Rational Design and Statistical Optimization of Polymer-Based Fast-Dissolving Films for Rapid Delivery of Naproxen and Aceclofenac

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ABSTRACT

Objective: In order to achieve quick medication release and better patient compliance, the current study set out to create and optimize fast-dissolving oral films (FDFs) of naproxen and aceclofenac.

Method: The solvent casting process was used to create fast-dissolving films utilizing polyethylene glycol 400 (PEG 400) as a plasticizer and hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA) as film-forming polymers. The physicochemical characteristics, mechanical strength, surface pH, drug content, and in-vitro drug release of the formulations were assessed. Response surface methodology (RSM) and multiple regression analysis were used in statistical optimization to examine how formulation variables affected drug release at 12 and 15 minutes.

Result: Every formulation had a flat surface morphology, consistent thickness, and little weight variance. When compared to Naproxen films, aceclofenac films had somewhat greater tensile strength and folding endurance. Both formulations showed rapid drug release, with almost full release occurring in 15 minutes. According to regression analysis, PVA mostly contributed to structural integrity, but HPMC significantly improved drug release. The constructed models were validated by checkpoint analysis with prediction error less than 1%, and they had good correlation coefficients ($R^2 > 0.99$). The formulations were stable under accelerated settings, according to stability studies, and the similarity factor ($f_2 > 50$) showed no discernible change in the dissolving profiles. First-order degradation kinetics were used in chemical stability investigations.

Conclusion: The produced fast-dissolving films of Aceclofenac and Naproxen showed good stability, quick drug release, and outstanding physicochemical characteristics, making them viable options for efficient oral drug delivery.

Keywords: Fast-dissolving oral films, Naproxen, Aceclofenac, HPMC, PVA, Solvent casting, Response surface methodology

How to cite this article: Ram T, Soni GK. Rational Design and Statistical Optimization of Polymer-Based Fast-Dissolving Films for Rapid Delivery of Naproxen and Aceclofenac. Int J Drug Deliv Technol. 2026;16(51s): 1036-1046. DOI: 10.25258/ijddt.16.51s.86

Source of support: Nil.

Conflict of interest: None

1. Introduction

Fast-dissolving oral films (FDFs) have become a cutting-edge medication administration method intended to increase patient compliance, especially in dysphagic, elderly, and pediatric populations. When these films come into touch with saliva, they quickly break down, releasing the medication without the need for water and offering a practical substitute for traditional oral dosing forms. FDFs include benefits such quick onset of action, increased bioavailability, and improved patient acceptance in addition to being simple to administer[1]. Aceclofenac and Naproxen are two examples of non-steroidal anti-inflammatory medications (NSAIDs) that are frequently used to treat pain and inflammation. However, gastrointestinal adverse effects and a delayed onset of action may be linked to their traditional oral forms. By facilitating quick drug release and absorption, including these medications into fast-dissolving films can get around these restrictions and increase therapeutic efficacy[2,3].

For FDFs to have the best possible mechanical strength, quick disintegration, and effective drug release, film-forming polymers must be carefully chosen. Because of their superior film-forming capacity, biocompatibility, and hydration properties, hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA) are often utilized polymers. The flexibility and handling qualities of films are

further improved by the addition of plasticizers such polyethylene glycol 400 (PEG 400)[4,5].
In order to get the necessary performance, formulation variable optimization is essential. In order to assess the impact of formulation variables and their interactions on drug release behavior, statistical approaches like response surface methodology (RSM) and multiple regression analysis are frequently used. This allows for systematic formulation development with fewer experimental trials.
Therefore, the current work used HPMC and PVA as film-forming polymers to generate and optimize fast-dissolving oral films containing naproxen and aceclofenac. In order to create a reliable and efficient oral drug delivery system, the formulations were assessed for physicochemical characteristics, mechanical strength, in-vitro drug release, release kinetics, and stability[6].

2. Materials and Methods

2.1 Materials

Due to their therapeutic significance and need for a quick onset of action, naproxen and aceclofenac were chosen as model non-steroidal anti-inflammatory medicines (NSAIDs) for the creation of fast-dissolving oral films. Both medications were acquired unadulterated and utilized as is[7]. The main hydrophilic film-forming polymer used was hydroxypropyl methylcellulose (HPMC) because of its superior film-forming capacity, quick hydration, and swelling properties, all of which greatly aid in quick disintegration and drug release. In order to improve the films' mechanical strength, flexibility, and structural integrity, polyvinyl alcohol (PVA) was employed as a secondary film-forming polymer[8].

2.2 Preparation of fast dissolving film

The solvent casting process was used to create fast-dissolving films (FDFs) of naproxen (F1–F9) and aceclofenac (A1–A9). To create a transparent polymeric solution, precisely weighed amounts of PVA and HPMC were dissolved in distilled water while being constantly stirred. The medication was added after PEG 400 was added as a plasticizer[9]. To create homogeneous films, the resultant solution was cast onto a level surface and dried at a regulated temperature. For additional analysis, dried films were carefully peeled and cut into the necessary sizes.

2.3 In vitro drug release study

Studies on the release of drugs in vitro were carried out under controlled settings with a suitable dissolving medium. At predefined intervals of 3, 6, 9, 12, and 15 minutes, samples were taken out and subjected to spectrophotometric analysis[10].

2.4 Release Kinetics

To ascertain the mechanism of drug release, the drug release data were fitted to a number of kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models[11,12].

2.5 Statistical analysis

The impact of independent variables, HPMC (X_1) and PVA (X_2), on drug release responses at 12 minutes (Y_{12}) and 15 minutes (Y_1^1) was assessed statistically using multiple regression analysis. The following second-order polynomial equation was used:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{11} X_1^2 + \beta_{22} X_2^2 + \beta_{12} X_1 X_2$$

Every experiment was carried out in triplicate, and the mean ± standard deviation was used to express the results[13,14].

2.6 Response Surface Methodology

RSM was used to assess the relationship between HPMC and PVA and optimize formulation factors. To see how independent variables affected drug release, three-dimensional response surface plots and contour plots were created[15].

2.7 Design Space and Checkpoint validation

Y_{12} and Y_{15} contour plots were superimposed to create the design space. To verify the regression model's prediction power, checkpoint formulations were created inside the optimized region[16].

2.8 Stability Studies

For four weeks, stability tests were carried out in accordance with ICH Q1A(R2) criteria at accelerated conditions (40 ± 2°C and 75 ± 5% RH). Samples were assessed for drug release, folding endurance, surface pH, and physical attractiveness[17].

3. RESULT AND DISCUSSION

3.1 Multiple regression analysis

Naproxen fast dissolving Film
The impact of formulation factors, specifically HPMC (X_1) and PVA (X_2), on drug release from Naproxen fast-dissolving films at 12 minutes (Y_{12}) and 15 minutes (Y_{15}), was quantitatively assessed using multiple regression analysis[18]. To explain the connection between independent factors and response, a second-order polynomial model was created. With a coefficient of determination (R^2 = 0.9944), the

polynomial equation for drug release at 15 minutes (Y_{15}) showed a very significant association between formulation variables and drug release. This shows that the chosen model can account for about 99.44% of the variation in drug release[19], demonstrating its appropriateness and robustness. Multiple regression analysis was used to quantify the effect of formulation parameters, namely HPMC (X_1) and PVA (X_2), on drug release from Naproxen fast-dissolving films at 12 minutes (Y_{12}) and 15 minutes (Y_{15})[20]. A second-order polynomial model was developed to describe the relationship between independent factors and response.

Table no. 1 - Regression Coefficients and Statistics for Naproxen FDFs
A – Drug Release at 15 min (Y_{15})

Parameter	Coefficient	p-value	Interpretation
Intercept (β_0)	77.4619	—	Baseline response
HPMC (X_1)	+3.8941	>0.05	Positive, not significant
PVA (X_2)	+3.8530	>0.05	Positive, not significant
X_1^2	+0.0736	>0.05	Minor curvature
X_2^2	−0.1325	>0.05	Slight negative curvature
X_1X_2	−0.3637	>0.05	Negative interaction

B- Drug Release at 12 min

Parameter	Coefficient	p-value	Interpretation
Intercept (β_0)	59.0068	—	Baseline response
HPMC (X_1)	+3.8955	>0.05	Positive effect
PVA (X_2)	+3.8531	>0.05	Positive effect
X_1^2	+0.0734	>0.05	Minor curvature
X_2^2	−0.1323	>0.05	Slight reduction effect
X_1X_2	−0.3638	>0.05	Negative interaction

The polynomial equation for drug release at 15 minutes (Y_{15}) demonstrated a highly significant correlation between formulation factors and drug release, with a coefficient of determination (R^2 = 0.9944). This demonstrates the suitability and resilience of the selected model, which can explain roughly 99.44% of the variation in drug release.
Similar patterns were displayed by the regression model for drug release at 12 minutes (Y_{12}), which had a good predictive capacity and little residual error. The strong agreement between the experimental and anticipated values attests to the model's dependability over a range of time periods.

Aceclofenac fast dissolving Film
In order to assess the impact of formulation variables on drug release behavior, a similar regression analysis was performed for Aceclofenac fast-dissolving films. The regression model showed an excellent correlation between predicted and experimental values, with a coefficient of determination (R^2 = 0.9977), indicating that 99.77% of the variation in drug release is explained by the model, confirming its high accuracy and predictive capability. The analysis of regression coefficients showed that HPMC (X_1) had a statistically significant positive effect on drug release ($p < 0.05$), indicating that it plays a dominant role in controlling drug diffusion.
Although its effect was not statistically significant ($p > 0.05$), PVA (X_2) also had a favorable contribution. This implies that rather than directly affecting drug release kinetics, PVA mostly aids in film generation and mechanical strength.

Table No -2 Regression Coefficients and Statistics for Aceclofenac FDFs
A - Drug Release at 15 min (Y_{15})

Parameter	Coefficient	p-value	Interpretation
Intercept (β_0)	82.0447	—	Baseline response
HPMC (X_1)	+2.5867	**<0.05**	Significant positive effect
PVA (X_2)	+2.1528	>0.05	Non-significant
X_1^2	+0.1291	>0.05	Positive curvature
X_2^2	+0.0290	>0.05	Minor effect

X_1X_2	−0.1745	>0.05	Negative interaction

B- Drug Release at 12 min

Parameter	Coefficient	p-value	Interpretation
Intercept (β_0)	65.8172	—	Baseline response
HPMC (X_1)	+2.5857	**<0.05**	Significant
PVA (X_2)	+2.1528	>0.05	Non-significant
X_1^2	+0.1293	>0.05	Minor curvature
X_2^2	+0.0290	>0.05	Minimal effect
X_1X_2	−0.1745	>0.05	Negative interaction

At moderate polymer concentrations, the quadratic terms (X_1^2 and X_2^2) showed positive coefficients, suggesting a small increase in drug release. These effects may not be statistically significant, though, based on their higher p-values.The interaction term (X_1X_2) displayed a negative coefficient, similar to Naproxen formulations, suggesting that concurrent increases in both polymers may decrease drug release because of increased matrix density and decreased diffusional routes. The coherence and robustness of the generated model across various response parameters were confirmed by the regression model for Y_{12}, which also exhibited the similar pattern.

3.2 Response surface analysis

The combined effect (Fig no – 1) of formulation factors, HPMC (X_1) and PVA (X_2), on the drug release behavior of fast-dissolving films was assessed using Response Surface Methodology (RSM). To give a visual depiction of the interaction between independent variables and their impact on the response parameters, namely % drug release at 12 minutes (Y_{12}) and 15 minutes (Y_{15}), three-dimensional (3D) response surface plots were created[21,22].

Drug release rise gradually with increasing HPMC and PVA concentrations up to an optimal level, as the 3D response surface plots amply illustrated. This activity is explained by HPMC's hydrophilic properties[23], which promote quick water absorption, swelling, and polymer relaxation, improving drug diffusion from the film matrix. PVA indirectly supports drug release by enhancing film formation and preserving structural integrity.

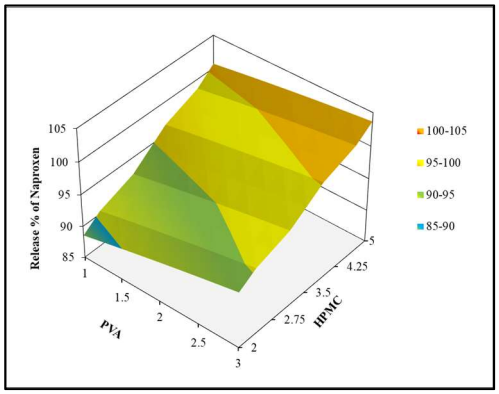
Nevertheless, a decrease or plateau in drug release was noted beyond the ideal concentration range. Increased matrix density and viscosity brought on by increasing polymer concentrations are the main causes of this phenomena. At higher concentrations, the polymer chains create a more densely packed network that decreases the matrix's porosity and limits the drug molecules' ability to diffuse.

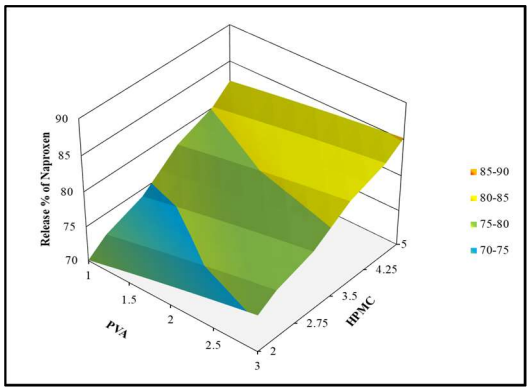
As a result, even with a higher polymer concentration, medication release slows down. The response surface plots for Naproxen formulations showed a comparatively steeper gradient, suggesting that drug release was more sensitive to variations in polymer content[24]. Aceclofenac formulations, on the other hand, displayed a smoother and wider response surface, indicating a more regulated release behavior and improved tolerance to formulation variable change. The response surface's curvature, which shows that the relationship between formulation variables and drug release is not strictly linear, further supports the existence of quadratic effects. Furthermore, the negative interaction impact (X_1X_2) found in the regression analysis is supported by the little surface depression at higher combined levels of HPMC and PVA[25].

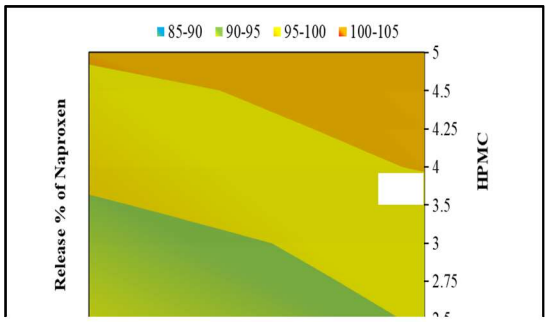
Overall, the response surface analysis helped determine the best area for accomplishing quick and effective drug delivery and gave a clear knowledge of how formulation variables interact to affect drug release.

3.3 Contour Plot Interpretation

To further clarify the connection between drug release responses (Y_{12} and Y_1^1) and formulation factors (HPMC (X_1) and PVA (X_2), contour plots—two-dimensional representations of the three-dimensional response surfaces were created[26]. When determining areas of ideal formulation circumstances where the intended drug release profile can be attained, these plots are especially helpful. Both the naproxen and aceclofenac formulations' contour plots showed elliptical contour







patterns, suggesting a substantial interaction between PVA and HPMC. As seen in the regression analysis, these non-linear contour shapes validate the existence of quadratic and interaction effects. The contour plots for Naproxen FDFs showed a comparatively small optimum region, indicating that drug release is extremely sensitive to changes in polymer content. A balanced mixture of PVA (2.75–3% w/v) and HPMC (around 3.5–4% w/v) produced quick and effective drug release in this area. Drug release changed noticeably when this ideal zone was slightly deviated from, underscoring the significance of exact formulation control[27]. The contour plots for Aceclofenac FDFs, on the other hand, showed a wider optimum region, suggesting more formulation variable flexibility. While keeping PVA within a similar range (2.75–3% w/v), the intended drug release profile was attained at relatively higher HPMC concentrations (4.75–5% w/v). This implies that aceclofenac formulations work better and are less susceptible to small changes in polymer content. Additionally, the contour lines confirmed HPMC's dominating function in regulating release behavior by showing that drug release increases along the gradient of rising HPMC concentration. PVA had a somewhat mild effect, mostly influencing the structure of the film rather than dramatically changing the release of the medication. The contour plots showed areas of decreased drug release at greater combined concentrations of both polymers. This can be explained by matrix densification and decreased diffusional routes, which restrict drug mobility within the polymer network.

3.4 Design Space

The multidimensional area of formulation variables where the intended product quality attributes are consistently attained is represented by the design space. In this work, contour plots for drug release responses at 12 minutes (Y_{12}) and 15 minutes (Y_1^1) were superimposed to create the design space using response surface methods. The optimal region for Naproxen fast-dissolving films was found at HPMC concentrations between 3.5 and 4% w/v and PVA values between 2.75 and 3% w/v[28]. The films demonstrated quick hydration, effective swelling, and quick breakdown within this range, which led to improved drug release within the intended time frame.

Table 3 : Optimized Design Space for FDFs Formulations

Drug	HPMC (X_1) Range	PVA (X_2) Range	Expected Drug Release Behaviour
Naproxen	3.5 – 4.0 mg	2.75 – 3.0 mg	Rapid drug release with quick film disintegration

Aceclofenac	4.75 – 5.0 mg	2.75 – 3.0 mg	Uniform and controlled drug release with good film integrity

To obtain the desired release profile, aceclofenac formulations, on the other hand, needed a comparatively higher HPMC content (4.75–5% w/v) while keeping a similar PVA range (2.75–3% w/v). This suggests that in order to guarantee consistent and regulated drug release, aceclofenac requires a relatively stronger and more cohesive polymeric matrix. Differences in drug–polymer interaction, solubility properties, and diffusion behavior within the wet matrix could be the cause of the increased polymer demand. The design space study further showed that balancing medication release and film integrity depends critically on polymer concentration. At ideal concentrations, HPMC facilitates drug diffusion by accelerating water absorption, swelling, and matrix degradation. On the other hand, excessive polymer causes increased matrix density and viscosity at higher concentrations, which may delay medication release.In a similar vein, PVA increases the strength and structural stability of films, but too much of it can also limit drug movement.
Naproxen was shown to have a relatively small design space, suggesting that drug release is more sensitive to slight changes in formulation parameters. Aceclofenac, on the other hand, showed a wider and slightly shifted design space, indicating increased robustness and better tolerance to formulation variability.

All things considered, the defined design space offers a variety of formulation variables that are optimized and supported by science, guaranteeing scalability, reproducibility, and consistent product performance. It also emphasizes how crucial it is to have polymer concentrations precisely balanced in order to produce fast-dissolving films with both desirable mechanical qualities and quick drug release.

3.5 Check Point Validation

The constructed polynomial regression models obtained by response surface methodology (RSM) were evaluated for prediction accuracy and reliability using checkpoint validation. Verifying that the mathematical models can correctly anticipate the experimental results within the specified design space is a crucial step.
From the optimal region found by contour and response surface analysis, checkpoint formulations were chosen. In order to ensure that validation was done within the experimental domain rather than at extreme values, these formulations included intermediate levels of HPMC (X_1) and PVA (X_2)[30].
For these checkpoint formulations, the percentage drug release at 12 minutes (Y_{12}) and 15 minutes (Y_{15}) was measured experimentally and compared with the corresponding values predicted by the regression equations.

With percentage error values less than 1% for both the naproxen and aceclofenac formulations, the results showed excellent agreement between anticipated and experimental values. Such a small deviation suggests Reliability of the polynomial equations for prediction, strong connection between expected and observed responses, and high accuracy of the constructed regression models. This strong agreement demonstrates that the models are both practically useful for formulation optimization and statistically significant.

Additionally, the low prediction error confirms that the model accurately captured the chosen independent variables (HPMC and PVA) and their interactions. Additionally, it verifies the robustness and reproducibility of the design space found using RSM.

Table 4 : Checkpoint Formulation for Validation of Design Space

Drug	HPMC (mg)	PVA (mg)	Predicted Y12 (%)	Experimental Y12 (%)	Predicted Y15 (%)	Experimental Y15 (%)	% Error
Naproxen	3.75	2.90	79.405	80.751	98.981	99.204	0.22
Aceclofenac	4.90	2.90	84.729	85.596	101.134	101.827	0.68

Overall, checkpoint validation effectively shows that the generated models have strong predictive power, which makes them appropriate for directing formulation development and guaranteeing fast-dissolving film performance.

3.6 Stability Analysis

In compliance with ICH guideline Q1A(R2), stability experiments of the optimized fast-dissolving film (FDF) formulations of naproxen and aceclofenac were carried out to assess their mechanical characteristics, drug release behavior, and physical integrity under accelerated storage circumstances.

For four weeks, the formulations were kept at 40 ± 2°C and 75 ± 5% relative humidity (RH). Samples were taken out at prearranged intervals and assessed for in-vitro drug release performance as well as important physicochemical characteristics such surface pH, folding endurance, and physical attractiveness[31].

Physical Stability Evaluation

The findings showed that there were no indications of discoloration, brittleness, or surface imperfections during the study period, and both Naproxen and Aceclofenac films maintained their homogeneity, smooth surface, and physical look. Over time, there was a minor decline in folding endurance, which may be explained by a little amount of moisture loss.

Table 5 : Stability Parameters of Optimized Naproxen FDFs under Accelerated Conditions

Quality Attribute	0 week	1st week	2nd week	3rd week	4th week
Surface pH	6.8 ± 0.1	6.8 ± 0.1	6.7 ± 0.2	6.7 ± 0.1	6.6 ± 0.2
Folding endurance	298 ± 5	295 ± 6	292 ± 5	289 ± 6	285 ± 7
Physical appearance	Uniform	Uniform	Uniform	Uniform	Uniform

Table 6 : Stability Parameters of Optimized Aceclofenac FDFs under Accelerated Conditions

Quality Attribute	0 week	1st week	2nd week	3rd week	4th week
Surface pH	6.7 ± 0.1	6.7 ± 0.2	6.6 ± 0.1	6.6 ± 0.2	6.5 ± 0.2
Folding endurance	285 ± 6	282 ± 5	279 ± 6	275 ± 7	270 ± 8
Physical appearance	Uniform	Uniform	Uniform	Uniform	Uniform

Polymer chains gradually rearranging, decreased impact of plasticization. Nonetheless, the values stayed within permissible bounds, suggesting that the films retained sufficient mechanical strength and flexibility. Surface pH also varied very little, staying around neutral, confirming the formulation's stability, Sustained harmony with the oral mucosa and Lack of pH changes brought on by deterioration.

Drug Release Stability

To evaluate any possible alterations in release behavior, the in-vitro drug release profiles of both formulations prior to and following storage were compared. After four weeks (Fig No – 2), there was a modest decrease in cumulative drug release, which could be caused by reduced polymer hydration efficiency, increased matrix density over time, or minor drug degradation.

In spite of this, the formulations continued to show quick drug release within 15 minutes, which is crucial for fast-dissolving films, and the overall release pattern stayed constant.

Table 7 : *In-vitro* release of the Naproxen from optimized check point formulation stored under accelerated stability condition

Time (min)	Cumulative amount (%)	
	0 week	**4th week**
3	12.755 ± 0.08	12.557 ± 0.08
6	38.003 ± 0.303	36.019 ± 0.303

Time (min)	Cumulative amount (%)	
	0 week	4th week
9	56.257 ± 0.413	54.272 ± 0.413
12	79.405 ± 0.198	77.421 ± 0.198
15	98.981 ± 0.115	96.997 ± 0.115
f2factor		62.402

Table 8 : *In-vitro* release of the Aceclofenac from optimized check point formulation stored under accelerated stability condition

Time (min)	Cumulative amount (%)	
	0 week	4th week
3	12.12 ± 0.106	11.882 ± 0.01
6	40.401 ± 1.062	36.853 ± 0.363
9	59.715 ± 1.023	57.679 ± 0.175
12	84.729 ± 0.605	82.461 ± 0.462
15	101.134 ± 0.462	94.212 ± 0.705
f2factor		55.765

Similarity Factor Analysis

To quantitatively compare the dissolution profiles before and after stability testing, the similarity factor (f_2) was calculated. For both Naproxen and Aceclofenac formulations, f_2 values were greater than 50 . This indicates that the release profiles are statistically similar According to regulatory criteria, an f_2 value between 50–100 confirms that there is no significant difference between two dissolution profiles.

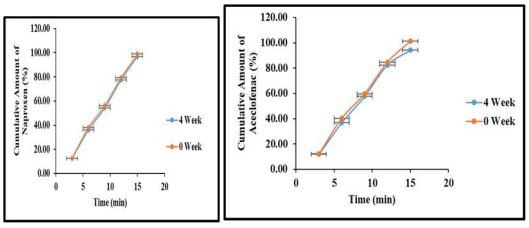


Figure 2 - *In-vitro* release of the Naproxen and Aceclofenac from optimized check point formulation stored under accelerated stability condition

he stability research verifies that all assessed physicochemical parameters were within acceptable bounds and that the optimized fast-dissolving film formulations maintained their physical stability under accelerated storage circumstances. The films maintained sufficient flexibility and structural integrity throughout time, as evidenced by the mechanical characteristics, such as folding endurance, which varied very little. Additionally, consistent dissolution profiles and similarity factor values indicate that the in-vitro drug release behavior was not considerably impacted during the study period. Overall, these results show that the created fast-dissolving films of Aceclofenac and Naproxen have good resilience and storage stability, making them good candidates for more research and possible commercialization.

3.7 Chemical Stability

In order to ascertain the drug's degradation behavior within the polymeric matrix, the chemical stability of the optimized fast-dissolving film formulations of naproxen and aceclofenac was assessed under accelerated storage circumstances. The study was carried out by tracking the percentage of medication that remained over time and employing suitable mathematical models to analyze the degradation kinetics.

The linear relationship between the logarithm of the proportion of medication remaining and time supported the findings, which showed that both formulations followed first-order degradation kinetics. This implies that, as is common for many pharmacological compounds, the rate of drug breakdown is concentration-dependent.

For all formulations, the computed correlation coefficient (R^2) values were found to be near unity, suggesting that the experimental data fit the first-order kinetic model quite well. This strong degree of connection attests to the degradation model's dependability in explaining the formulations' stability behavior. The intercept values were near the starting

drug content, further confirming the quality of the experimental data, and the slope values from the regression analysis were extremely low, indicating a modest rate of degradation. Furthermore, the measurements' accuracy and consistency are reflected in the small confidence intervals (UCI and LCI).

Table 9 : Chemical stability data of the developed NaproxenFDFs in check point formulation at accelerated stability condition

Time (week)	% Drug remaining (mean ± S.D.)	Log % drug remaining (mean ± S.D.)	95%	
			UCI	LCI
0	99.633 ± 0.379	1.998 ± 0.002	2.000	1.997
1	98.633 ± 0.379	1.994 ± 0.002	1.996	1.992
2	98.367 ± 0.252	1.993 ± 0.001	1.994	1.992
3	97.533 ± 0.153	1.989 ± 0.001	1.990	1.988
4	97.167 ± 0.058	1.988 ± 0	1.988	1.987
Slope	-0.0004	-0.0004	-0.0004	-0.0003
Intercept	99.47	1.9977	1.9998	1.9956
R^2	0.9689	0.9689	0.9835	0.9404

Table 10 : Chemical stability data of the developed Aceclofenac FDFs in check point formulation at accelerated stability condition

Time (week)	% Drug remaining (mean ± S.D.)	Log % drug remaining (mean ± S.D.)	95%	
			UCI	LCI
0	101.233 ± 0.058	2.005 ± 0	2.006	2.005
1	100.4 ± 0.3	2.002 ± 0.001	2.003	2.000
2	99.7 ± 0.173	1.999 ± 0.001	2.000	1.998
3	98.8 ± 0.1	1.995 ± 0	1.995	1.994
4	97.867 ± 0.058	1.991 ± 0	1.991	1.990
Slope	-0.0005	-0.0005	-0.0005	-0.0005
Intercept	101.27	2.0055	2.0064	2.0046
R^2	0.997	0.997	0.9887	0.992

Over the course of the storage period, a minor drop in drug content was noted; this might be explained by negligible degradation at accelerated settings. Nonetheless, the total drug content stayed within permissible bounds, suggesting that the medication was protected by the polymeric matrix.

Effective drug encapsulation inside the polymer network, less exposure to environmental elements including heat and moisture, and drug-excipient compatibility are all responsible for the formulations' durability.

3.8 Comparative Evaluation of Physicochemical and Mechanical Properties

Physicochemical Properties

The homogeneity and general quality of the fast-dissolving film formulations of naproxen and aceclofenac were evaluated by comparing their physicochemical properties. Both formulas showed

constant film development and exact control over the solvent casting process throughout all batches.

The homogeneous distribution of medication and excipients inside the polymeric matrix was confirmed by the low standard deviation values and minimal weight variation amongst films. This indicates that the formulation approach is reproducible and has acceptable content homogeneity.

Furthermore, there were no obvious flaws like air bubbles, cracks, or drug crystallization, and all films had a smooth and uniform surface morphology. By lowering intermolecular tensions inside the polymer matrix, PEG 400, a plasticizer, enhanced film flexibility and surface homogeneity. All things considered, these findings verify that the physicochemical properties of naproxen and aceclofenac films are suitable for oral film applications.

Mechanical Properties

Tensile strength and folding endurance, which are essential for handling, packaging, and patient usage, were used to assess the films' mechanical qualities. When compared to Naproxen films, aceclofenac films showed a somewhat higher tensile strength, suggesting better resistance to mechanical stress. This could be explained by both the comparatively larger polymer concentration utilized in these formulations and the stronger interactions between Aceclofenac and the polymer matrix.

Aceclofenac films also had greater folding endurance values, indicating better flexibility and resilience to repetitive mechanical deformation. Because of increased matrix density and polymer chain entanglement, higher polymer concentrations in both formulations led to improved mechanical strength. Despite these variations, all formulations demonstrated sufficient mechanical integrity and showed no signs of cracking or brittleness, demonstrating the efficacy of the chosen polymer-plasticizer system.

Surface pH and Drug Content

It was discovered that the surface pH of both naproxen and aceclofenac films was almost neutral, suggesting good compatibility with the oral mucosa and little chance of discomfort after administration. There was no discernible difference in pH between the various formulations, indicating that the excipients had no negative effect on the films' pH.

All formulations' medication contents were within permissible bounds, indicating consistent drug distribution throughout the films. The solvent casting method's dependability is further supported by its minimal variability. Improved drug trapping within a denser polymeric network may account for a small increase in drug content in higher polymer formulations.

According to the comparative analysis, the physicochemical and mechanical features of Naproxen and Aceclofenac fast-dissolving films are similar and satisfactory. Naproxen films likewise performed satisfactorily across all assessed metrics, however Aceclofenac films had somewhat better mechanical strength and flexibility. Overall, the findings support both film systems' viability for further development as fast-dissolving oral drug delivery platforms by confirming their good formulation, homogeneity, and reproducibility.

4. Conclusion

Using HPMC and PVA, the solvent casting process was effectively used to create fast-dissolving oral films containing naproxen and aceclofenac. The formulations showed quick drug release in less than 15 minutes, as well as acceptable physicochemical and mechanical characteristics. Checkpoint investigations further corroborated the statistical analysis's good model prediction and confirmation of HPMC's important function in regulating medication release. According to stability experiments, there were no appreciable alterations in the drug release behavior of the formulations under accelerated settings. All things considered, the produced films are strong, efficient, and appropriate for further development as quick-dissolving medication delivery systems.

5. Reference

1. Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm. 2008;70(3):895–900.
2. Dinge A, Nagarsenker M. Formulation and evaluation of fast dissolving films. Indian J Pharm Sci. 2008;70(4):544–547.
3. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: An innovative drug delivery system. Int J ChemTech Res. 2010;2(1):576–583.
4. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films: Innovations in formulation and technology. Int J Pharm Sci Rev Res. 2011;9(2):50–57.
5. Prashant Purohit, Mahesh Kumar Kataria. Phytochemicals screening, antioxidant and antimicrobial activity of *Carica Papaya* leaf

extracts. Int J Curr Pharm Sci. 2024 May 15; 16(3):95-98.
6. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Control Release. 2009;139(2):94–107.
7. Kunte S, Tandale P. Fast dissolving strips: A novel approach. Int J Pharm Bio Sci. 2010;1(2):1–13.
8. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Control Release. 2011;153(2):106–116.
9. Boateng JS, Auffret AD, Matthews KH, Humphrey MJ, Stevens HNE, Eccleston GM. Characterization of freeze-dried wafers. J Pharm Sci. 2010;99(6):2594–2606.
10. Bansal S, Garg A, Sharma PK. Fast dissolving films: A review. Int J Pharm Sci Rev Res. 2013;18(2):31–36.
11. Khan S, Boateng JS. Effect of polymer composition on films. Int J Pharm. 2012;436(1–2):105–111.
12. Preis M, Knop K, Breitkreutz J. Mechanical properties of orodispersible films. Int J Pharm. 2014;461(1–2):22–29.
13. Garsuch V, Breitkreutz J. Novel analytical methods for ODFs. J Pharm Biomed Anal. 2010;53(3):497–503.
14. Morales JO, McConville JT. Manufacture and characterization of mucoadhesive films. Drug Dev Ind Pharm. 2011;37(3):323–330.
15. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 6th ed. London: Pharmaceutical Press; 2009.
16. Banker GS. Film coating theory. In: Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. 3rd ed. 1987.
17. Peh KK, Wong CF. Polymeric films as drug delivery systems. Drug Dev Ind Pharm. 1999;25(11):1209–1218.
18. Kulkarni AS, Deokule HA, Mane MS, Ghadge DM. Exploration of different polymers. Int J Pharm Pharm Sci. 2010;2(3):33–35.
19. Rao NG, Chowdary KPR. Design and evaluation of mucoadhesive films. Indian J Pharm Sci. 2004;66(5):541–545.
20. Desai KG, Mallery SR, Schwendeman SP. Formulation of films. J Pharm Sci. 2011;100(10):4133–4144.
21. Tejaram, Rajesh Sharma, Prashant Purohit, Sanju, Kashi Ram, Formulation and Evaluation of Cefixime Loaded Grafted Gellan Gum Tablet, International Journal of Pharmacy and Biological Sciences (2023) 13 (3): 89-98
22. Prashant Purohit, Mahesh Kumar Kataria. Formulation and Evaluation of Polyherbal Ointment Using Carica Papaya and Leptadenia Pyrotechnica International Journal of Current Pharmaceutical Review and Research 2024; 16(5); 22-27
23. Singh B, Kumar R, Ahuja N. Optimizing drug delivery systems using RSM. Crit Rev Ther Drug Carrier Syst. 2005;22(1):27–105.
24. Ferreira SL, Bruns RE, Ferreira HS, et al. Box–Behnken design. Anal Chim Acta. 2007;597(2):179–186.
25. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13(2):123–133.
26. Sheikh SA, Purohit P, Teja Ram, Shrimali A. Concomitant Effect Of Present Herbal Formulation With Marketed Allopathic Formulation For The Evaluation Of Hair Growth. Int J Drug Deliv Technol. 2026;16 (40s): 133-136. DOI: 10.25258/ijddt.16.40s.14
27. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of drug release. Int J Pharm. 1983;15(1):25–35.
28. ICH Q1A(R2). Stability Testing of New Drug Substances and Products. Geneva: ICH; 2003.
29. Shah VP, Tsong Y, Sathe P, Liu JP. Dissolution profile comparison using f2 factor. Pharm Res. 1998;15(6):889–896.
30. Sweetman SC. Martindale: The Complete Drug Reference. 36th ed. London: Pharmaceutical Press; 2009.
31. Tripathi KD. Essentials of Medical Pharmacology. 8th ed. New Delhi: Jaypee Brothers; 2019.