HPMC E 15)	200 mg	300 mg	400 mg
B	Poly vinyl Alcohol (PVA)	50 mg	150 mg	250 mg
Responses	**Dependent variables**			
X	Disintegration time (sec)			
Y	% cumulative amount of drug release (%)			

4.3. Formulation of Nicorandil Fast Dissolving Buccal Films[10]

Nicorandil fast dissolving buccal films were prepared by solvent casting method. Polymers and drug are dissolved in distilled water, which is poured into polymeric solution and stirred to form a homogenous solution for 15 minutes. Finally, plasticizers, sweeteners as mannitol and citric acid were added to the solution and kept for stirring for 5 minutes. The solution was casted in mould 6 × 8 cm (length and width). Then kept in a hot air oven at 60°C for 2 hours. Thus, formed film was cut into size of 2*2 cm square films and conduct the evaluation studies.

Table 2: Formulation of fast dissolving buccal films.

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Nicorandil (mg)	60	60	60	60	60	60	60	60	60	60	60	60	60
HPMC E15 (mg)	300	400	200	300	400	200	300	300	300	200	300	300	400
PVA (mg)	150	50	50	150	150	250	50	150	250	150	150	150	250
Distilled water (ml)	10	10	10	10	10	10	10	10	10	10	10	10	10
PEG 400 (ml)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Mannitol (mg)	10	10	10	10	10	10	10	10	10	10	10	10	10
Citric acid (mg)	5	5	5	5	5	5	5	5	5	5	5	5	5

5. Evaluation and physicochemical characterization of Nicorandil fast dissolving buccal films

5.1. Physical appearance of films

The films were observed visually for their physical appearance such as colour, transparency and texture by feel or touch.

5.2. Weight uniformityof films

Three films of the size 2×2 cm were weighed individually using digital balance and the average weights were calculated.

5.3. Thickness of films

Thickness of the films was measured using screw gauge with a least count of 0.01mm at different spots of the films. The thickness was measured at three different spots of the films and average was taken.

5.4. Folding endurance of films

The flexibility of films can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the films was determined by repeatedly folding a small films (approximately 2x2 cm) at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

5.5. Drug content of films

The films were tested for drug content uniformity by UV Spectrophotometric method.m Films of 2×2 cm size were cut from three different places from the casted films. Each film was placed in 100 mL volumetric flask and dissolved in simulated saliva pH 6.8 and 2 mL is taken and diluted with water up to 10 ml. The absorbance of the solution was measured at λ max 262 nm using UV/visible spectrophotometer (Shimadzu, japan). The percentage drug content was determined.

5.6. Fourier-transformed infrared study[11]

An FT-IR spectroscopy study has been carried out separately to check the compatibility assessment was performed between the drug and excipients using FT-IR analysis. This evaluation was conducted for each specific component, including drug (Nicorandil) and the polymers (HPMC E15, PVA) used for the preparation of films. Additionally, the investigation also included their Nicorandil loaded fast dissolving buccal films.

5.7. *In-vitro* drug release[10]

The drug release rate of Nicorandil fast dissolving Buccal films was determined by using the Diffusion method by using Franz diffusion cell The film with 2×2 cm was placed in the phosphate buffer of 6.8 pH simulated saliva as diffusion medium. From this dissolution medium, 2mL of the sample solution was withdrawn at different time intervals. The samples were collected by 2,4,6,8,10,12 up to 14 minutes and absorbance was analyzed by UV spectrophotometer at 262nm.

5.8. Disintegration time

Disintegration test of films was carried out by petridish method. In this method one film at a time was placed in petridish containing a 5ml of buffer and the time required to dissolve the film completely was measured. Estimation was carried out in triplicate.

6. RESULTS AND DISCUSSION

6.1. FTIR studies

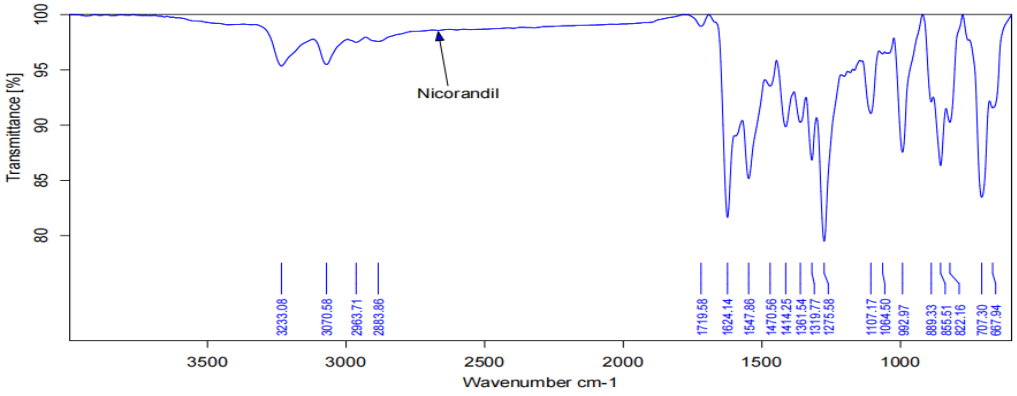


Figure 1: FTIR spectrum of pure Nicorandil.

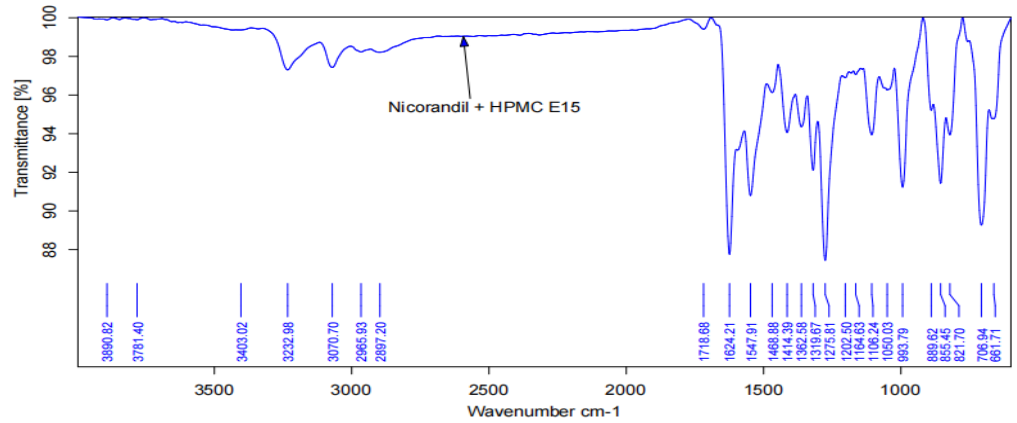


Figure 2: FTIR spectrum of Nicorandil + HPMC E15.

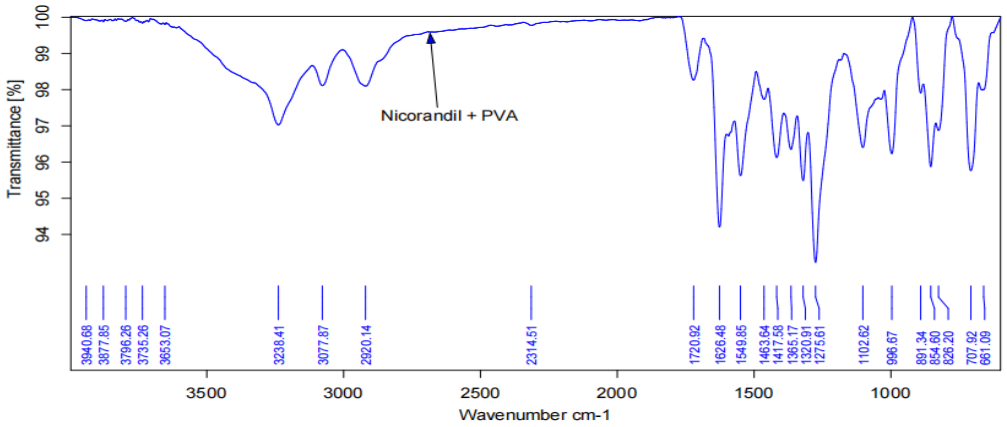


Figure 3: FTIR spectrum of Nicorandil + PVA.

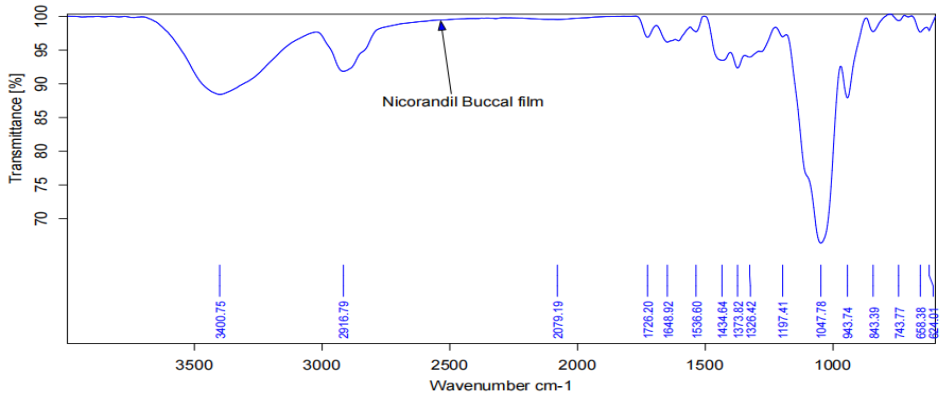


Figure 4: FTIR spectrum of Buccal film containing Drug + Polymers (HPMC E15+ PVA)

The FT-IR Spectra were analyzed within the frequency range of 600-4000 cm^{-1}. Based on the FTIR studies appear to be no possibility of interaction between the Nicorandil and polymers of other excipients used in the films.

6.2. Wavelength

The lambda max was observed at 262nm

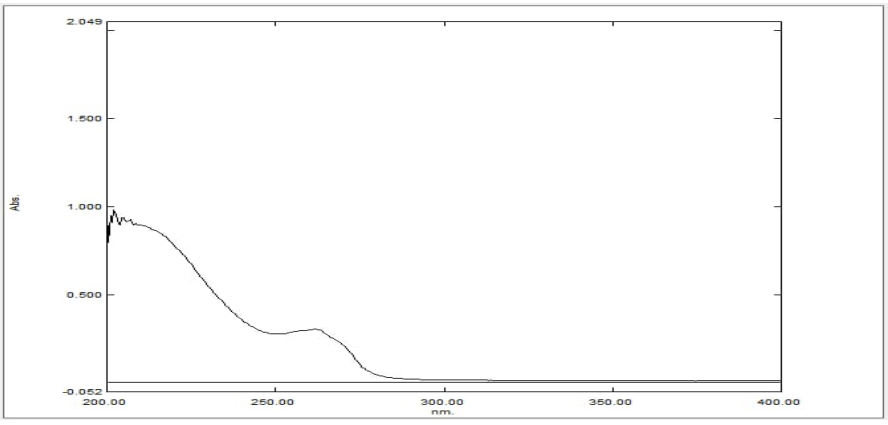


Figure 5: Wavelength of Nicorandil.

6.3. Standard graph

Table 3: Standard graph.

SL. NO	Concentration (µg/ml)	Absorbance @262nm
1	5	0.1019
2	10	0.1898
3	15	0.2616
4	20	0.3412
5	25	0.4325
6	30	0.5188
7	35	0.6081
8	40	0.7147
9	45	0.8018
10	50	0.8788

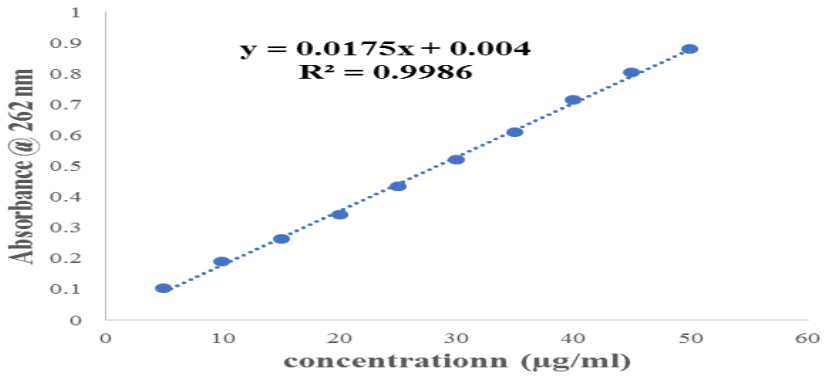


Figure 6: Standard curve of Nicorandil.

6.4. Characterization of Nicorandil films

Total 13 formulations were prepared and subjected to different evaluation parameters. Among these formulations, F7 shows good results. The appearances of films were evaluated by visual examination such as transparent and opaque. The films were thin, flexible, elastic, smooth and transparent (figure 7).

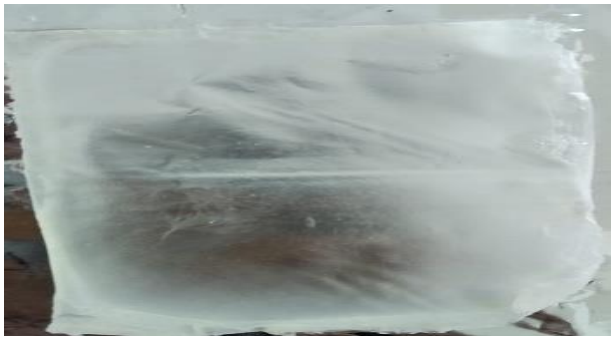


Figure 7: Appearance of film.

The weight uniformity of films ranged between 50.8±0.59 to 58.02±0.28 showed that there was no significant difference in the weight of films. This ensured the uniformity of the films.

The thickness of all the formulations was varied from 0.20±0.02 mm to 0.25±0.03 mm and ensured the uniformity of films.

The films were subjected to folding endurance to evaluate the flexibility studies. All the formulations showed >150. This revealed that the prepared films were having capacity to withstand the mechanical pressure along with good flexibility.

Table 4: Evaluation parameters of Nicorandil Buccal Films.

Formulation	Weight uniformity (mg)	Thickness (mm)	Folding Endurance	Disintegration time (sec)	Drug Content (%)
F1	56.44±1.308	0.20±0.02	245.33±2.08	44.00±1.00	97.35±0.17
F2	52.13±0.176	0.23±0.01	221.66±2.88	46.00±1.73	95.42±0.14
F3	55.33±1.258	0.21±0.01	253.00±1.00	42.66±0.57	98.76±0.31
F4	56.55±1.189	0.20±0.02	244.33±2.08	44.00±1.00	97.46±0.42
F5	52.01±0.150	0.25±0.02	251.00±1.00	51.66±1.52	95.21±0.23
F6	54.15±0.230	0.22±0.03	219.00±1.00	45.00±1.00	96.76±0.24
F7	58.01±0.340	0.24±0.03	252.33±2.08	38.00±1.00	99.26±0.54
F8	56.55±1.187	0.20±0.02	245.66±1.52	43.66±1.15	97.25±0.05
F9	58.35±0.490	0.21±0.01	279.33±1.52	42.66±0.57	99.04±0.01
F10	55.81±1.885	0.22±0.02	254.66±2.08	46.00±1.73	98.32±0.25
F11	56.55±1.184	0.20±0.02	244.66±1.52	44.00±1.00	97.35±0.17
F12	56.53±1.198	0.22±0.02	245.00±1.00	44.33±1.15	97.58±0.64
F13	51.03±1.050	0.24±0.01	223.00±2.00	53.00±1.00	95.49±0.26

n = 3 observations ± SD.

The percentage of drug content in various formulations were ranged from 95.21±0.23 to 99.26±0.54 %.

The in-vitro disintegration time studies suggested that films prepared by using all the grades of polymers showed the disintegration time below 53 sec and was in acceptable range.

A rapid diffusion of all the films was observed by the diffusion studies, in which above 90% of Nicorandil was released within 12min. The formulation F7 showed maximum drug release 95.3% within 8 minutes. ***In-vitro*** **Drug Release of Fast dissolving buccal films.**

Table 5*: In-vitro* release data of various Nicorandil fast dissolving buccal films (F1-F7)

Time (min)	Cumulative Percentage Drug release (%)						
	F1	F2	F3	F4	F5	F6	F7
2	42.12	40	54	43.12	47.1	44.31	59.14
4	56.15	51.42	66.14	57.15	62.1	59.31	70.21

6	62.14	70.07	78.49	63.12	72.5	70.32	83.55
8	72.11	76	88.07	72.12	80	79.35	95.3
10	85.14	87.52	95.91	86.15	90.2	94.36	-
12	93	91.47	-	92.15	-	-	-

Table 6: *Invitro* release data of various Nicorandil fast dissolving buccal films (F8-F13)

Time (min)	Cumulative Percentage Drug release (%)					
	F8	F9	F10	F11	F12	F13
2	46.11	48.6	35.4	47.1	49.1	40.2
4	59.12	56.3	45.1	59.22	59.2	48.3
6	62.14	66.8	58.2	69.11	68.3	62.3
8	75.12	75.1	65.4	79.12	79.5	69.2
10	86.14	83.1	78.2	82.14	85.1	78.3
12	92.14	93.3	84.36	92.14	93.5	85.2
14	-	-	95.23	-	-	90.33

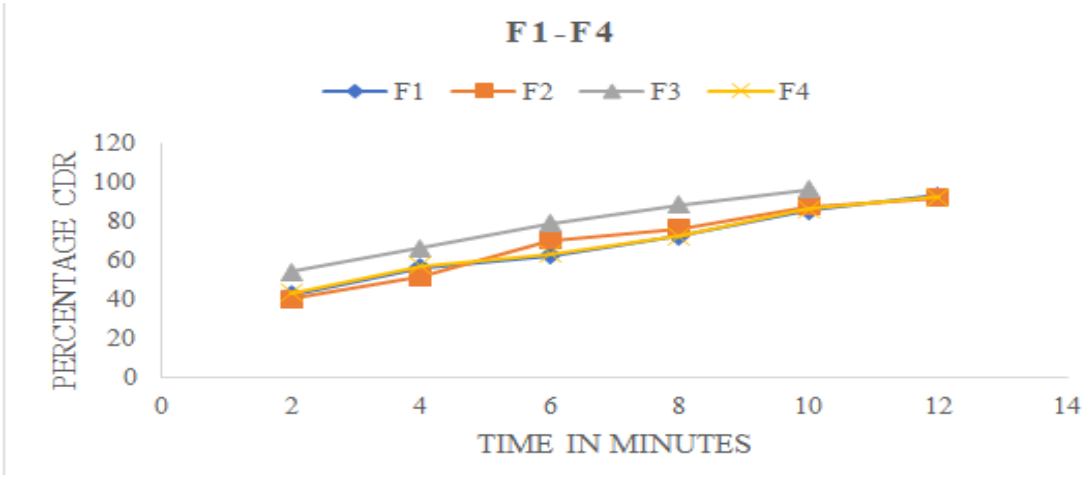


Figure 8: *In-vitro* drug release profile of formulations (F1-F4).

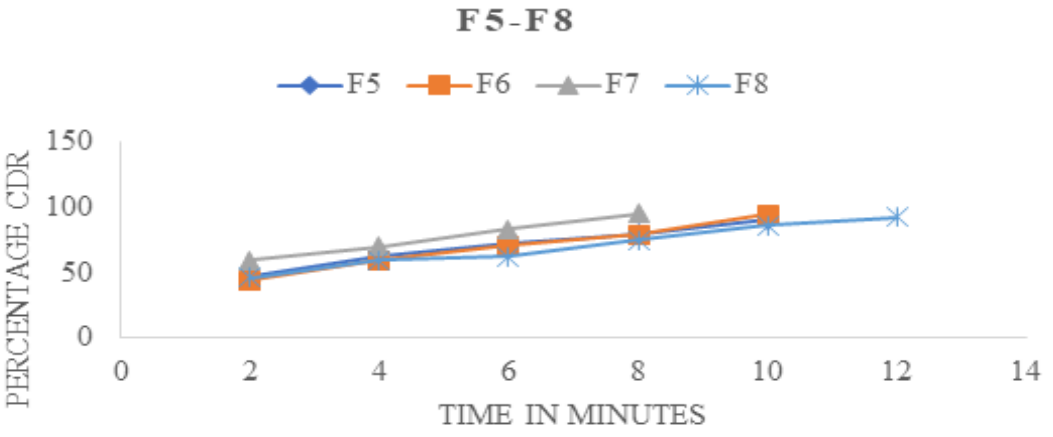


Figure 9: In-vitro drug release profile of formulations (F5-F8).

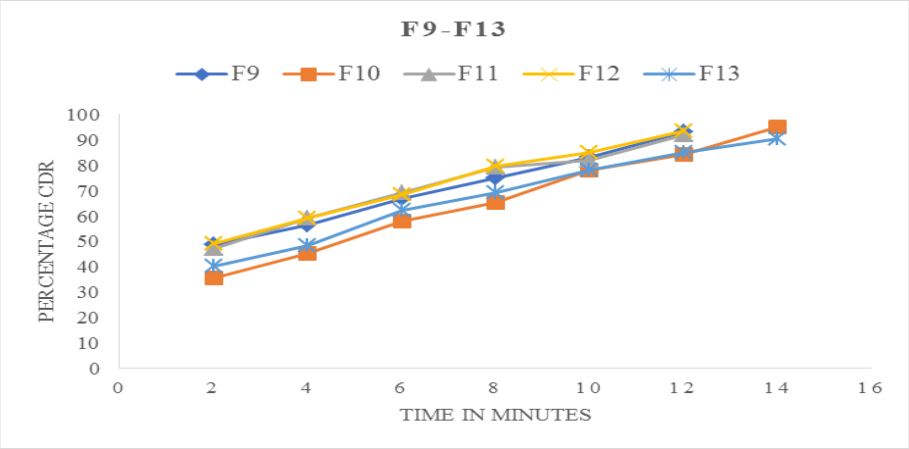


Figure 10: In-vitro drug release profile of formulations (F9-F13)

Optimization Results of Nicorandil loaded Fast dissolving buccal films

Employing experimental design to optimize various parameters on the Nicorandil fast dissolving buccal films A Factorial Design consisting of 2 factors and 3 levels was performed in order to optimize fast dissolving buccal films using Design Expert software version 12.0.1.0. It provides a total of 13 experimental runs to evaluate the impact of two independent variables such as HPMC E 15 polymer and PVA polymer were taken as factors and their effects on Disintegration time and cumulative amount of drug release were considered as the responses, as specified in Table 7.

Table 7: Experimental Design Matrix and Reponses of Nicorandil loaded Fast Dissolving Buccal Film formulations.

Formulation	Factors (Independent variables)		Responses (Dependent variables)	
	HPMC E 15 (mg)	PVA (mg)	Disintegration time (sec)	%CDR (%)
Sl.no	A	B	X	Y
1	300	150	44	93
2	400	50	46	91.47
3	200	50	42.66	95.91
4	300	150	44	92.15
5	400	150	51.66	90.2
6	200	250	45	94.36
7	300	50	38	95.3
8	300	150	43.66	92.14
9	300	250	42.66	93.3
10	200	150	46	95.23
11	300	150	44	92.15
12	300	150	44.33	93.5
13	400	250	53	90.33

Analysis of data obtained from the factorial design

Effect of Independent Variables on Disintegration time (Response X)

Disintegration time of the entire prepared oral film was carried by petri dish method. The disintegration time for all the formulation was found to be 38±1.00 to 53±1.00 seconds. All the formulations of fast dissolving films were found to disintegrate in less than 60 sec. The quadratic model demonstrated a statistically significant, indicating a strong influence of independent variables on the Disintegration time of Fast dissolving buccal films. A model F value was found to be 116.62, showing just a 0.01% probability that such a high F-value could be attributed to random variation. p-value, which is less than 0.0500, indicates its statistical significance. In this model, the significant terms were A, B, AB, A^2, and B^2. Among these, the HPMC E15 (Factor A) had the most pronounced effect ($F = 161.59$, $p < 0.0001$), followed by PVA (Factor B), their interaction (AB), and the quadratic term of A (A^2), quadratic term of B (B^2), all of which were significant contributors. Lack of fit was not significant ($p = 0.3550$), ensuring that the model is adequate, which is given in Table 8 The Predicted R^2 value of the model is 0.9495, which is in close agreement with the Adjusted R^2 value of 0.9797, suggesting a strong goodness of fit. Additionally, the Adequate precision value of 38.3192 validates the model's capability in exploring the design space.

The resulting polynomial equation 1, can be used to illustrate the total impact of independent variables and their interaction on Disintegration time: Disintegration time = 43.6238 + 2.86 A + 2.36 B + 1.125 AB + 5.64172 A^2 - 2.85828 B^2 (Equation 1)

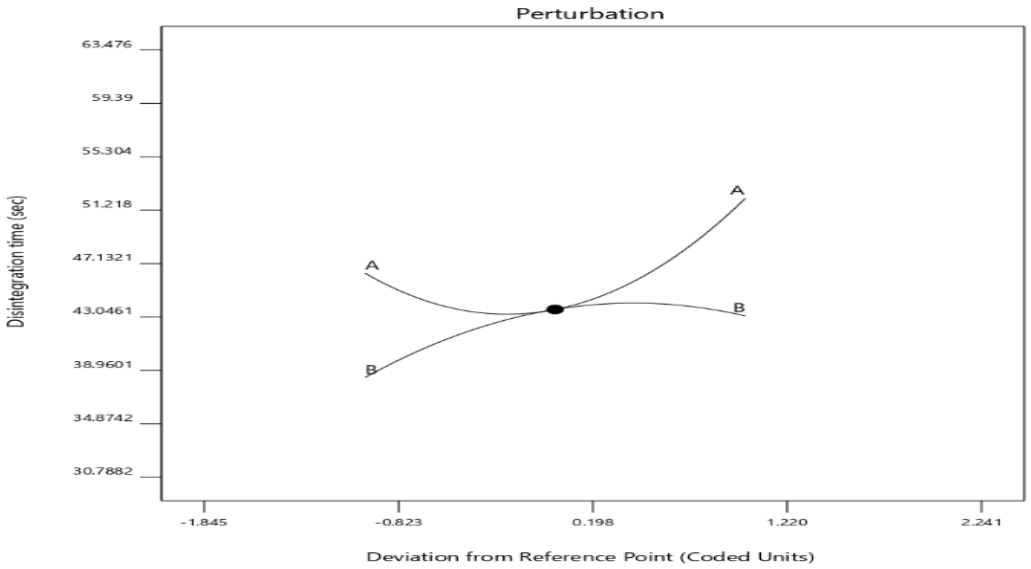
In equation 1, the positive value of the coefficient indicates that the factors and the responses are directly related. Similarly, the negative value indicates the inverse relationship between them. The positive coefficient of Factor A & B indicated the synergistic effect on disintegration time. Increasing the concentration of HPMC E 15 and PVA polymer increases the disintegration time of fast dissolving buccal films. The equation concludes that factor A has a higher impact on disintegration time than factor B.

Table 8: ANOVA for the quadratic model of Disintegration time.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	177.09	5	35.42	116.62	< 0.0001	**significant**
A-HPMC E 15	49.08	1	49.08	161.59	< 0.0001	
B-PVA	33.42	1	33.42	110.03	< 0.0001	
AB	5.06	1	5.06	16.67	0.0047	

A^2	87.91	1	87.91	289.45	< 0.0001	
B^2	22.56	1	22.56	74.29	< 0.0001	
Residual	2.13	7	0.3037			
Lack of Fit	1.11	3	0.3685	1.44	0.355	**not significant**
Pure Error	1.02	4	0.2551			
Corrected Total	179.22	12				

The graphical representations derived from the factorial design illustrate the influence of two independent variables – HPMC E15 (A) and PVA (B) on the Disintegration time of fast dissolving buccal films. The perturbation graph (Figure 11) demonstrates the individual effects of each variable, revealing how variations in HPMC E15 and PVA impact the Disintegration time. increasing HPMC E 15 from 200 mg to 400 mg leads to increase in disintegration time until a saturation point is reached. Beyond the optimal amount of HPMC E 15 (like 400 mg) significantly increases in disintegration time. Increase in HPMC E 15 As the quantity of HPMC E 15 rises from 200 mg to approximately 300 mg, the disintegration time reduces, Increase in PVA increases from 50 mg to 150 mg, the disintegration time increases. Beyond 150 mg, the disintegration time begins to decrease. Decrease in PVA from 250 mg to 150 mg, the disintegration time decreases. Below 150 mg, the disintegration time starts to rise.



The contour surface plot provides a visualization of the interaction between factors, highlighting optimal regions for maximizing through colour gradients. Complementing this, the 3D response surface plot offers a comprehensive three-dimensional perspective, showcasing the synergistic effects of both variables and identifying peak time zones.

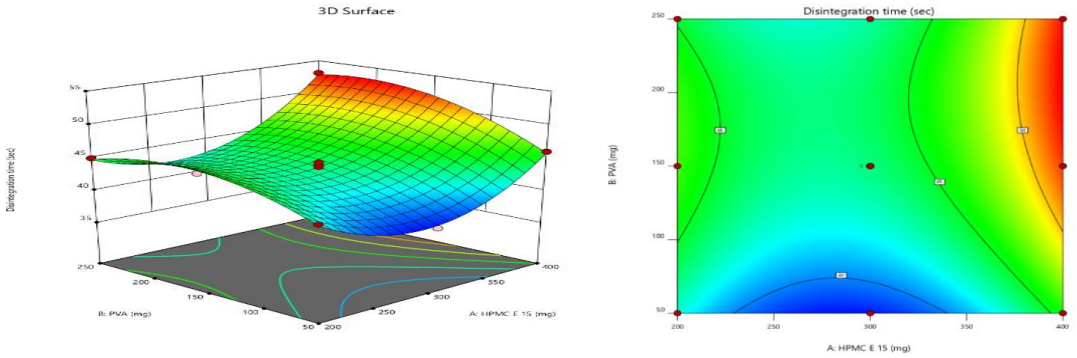


Figure 11: Graphical depiction of perturbation plot, contour and 3-D response surface plots illustrating effects of independent variables on disintegration time.

Effect of Independent Variables on %CDR (Response Y)

%CDR of Nicorandil-loaded fast dissolving buccal films were subjected to *in-vitro* drug release studying for a period of 14 min and the %CDR were ranged between 35.4 to 95.91% among these total 13 formulations. The quadratic model demonstrated a statistically significant, indicating a strong influence of independent variables on the %CDR of fast dissolving buccal films. A model F value was found to be 26.63, showing just a 0.01% probability that such a high F-value could be attributed to random variation. p-value, which is less than 0.0500, indicates its statistical significance, HPMC E15 (Factor A) had the most pronounced effect ($F = 47.53$, $p < 0.0001$), followed by PVA (Factor B). Lack of fit was not significant ($p = 0.2609$), ensuring that the model is adequate, which is given in Table 9 The Predicted R^2 value of the model is 0.7542, which is in close agreement with the Adjusted R^2 value of 0.8103, suggesting a strong goodness of fit. Additionally, the Adequate precision value of 15.7884 validates the model's capability in exploring the design space. The resulting polynomial equation 2, can be used to illustrate the total impact of independent variables and their interaction on %CDR: % CDR = 93.0023 + -2.25 * A - 0.781667 * B (Equation 2)

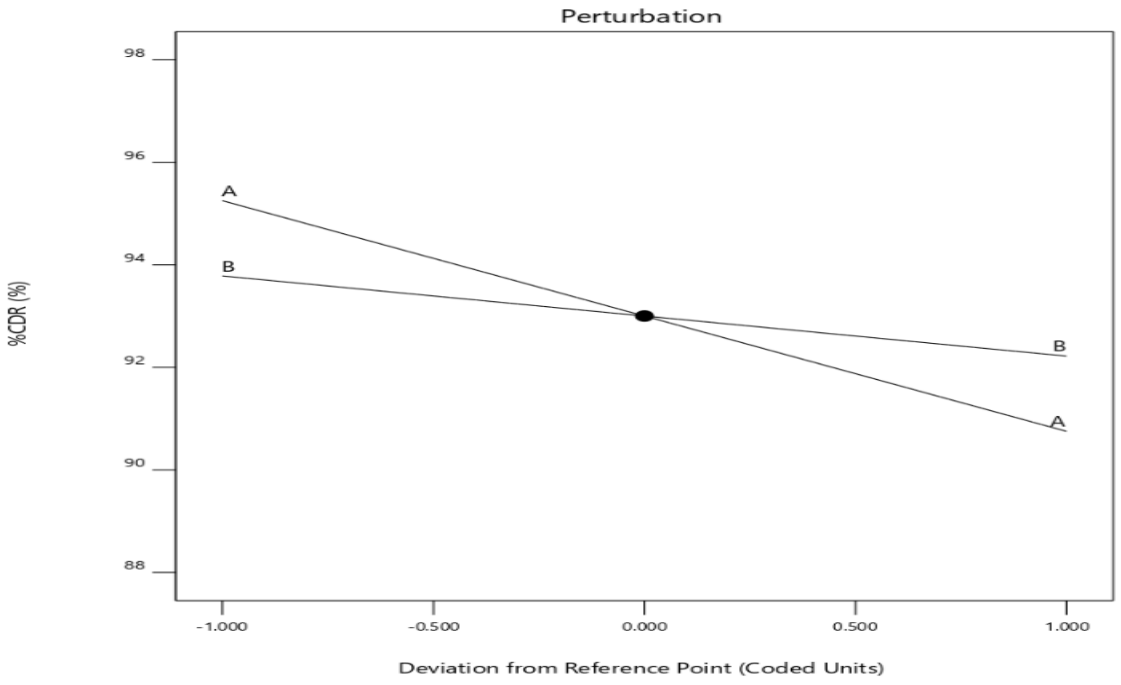
In equation 2, the positive value of the coefficient indicates that the factors and the responses are directly related. Similarly, the negative value indicates the inverse relationship between them. The positive coefficient of Factor A & B indicated the synergistic effect on %CDR. Increasing the concentration of HPMC E15 and PVA decrease the %CDR of FDBF's. The equation concludes that factor A (HPMC E15) has a higher impact on %CDR compared to factor B (PVA).

Table 9: ANOVA for the quadratic model of percentage cumulative drug release (%CDR)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	34.04	2	17.02	26.63	< 0.0001	**significant**
A-HPMC E 15	30.38	1	30.38	47.53	< 0.0001	
B-PVA	3.67	1	3.67	5.74	0.0376	
Residual	6.39	10	0.6391			
Lack of Fit	4.8	6	0.7994	2.01	0.2609	**not significant**
Pure Error	1.59	4	0.3987			
Corrected Total	40.43	12				

The graphical representations derived from the factorial design illustrate the influence of two independent variables – HPMC E15 (A) and PVA (B) on the %CDR of fast dissolving buccal films. The perturbation graph (Figure 12) demonstrates the individual effects of each variable, revealing how variations in HPMC E15 and PVA impact the %CDR.

The contour surface plot provides a visualization of the interaction between factors, highlighting optimal regions for maximizing through colour gradients. Complementing this, the 3D response surface plot offers a comprehensive three-dimensional perspective, showcasing the synergistic effects of both variables and identifying peak %CDR zones.



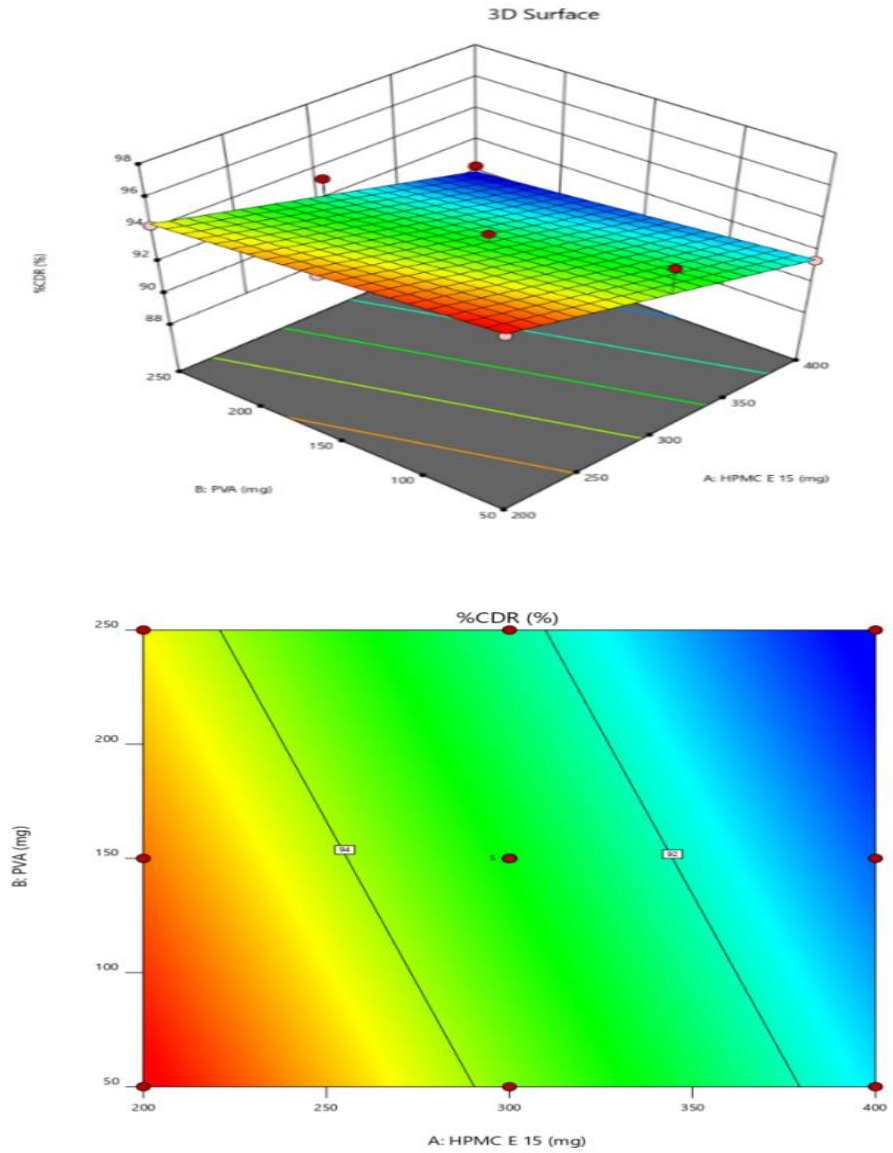


Figure 12: Graphical depiction of perturbation plot, contour, and 3-D response surface plots illustrating effects of independent variables on percentage cumulative drug release (%CDR).

Stability studies

Finally based on the thickness, weight uniformity, drug content uniformity, disintegration study and *in-vitro* drug release study confirmed that F7 was the best formulation. Stability studies were conducted as per ICH guidelines. Samples were taken at 30 days for drug content and *in-vitro* release estimation. The formulated films F7 were stored over period of four weeks. At the end of four weeks films were tested for drug content and *in-vitro* release profiles. The drug content and *in-vitro* release results were suggesting that there was no significant change in drug content and *in-vitro* drug release.

Table 10: Drug content of formulation F7 on 1st day & 30th day (n=3, Avg ± SD).

SL.NO	Trial no.	Before stability storage	30 days
1	I	99.26	97.35
2	II	98.76	97.46
3	III	99.04	98.32
4	Mean	99.02±0.25	97.71±0.82

Table 11: In-vitro release data of optimized formulation (F7) on 1st day & after 30 days (n=3, Avg ± SD).

Time (min)	Percentage cumulative drug release	
	Before stability storage	After 30 days
2	60.13±0.72	58.01±0.51
4	71.32±0.91	69.15±0.52
6	82.53±0.75	80.58±0.92
8	95.21±0.86	93.04±0.61

CONCLUSION

The present research work successfully developed and optimized that is "Design, Optimization and Evaluation of Buccal Films of Nicorandil using Design of Experiments" for Angina Pectoris using a 3- level factorial design by various types of polymers such as HPMC E15 and PVA by solvent casting method, to overcome the first-pass metabolism and the subsequent low bioavailability of the drug. The method of formulation was found to be modern and economic. Among all the 13 formulations, F7 was found as a best formulation which contains Nicorandil, HPMC E15 and PVA showed a excellent film forming characteristics such as disintegration time 38 sec and percentage drug release was 95.3 % within 8 minutes. The results suggest that the developed fast release films of Nicorandil could perform better than conventional dosage form leading to improved efficacy and better patient compliance.

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