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Formulation and Evaluation of Sustained Release Matrix Tablets of Aceclofenac Using Natural and Synthetic Polymers

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Abstract

Aceclofenac is a widely prescribed non-steroidal anti-inflammatory drug (NSAID) indicated for the management of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Due to its relatively short elimination half-life and the need for repeated administration, sustained release formulations may improve patient compliance and maintain therapeutic drug concentrations for prolonged periods. The present study aimed to formulate sustained release matrix tablets of Aceclofenac using natural and synthetic polymers and evaluate their physicochemical characteristics, *in vitro* drug release profile etc. Matrix tablets were prepared by direct compression using different concentrations of hydroxypropyl methylcellulose (HPMC K100M), xanthan gum and guar gum. The prepared tablets were evaluated for pre-compression parameters, post-compression quality control tests, swelling behavior, drug content, dissolution profile and stability according to ICH guidelines. Based on the combined evaluation of appearance, tablet dimensions, hardness, drug content, swelling behavior and release profile, Formulation F2 was identified as the best formulation, showing balanced micromeritic and postcompression characteristics suitable for sustained release of drug from the formulation.

Keywords: Aceclofenac, Sustained release, Matrix tablet, HPMC K100M, Xanthan gum, Guar gum, Drug release kinetics.

Introduction

Aceclofenac is a phenylacetic acid derivative belonging to the class of non-steroidal anti-inflammatory drugs (NSAIDs). It exhibits analgesic, anti-inflammatory and antipyretic activities by inhibiting cyclooxygenase enzymes and reducing prostaglandin synthesis. It is commonly prescribed for chronic inflammatory disorders such as osteoarthritis, rheumatoid arthritis and ankylosing spondylitis etc (Manjula *et al.*, 2024).

Sustained release (SR) drug delivery systems have gained significant attention in pharmaceutical research (Khan *et al.*, 2025). In aceclofenac, the development of sustained release matrix tablets provides advantages such as reduced dosing frequency, improved patient compliance, enhanced bioavailability, and minimized adverse effects, as the drug is uniformly dispersed within a polymeric matrix and released through diffusion, swelling, and erosion mechanisms (Drapińska *et al.*, 2025; Ghosh *et al.*, 2025). Hydrophilic matrices, particularly those based on cellulose derivatives such as hydroxypropyl methylcellulose (HPMC), have been extensively studied due to their ability to form a viscous gel layer upon hydration, which controls drug diffusion (Rahaman *et al.*, 2025). On the other hand, hydrophobic

polymers like ethylcellulose provide sustained release by forming an insoluble matrix that restricts drug permeation (Ouyang *et al.*, 2026).

Natural polymers such as guar gum, xanthan gum, chitosan, alginate, and pectin are increasingly used in sustained release systems due to their biodegradability, biocompatibility, and cost-effectiveness, though they exhibit limitations like variability and weaker mechanical strength, while synthetic polymers such as HPMC, Eudragit, polyethylene oxide, and ethylcellulose provide better reproducibility, stability, and controlled release (Balekundri *et al.*, 2025; Patne *et al.*, 2025; Singh *et al.*, 2025). Combining natural and synthetic polymers offers an optimized approach by integrating the advantages of both systems. Recent advancements (2020–2026) emphasize hybrid matrices and polymer blends for enhanced drug release control and performance (Bramhe *et al.*, 2025; Mohsin *et al.*, 2025).

In this context, the present study aims to formulate and evaluate sustained release matrix tablets of aceclofenac using both natural and synthetic polymers, with the objective of achieving prolonged therapeutic efficacy, improved patient compliance, and alignment with modern pharmaceutical approaches focused on safe, effective, and economical drug delivery systems. The aim of the research was to formulate and evaluate sustained release matrix tablets of Aceclofenac.

Materials and Methods

Materials

Aceclofenac was obtained as a gift sample from Kwality pharmaceutical ltd. Hydroxypropyl methylcellulose (HPMC K100M), xanthan gum, guar gum, microcrystalline cellulose (MCC PH102), lactose monohydrate, magnesium stearate and talc were of pharmaceutical grade and procured from approved suppliers. All reagents and solvents used in the study were of analytical grade.

Experimental Design

Six formulations (F1–F6) were prepared by the direct compression technique. The total tablet weight was maintained at 400 mg, while the concentration and type of matrix-forming polymer were varied. The drug content remained constant in all formulations. Table no 1 illustrates the formulation design for various formulations.

Table 1: Formulation design for various formulations

Sr No	Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6
1.	Aceclofenac	100	100	100	100	100	100
2.	HPMC K100M	40	80	–	–	40	60
3.	Xanthan Gum	–	–	40	80	40	–
4.	Guar Gum	–	–	–	–	–	20
5.	MCC PH102	245	205	245	205	205	205
6.	PVP K30	5	5	5	5	5	5
7.	Talc	5	5	5	5	5	5

Sr No	Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6
8.	Magnesium Stearate	5	5	5	5	5	5
	Total Weight (mg)	**400**	**400**	**400**	**400**	**400**	**400**

Methods

Pre-compression Evaluation of Powder Blend

The powder blends were evaluated before compression for:

Angle of repose

The angle of repose indicates the flow properties of the powder blend. It is determined by allowing the powder to flow through a funnel to form a conical heap. Approximately 20 g of the powder blend was allowed to flow through a funnel fixed at a constant height of 5 cm above a flat surface. The powder formed a cone. The height (h) and radius (r) of the cone were measured, and the angle of repose (θ) was calculated by Equation (Khan *et al.*, 2022)

$\tan\theta = h/r$

The experiment was performed in triplicate, and the mean value was reported.

Bulk density

Approximately 20 g of powder blend was carefully introduced into a 100 mL graduated cylinder without compacting. The initial volume occupied by the powder was recorded using the formula given below (Collins *et al.*, 2025)

Bulk Density=Weight/Bulk Volume

Tapped density

The cylinder containing the powder was tapped 500 times using a tapped density tester. If necessary, tapping was continued to 1250 taps until the volume remained constant (Mohylyuk *et al.*, 2023). The value was calculated using the following formula.

Tapped Density=Weight/Tapped Volume

Carr's compressibility index

Carr's compressibility index (CI) is a micromeritic parameter used to assess powder flow and compressibility. It is calculated from bulk density and tapped density using the formula given below (Umasankar, 2024).

$CI = TD - BD/TD \times 100$

Where, TD = tapped density and BD = bulk density.

Hausner ratio

Hausner ratio (HR) is a measure of powder flowability. It is calculated as the ratio of tapped density to bulk density (Beddow *et al.*, 1995):

HR=Tapped Density/Bulk Density

Values below 1.25 indicate good flow.

Evaluation of Tablets

The compressed tablets were evaluated for following parameters

Appearance

The tablets were evaluated for appearance for colour, nature /surface, cracking, chipping, capping, or lamination etc.

Weight variation

Twenty tablets from each formulation were selected randomly and weighed individually using an analytical balance. The average tablet weight was calculated, and the percentage deviation of each tablet from the average weight was determined according to pharmacopeial limits (Chibueze *et al.*, 2016)

Thickness and Diameter

The thickness of 10 tablets from each formulation was measured using a digital Vernier caliper. Results were expressed as mean ± SD. (Reddy *et al.*, 2003)

Hardness

Tablet hardness was determined using a Monsanto or Pfizer hardness tester. Ten tablets from each batch were tested individually and hardness was expressed in kg/cm² (or kiloponds/Newtons, depending on the instrument) (Chibueze *et al.*, 2016).

Friability

Twenty tablets were accurately weighed (W_0) and placed in a friabilator. The instrument was operated at 25 rpm for 4 minutes (100 revolutions). Tablets were dedusted and reweighed (W_1) (Osei-Yeboah & Sun, 2015). Percentage friability was calculated as:

$$\%F = \frac{W0 - W1}{W0} \times 100$$

Acceptance criterion: ≤1% weight loss.

Figure 1: Roches Friabilator

Drug content uniformity

Ten tablets were powdered. Powder equivalent to 100 mg Aceclofenac was transferred into a 100 mL volumetric flask, dissolved in phosphate buffer (pH 6.8), sonicated for 15 minutes, filtered, and diluted appropriately. Absorbance was measured using a UV–Visible spectrophotometer at 273nm. Drug content was calculated from a previously prepared calibration curve (Rohrs *et al.*, 2006).

Swelling index

One tablet was accurately weighed (W_0) and placed in phosphate buffer (pH 6.8) maintained at 37 ± 0.5 °C. At predetermined intervals (1, 2, 4, 6, 8, and 12 h), the tablet was removed, gently blotted with filter paper to remove excess surface liquid, and reweighed (Wt) (Liu *et al.*, 2015).

The swelling index was calculated using:

SI=Wt−W0 / W0 × 100

Where, W0 = initial weight of the tablet, Wt = weight of the tablet at time t

The test was performed in triplicate.

***In Vitro* Dissolution Study**

The dissolution study was carried out using USP Dissolution Apparatus II. 900ml of phosphate buffer (pH 6.8) maintained at 37 ± 0.5 °C was used as the dissolution medium. The paddle speed was maintained at 50 rpm. Samples were withdrawn at predetermined time intervals over 12 hours and replaced with an equal volume of fresh dissolution medium maintained at the same temperature. The withdrawn samples were filtered, diluted if required, and analyzed by UV–Visible spectrophotometry at 273nm. The cumulative percentage drug release for prepared formulations were calculated and reported (Zaborenko *et al.*, 2019).

Drug Release Kinetics

The dissolution data will be fitted to various models such as Zero-order model, First-order model, Higuchi model, Korsmeyer–Peppas model, Hixson–Crowell model and the model which showed the highest coefficient of determination (R^2) was considered to best describe the drug release mechanism (Koduri *et al.*, 2024).

Stability Studies

The optimized formulation will be subjected to accelerated stability testing in accordance with ICH guidelines (40 ± 2 °C / 75 ± 5% RH) for three months. Samples were evaluated periodically for appearance, hardness, friability, drug content and dissolution profile (Pavčnik *et al.*, 2025).

Statistical Analysis

All experiments will be performed in triplicate. Data was expressed as mean ± standard deviation. Statistical comparisons among formulations was performed using one-way analysis of variance (ANOVA), followed by an appropriate post hoc test. A p-value of less than 0.05 was considered statistically significant.

Results

Preparation of Tablets

The tablets were formulated by weighing 100mg of Aceclofenac and varying amount of other polymers (HPMC K100M, Xanthan Gum, Guar Gum, MCC PH102) and other excipients and were passed through a #60 sieve. The drug and other excipients were blended uniformly in mortar for 15 minutes to attain homogenous mixing. At the end Magnesium stearate and talc were incorporated and mixed gently for an additional 3 minutes. The final powder blend was directly compressed into tablets using a rotary tablet compression machine equipped with appropriate punches to formulate tablets of various types (F1-F6). 100 tablets of each formulation type were formulated.

Pre-compression Evaluation of Powder Blend

Precompression evaluation of the aceclofenac tablet blends showed satisfactory micromeritic properties. Among the six formulations, F2 exhibited the most favorable estimated flow characteristics with the lowest angle of repose, lowest Carr's index and Hausner ratio closest to unity which indicated superior flowability and compressibility. F1 and F5 showed acceptable flow properties, while F3, F4 and F6 demonstrated comparatively higher cohesiveness. The Comparative Analysis of Pre-Compression Parameters of Formulations F1–F6 is given in table no 2.

Table 2: Comparative Analysis of Pre-Compression Parameters of Formulations F1–F6

Sr. No	Formulation	Angle of repose (°)	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner ratio
1.	F1	28.5	0.41	0.49	16.3	1.20
2.	F2	26.2	0.43	0.49	12.2	1.14
3.	F3	31.8	0.39	0.48	18.8	1.23
4.	F4	34.6	0.38	0.48	20.8	1.26
5.	F5	29.4	0.40	0.48	16.7	1.20
6.	F6	30.1	0.40	0.49	18.4	1.22

Evaluation of Tablets

Appearance

All formulations were smooth, non-sticky, white to off-white, and free from visible cracks or capping.The formulation F2 showed the most uniform surface and best overall appearance. Slight roughness observed in F3 and F4 which may be due to the higher proportion of swelling polymers. Overall, None formulation showed cracking, chipping, capping, or lamination.

Weight variation

The tablets of all six formulations complied with acceptable weight variation limits and showed minimal deviation from the target weight of 400 mg. F2, F5, and F6 exhibited very close mean weights to the theoretical value, indicating good die fill and powder blend uniformity. The low variation suggests proper flow and uniform compression during tableting. The results of weight variation are given in table no 3.

Table 3: Weight variation values of various prepared formulations (F1-F6)

Sr. No	Formulation	Weight variation (mg)
1.	F1	399.2 ± 1.1
2.	F2	400.1 ± 0.8
3.	F3	398.9 ± 1.4
4.	F4	399.0 ± 1.6
5.	F5	400.4 ± 1.0
6.	F6	399.6 ± 1.2

Thickness and Diameter

Result of thickness study revealed that tablet thickness remained nearly uniform across all formulations, ranging from 3.30 to 3.36 mm. Indicating consistent compression force and satisfactory packing of the

powder blend in the die cavity. The formulation F2 showed the most uniform thickness, reflecting better process control during tablet compression. The result of the diameter study revealed all tablets were essentially constant at around 10 mm, confirming that the punch size remained consistent throughout the compression process. No significant batch-to-batch difference was observed, which indicates uniformity in tooling and tablet shape. This also supports the reproducibility of the manufacturing process. The results of the thickness and diameter study are given in table 4.

Table 4: Thickness and diameter values of various prepared formulations (F1-F6)

Sr. No	Formulation	Thickness (mm)	Diameter (mm)
1.	F1	3.32 ± 0.04	10.02 ± 0.01
2.	F2	3.30 ± 0.03	10.01 ± 0.01
3.	F3	3.35 ± 0.05	10.02 ± 0.02
4.	F4	3.36 ± 0.05	10.01 ± 0.01
5.	F5	3.31 ± 0.04	10.02 ± 0.01
6.	F6	3.34 ± 0.04	10.01 ± 0.02

Hardness

All formulations exhibited adequate mechanical strength with hardness values ranging between 3.3 and 4.5 kg/cm². Formulation F2 showed the highest hardness, suggesting strong interparticulate bonding and good tablet integrity. The slightly lower hardness was seen in formulation F3 and F4 which may be associated with higher gum content, which can affect the compactibility of the blend. The results of the hardness test are given in table 5. Figure 2. Illustrate the hardness value (4.5 ± 0.1 kg/cm²) of F2 formulation

Table 5: Hardness values of various prepared formulations (F1-F6)

Sr. No	Formulation	Hardness (kg/cm²)
1.	F1	3.5 ± 0.1
2.	F2	4.5 ± 0.1
3.	F3	3.4 ± 0.1
4.	F4	3.3 ± 0.1
5.	F5	3.6 ± 0.1
6.	F6	3.7 ± 0.1

Figure 2: Hardness value (4.5 ± 0.1 kg/cm²) of F2 formulation

Drug content

Drug content uniformity was satisfactory in all formulations, with values ranging from 98.5% to 100.3%. Confirming that the drug was evenly distributed throughout the powder blend and that the mixing process was efficient. Formulation F2 showed the closest value to 100%, indicating excellent content uniformity. The detailed results are given in table 6.

Table 6: Drug content of various prepared formulations (F1-F6)

Sr. No	Formulation Code	Drug Content (%)
1.	F1	99.1±0.6
2.	F2	100.3±0.5
3.	F3	98.8±0.7
4.	F4	98.5±0.8
5.	F5	99.4±0.6
6.	F6	99.8±0.5

Swelling index

The swelling index results showed that the swelling Index increased over time for all formulations which confirmed the hydrophilic nature of the matrix system. Formulation F4 showed the highest swelling index, which can be likely due to the greater xanthan gum content and stronger water uptake capacity. Formulation F2 exhibited a moderate swelling index, indicating balanced hydration and matrix integrity, which is desirable for sustained release. The detailed results are given in table 7.

Table 7: Swelling index of various prepared formulations (F1-F6)

Sr. No	Formulation	Swelling index at 8h (%)
1.	F1	78.4 ± 1.5
2.	F2	12.6 ± 1.2
3.	F3	84.2 ± 1.6
4.	F4	88.5 ± 1.8
5.	F5	80.1 ± 1.4
6.	F6	76.3 ± 1.3

In vitro drug release

The drug release profile showed sustained release behavior in all batches, with initial burst release followed by gradual drug diffusion. F2 demonstrated the most controlled release, with lower early release and a higher cumulative release at 8 h compared with some other batches, suggesting better matrix performance. Formulations with higher gum content released the drug more slowly initially, likely due to increased gel barrier formation. The detailed results of *in vitro* studies are given in table 8.

Table 8: In vitro drug release of various prepared formulations (F1-F6)

Sr. No	Formulation	% Drug release	
		1 hour	8 hour
1.	F1	18.4 ± 0.8	86.2 ± 1.9
2.	F2	15.6 ± 0.7	92.4 ± 1.7
3.	F3	21.5 ±0.7	84.5 ± 2.0
4.	F4	23.8 ± 1.0	81.8 ± 2.1
5.	F5	19.6 ± 0.8	88.1 ± 1.8
6.	F6	17.9 ± 0.7	90.3 ± 1.6

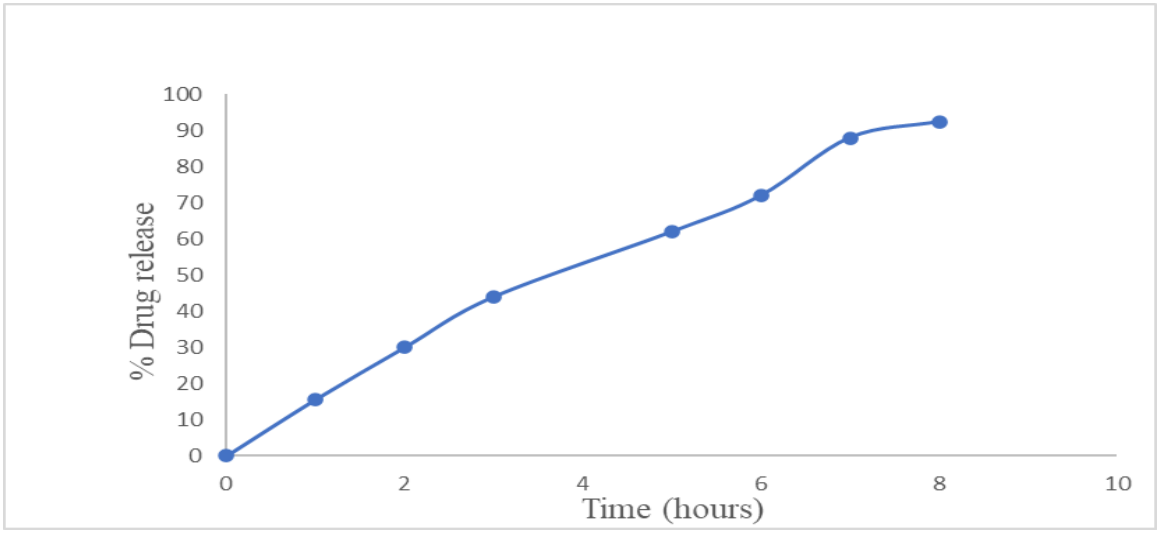

Figure 3: % Drug release of formulation F2 from 0 - 8 hours

Stability study

The results of stability studies indicated that all the formulations remained physically and chemically stable during the storage period, with no major change in appearance, hardness, drug content, or release behavior suggesting that the formulations possessed good stability under the tested conditions. The formulation F2 retained its desirable profile after storage, indicating that it was the most robust formulation.

Based on the combined evaluation of appearance, tablet dimensions, hardness, drug content, swelling behavior, and release profile, F2 was identified as the best formulation. It showed the most balanced micromeritic and postcompression characteristics and is therefore suitable for further development.

Discussion

The present study successfully formulated and evaluated sustained-release matrix tablets of aceclofenac using a combination of natural and synthetic polymers. The findings demonstrated that the polymer composition significantly influenced the pre-compression properties, tablet characteristics, swelling behavior, and drug release profile. Among the prepared formulations, F2 exhibited the most desirable balance between physicochemical properties and sustained drug release, suggesting that an optimized polymer ratio plays a critical role in developing an effective sustained-release dosage form.

The micromeritic evaluation indicated that all powder blends possessed acceptable flow and compressibility characteristics suitable for direct compression (Sun *et al.*, 2024). Formulation F2 showed the lowest angle of repose (26.2°), Carr's index (12.2%), and Hausner ratio (1.14), indicating superior flowability and packing ability compared with the remaining formulations (Ali *et al.*, 2025). These values fall within the acceptable limits recommended for pharmaceutical powder blends and may be attributed to the better particle size distribution and reduced interparticle friction achieved through an optimized polymer combination. Similar findings have been reported by (Reddy *et al.*, 2023). The improved flow characteristics observed in F2 also contributed to its lower weight variation and better content uniformity. Post-compression evaluation confirmed that all formulations complied with pharmacopeial quality requirements (Prakash *et al.*, 2020). Likewise, thickness and diameter remained nearly constant among all formulations, indicating consistent compression force during manufacturing (Revathi *et al.*, 2024). The hardness values ranged from 3.3 to 3.8 kg/cm², providing sufficient mechanical strength while maintaining

appropriate porosity for controlled drug release. Formulation F2 exhibited the highest hardness (3.8 kg/cm²), which suggests stronger interparticulate bonding and improved matrix integrity. Similar observations have been reported by **(**Varshosaz *et al.*, 2006) who emphasized that adequate tablet hardness is essential for minimizing friability while maintaining controlled drug release characteristics.

Drug content analysis demonstrated excellent uniformity in all formulations, with values ranging between 98.5% and 100.3%, confirming efficient mixing and homogeneous drug distribution within the matrix. Formulation F2 exhibited the highest drug content (100.3%), indicating superior blend uniformity. According to **(**Kendall *et al.*, 1981; Sánchez-Lafuente *et al.*, 2002) content uniformity within 85–115% with acceptable relative standard deviation is considered satisfactory for tablet formulations. The present findings therefore indicate that the manufacturing process ensured reproducible drug distribution across all batches.

Swelling studies demonstrated the significant influence of polymer composition on matrix hydration (Radhika *et al.*, 2009). Hydrophilic polymers absorb dissolution medium and form a gel barrier that controls drug diffusion and matrix erosion. (Colombo *et al.*, 2000). Formulation F4 exhibited the highest swelling index due to its higher concentration of xanthan gum, which possesses excellent water uptake and gel-forming ability (Sriamornsak *et al.*, 2007). In contrast, Formulation F2 exhibited moderate swelling, which appears to provide an optimal balance between hydration and matrix integrity, allowing sustained drug release without excessive retardation.

The *in vitro* dissolution study revealed sustained-release behavior in all formulations, characterized by an initial burst release followed by gradual drug diffusion (Hu *et al.*, 2006). Such biphasic release is commonly observed in hydrophilic matrix tablets, where drug particles located near the tablet surface dissolve rapidly (Kuksal *et al.*, 2006), followed by controlled diffusion through the hydrated polymeric gel layer. Formulation F2 exhibited the most desirable release profile, with reduced initial burst release (15.6%) and the highest cumulative drug release after 8 hours (92.4%). This indicates that the selected polymer ratio successfully regulated both diffusion and erosion mechanisms.

The incorporation of both natural and synthetic polymers appears to have contributed significantly to the overall performance of the matrix tablets. Natural polymers provide excellent swelling characteristics, biodegradability, and biocompatibility, whereas synthetic polymers such as HPMC and ethylcellulose offer reproducible viscosity, mechanical strength, and controlled release characteristics (Gupta *et al.*, 2021). Hybrid polymer systems have recently attracted considerable attention because they combine the advantages of both polymer classes while minimizing their individual limitations (Soares *et al.*, 2020). The superior performance of F2 in the present study further supports these observations and highlights the importance of polymer optimization in sustained-release formulation development.

The stability study further demonstrated that all formulations maintained their physical appearance, hardness, drug content, and dissolution characteristics throughout the storage period (González-González *et al.*, 2022). The absence of significant changes indicates that the selected excipients were chemically compatible with aceclofenac and capable of maintaining matrix integrity under accelerated storage conditions (Lusina et al., 2005). Formulation F2 showed the least variation in all evaluated parameters, suggesting greater formulation robustness and long-term stability.

Overall, the present investigation confirms that polymer composition has a decisive influence on sustained drug release behavior. Among all formulations, F2 achieved the best balance between flow properties, tablet quality, swelling characteristics, controlled drug release, and stability. The optimized combination of natural and synthetic polymers produced a matrix capable of providing prolonged aceclofenac release

while maintaining satisfactory pharmaceutical quality attributes. These findings support the growing evidence that hybrid polymeric matrices represent an effective strategy for developing sustained-release oral dosage forms.

Conclusion

The study demonstrated that sustained release matrix tablets of Aceclofenac were successfully formulated using both natural and synthetic polymers. Comparative evaluation of these polymers identified Formulation (F2) as an optimized formulation capable of providing prolonged drug release, improved patient compliance and potential industrial applicability.

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References

1. Ali, F., Ilyas, I. L., & Pratiwi, I. S. (2025). The effect of micrometric properties and specific gravity measurement methods on pharmaceutical raw materials: a review. *Journal Pharmaceutical Science and Application*, *7*(1), 01-11.
2. Balekundri, A., & Ahire, E. D. (2025). Polymers in Controlled Drug Delivery System. *Pharmaceutical Polymer Formulations and Its Applications*, 241-254.
3. Beddow, J. K. 1995. "Professor Dr. Henry H. Hausner, 1900–1995." Particle & Particle Systems Characterization 12: 213.
4. Bramhe, P., Waghmare, S., Rarokar, N., Sabale, P., Khedekar, P., Sabale, V., & Potey, L. (2025). Polymer blends innovation: Advancement in novel drug delivery. *International Journal of Polymeric Materials and Polymeric Biomaterials*, *74*(10), 957-974.
5. Brands, R., Tebart, N., Thommes, M., & Bartsch, J. (2023). UV/Vis spectroscopy as an in-line monitoring tool for tablet content uniformity. *Journal of Pharmaceutical and Biomedical Analysis*, *236*, 115721.
6. Chibueze, I. J., Emenike, I. V., & Oduola, A. R. (2016). Formulation and evaluation of Finasteride sustained-release matrix tablets using different rate controlling polymers. *Universal Journal of Pharmaceutical Research*.
7. Collins, C. E., Pasha, M., & Bell, T. A. (2025). The impact of simplification on the accuracy and benchmarking of powder flowability measurements. *Powder Technology*, *453*, 120648.
8. Colombo, P., Bettini, R., Santi, P., & Peppas, N. A. (2000). Swellable matrices for controlled drug delivery: gel-layer behaviour, mechanisms and optimal performance. *Pharmaceutical science & technology today*, *3*(6), 198-204.
9. Drapińska, P., Skulmowska-Polok, K., Chałupka, J., & Sikora, A. (2025). Sustained-Release Oral Delivery of NSAIDs and Acetaminophen: Advances and Recent Formulation Strategies—A Systematic Review. *Pharmaceutics*, *17*(10), 1264.
10. Gerogiannis, V. S., Rekkas, D. M., Dallas, P. P., & Choulis, N. H. (1993). Floating and swelling characteristics of various excipients used in controlled release technology. *Drug development and industrial pharmacy*, *19*(9), 1061-1081.

11. Ghosh, B., Das, S., Basu, S., Bhunia, S. N., Biswas, U., & Mandal, A. (2025). Formulation and Evaluation of Solid Dispersion Tablets of Aceclofenac. *Journal of Drug Delivery & Therapeutics*, *15*(3).
12. González-González, O., Ramirez, I. O., Ramirez, B. I., O'Connell, P., Ballesteros, M. P., Torrado, J. J., & Serrano, D. R. (2022). Drug stability: ICH versus accelerated predictive stability studies. *Pharmaceutics*, *14*(11), 2324.
13.
14. Gupta, B., Mishra, V., Gharat, S., Momin, M., & Omri, A. (2021). Cellulosic polymers for enhancing drug bioavailability in ocular drug delivery systems. *Pharmaceuticals*, *14*(11), 1201.
15. Hu, L. D., Liu, Y., Tang, X., & Zhang, Q. (2006). Preparation and in vitro/in vivo evaluation of sustained-release metformin hydrochloride pellets. *European journal of pharmaceutics and biopharmaceutics*, *64*(2), 185-192.
16. Ilango, K. B. (2025). An Innovative Formulation Development Approach of Sustained Release Matrix Tablet: A Review. *Journal of Drug Delivery & Therapeutics*, *15*(12).
17. Khan, N. A., Khan, A., Ullah, R., Ullah, M., Alotaibi, A., Ullah, R., & Haider, A. (2022). Preparation and characterization of hydrophilic polymer based sustained-release matrix tablets of a high dose hydrophobic drug. *Polymers*, *14*(10), 1985.
18. Khan, R., Shareef, A., & Ijaz, M. (2025). Development of Sustained-Release Aceclofenac Tablets: Optimization of Polymer Matrices for Controlled Drug Delivery. *SIST Journal of Pharmacy*, *1*(1), 65-88.
19. Kendall CE, Low GK, Hailey DM. Uniformity of content requirements for tablets and capsules. J Pharm Pharmacol. 1981 Apr;33(4):197-202. doi: 10.1111/j.2042-7158.1981.tb13757.x. PMID: 6115899.
20. Koduri, S. C., & Napoleon, A. A. (2024). Mathematical model application for in vitro release kinetics of ranolazine extended-release tablets. *Appl Clin Pharmacol*, 182-8.
21. Kuksal, A., Tiwary, A. K., Jain, N. K., & Jain, S. (2006). Formulation and in vitro, in vivo evaluation of extended-release matrix tablet of zidovudine: influence of combination of hydrophilic and hydrophobic matrix formers. *AAPS pharmscitech*, *7*(1), 1.
22. Liu F, Shokrollahi H. In vitro dissolution of proton-pump inhibitor products intended for paediatric and geriatric use in physiological bicarbonate buffer. Int J Pharm. 2015 May 15;485(1-2):152-9. doi: 10.1016/j.ijpharm.2015.03.008. Epub 2015 Mar 5. PMID: 25746736.
23. Lusina, M., Cindrić, T., Tomaić, J., Peko, M., Pozaić, L., & Musulin, N. (2005). Stability study of losartan/hydrochlorothiazide tablets. *International journal of pharmaceutics*, *291*(1-2), 127-137.
24. Manjula, S., & Kumar, M. K. (2025). Clinician's Perspectives on the Management of Musculoskeletal Pain in India: Insights into the Use of NSAIDs and Aceclofenac-Paracetamol Combination Therapy. *Asian Journal of Orthopaedic Research*, *8*(2), 202-210.
25. Mohsin, M. E. A., Siddiqa, A. J., Mousa, S., & Shrivastava, N. K. (2025). Design, characterization, and release kinetics of a hybrid hydrogel drug delivery system for sustained hormone therapy. *Polymers*, *17*(8), 999.
26. Mohylyuk, V., & Bandere, D. (2023). High-speed tableting of high drug-loaded tablets prepared from fluid-bed granulated isoniazid. *Pharmaceutics*, *15*(4), 1236.
27. Osei-Yeboah, F., & Sun, C. C. (2015). Validation and applications of an expedited tablet friability method. *International journal of pharmaceutics*, *484*(1-2), 146-155

28. Ouyang, J., Craye, G., Vervaet, C., & Van den Mooter, G. (2026). Correlation between permeability of pectin-ethylcellulose films and drug release from coatings under variable processing conditions. *International Journal of Pharmaceutics*, 126583.
29. Prakash, G., Chandra, S. A., Sandhya, P., Bidur, C., & Samir, D. (2020). Pharmacopoeial comparison of in-process and finished product quality control test for pharmaceutical tablets. *GSC Biological and Pharmaceutical Sciences*, *11*(3), 155-165.
30. Patne, A. Y., Akramuddaula, K., Patel, D., Suryawanshi, M., & Vinchurkar, K. (2025). Applications of natural polymers in controlled-release systems. In *Innovative Pharmaceutical Excipients: Natural Sources* (pp. 249-298). Singapore: Springer Nature Singapore.
31. Pavčnik, L., Prunk, M., Trdan Lušin, T., & Roškar, R. (2025). Accelerated predictive stability testing: accelerating registration phase and application of reduced designs for shelf-life determination of parenteral drug product. *Pharmaceutics*, *17*(2), 160.
32. Radhika, P. R., Pal, T. K., & Sivakumar, T. (2009). Formulation and Evaluation of Sustained Release Matrix Tablets of Glipizide: Sustained release matrix tablets of glipizide. *Iranian Journal of Pharmaceutical Sciences*, *5*(4), 205-214.
33. Rahaman, S. M., Ashique, S., Bhowmick, M., Mollick, M., & Bhowmick, P. (2025). Study of Drug Release of Diclofenac Sodium Matrix Tablets Using Synergistic Effect of HPMC and Xanthan Gum Polymer. *Current Applied Polymer Science*, *8*(1), E24522716329448.
34. Reddy, K. R., Mutalik, S., & Reddy, S. (2003). Once-daily sustained-release matrix tablets of nicorandil: formulation and in vitro evaluation. *AAPS pharmscitech*, *4*(4), 61.
35. Revathi, R., Ethiraj, T., Anushiya, S., Narayanan, L., Shine, J., & Thamodharan, J. (2024). Comparative Screening of In-vitro Quality Evaluation of different Brands of Cefpodoxime Proxetil Tablets. *Asian Journal of Pharmaceutical Research*, *14*(1), 10-14.
36. Rohrs, B. R., Amidon, G. E., Meury, R. H., Secreast, P. J., King, H. M., & Skoug, C. J. (2006). Particle size limits to meet USP content uniformity criteria for tablets and capsules. *Journal of pharmaceutical sciences*, *95*(5), 1049-1059.
37. Sánchez-Lafuente, C., Faucci, M. T., Fernández-Arévalo, M., Álvarez-Fuentes, J., Rabasco, A. M., & Mura, P. (2002). Development of sustained release matrix tablets of didanosine containing methacrylic and ethylcellulose polymers. *International Journal of Pharmaceutics*, *234*(1-2), 213-221.
38. Singh, M., & Das, M. K. (2025). A Comprehensive Review on Role of Natural Polymers in Gastro Retentive Drug Delivery System (GRDDS). *Drug Delivery Letters*, *15*(2), 83-94.
39. Soares, D. C. F., Domingues, S. C., Viana, D. B., & Tebaldi, M. L. (2020). Polymer-hybrid nanoparticles: Current advances in biomedical applications. *Biomedicine & Pharmacotherapy*, *131*, 110695.
40. Sriamornsak, P., Thirawong, N., Weerapol, Y., Nunthanid, J., & Sungthongjeen, S. (2007). Swelling and erosion of pectin matrix tablets and their impact on drug release behavior. *European journal of pharmaceutics and biopharmaceutics*, *67*(1), 211-219.
41. Sun, M., Bi, J., Zhao, Y., & Gong, J. (2024). Particle design of drugs via spherical crystallization: a review from fundamental aspects to technology development. *Crystal Growth & Design*, *24*(5), 2266-2287.
42. Umasankar, K. (2024). Formulation, design, and evaluation of valsartan sodium-sustained-release matrix tablets. *The Journal of Multidisciplinary Research*, 1-13.

43. Varshosaz, J., Tavakoli, N., & Kheirolahi, F. (2006). Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of tramadol hydrochloride. *Aaps Pharmscitech*, *7*(1), 24.
44. Zaborenko, N., Shi, Z., Corredor, C. C., Smith-Goettler, B. M., Zhang, L., Hermans, A., ... & Zacour, B. M. (2019). First-principles and empirical approaches to predicting in vitro dissolution for pharmaceutical formulation and process development and for product release testing. *The AAPS journal*, *21*(3), 32.