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Research Paper

Development, Optimization and Comparative Evaluation of Diclofenac Sodium Sustained Release Matrix Tablets Using Polymers

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ABSTRACT

The present study was aimed at the formulation and evaluation of sustained release matrix tablets of Diclofenac Sodium using different hydrophilic and hydrophobic polymers to achieve prolonged drug release, improve therapeutic efficacy, and enhance patient compliance. Diclofenac Sodium, a widely used non-steroidal anti-inflammatory drug (NSAID), possesses a short biological half-life and requires frequent administration, which may lead to poor patient adherence and gastrointestinal side effects. To overcome these limitations, sustained release matrix tablets were prepared using various grades of Hydroxypropyl Methylcellulose (HPMC K4M, HPMC K15M, and HPMC K100M) along with Ethylcellulose as release-retarding polymers. The tablets were formulated by wet granulation technique and evaluated for pre-compression and post-compression parameters including angle of repose, bulk density, tapped density, hardness, friability, weight variation, thickness, and drug content uniformity. Drug-excipient compatibility studies were carried out using FTIR and DSC analyses, which confirmed the absence of significant interactions between the drug and excipients. In-vitro dissolution studies were performed using USP type II paddle apparatus in phosphate buffer pH 6.8 for 12 hours. Among all formulations, batch F4 containing HPMC K15M and Ethylcellulose exhibited the most desirable sustained release profile with 92% drug release over 12 hours, acceptable mechanical strength, and minimal burst release. Release kinetics studies indicated that the optimized formulation followed near zero-order kinetics, demonstrating controlled and concentration-independent drug release. Comparative dissolution studies with marketed formulation (Voveran SR) revealed similar release behavior. The study concluded that the developed sustained release matrix tablet of Diclofenac Sodium can serve as a promising alternative to conventional dosage forms for prolonged therapeutic action and improved patient compliance

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INTRODUCTION

The kinetics of Drug release is divided into three parts: immediate release (IR), modified release (MR), and specialized forms **(1)**. IR tablets breakdown quickly (within 15-30 minutes), delivering the complete dose for immediate absorption-ideal for acute situations but prone to plasma peaks. MR tablets, which include Sustained Release (SR) **(2)**, Controlled Release (CR), and Extended Release (ER), regulate release to improve bioavailability, reduce dose frequency, and reduce side effects such as gastrointestinal. Among the most common and adaptable solid unit dosage form used in pharmaceutical sciences are Tablets, consisting of powdered medicinal ingredients and excipients crushed into compact, discoid shapes for oral administration. Manufacturing Methods **(3)**.

a. Direct compression: Pre-blended granules compressed directly into tablets, making the process very fast, simple and cost-effective. Direct compression is a tablet manufacturing method where active pharmaceutical ingredients (API) and excipients are blended and compressed directly into tablets without granulation steps **(4)**. Process Steps includes:

I. API blended with fillers (e.g., lactose, microcrystalline cellulose) for uniformity of tablets.

II. Then add lubricants or glidant (e.g., magnesium stearate) and disintegrates.

III. Finally compress the granules using rotary presses with induced die feeders to aid powder flow and reduce air entrapment.

Advantages

- ❖ Fewer unit operations, no moisture/heat, cutting time and costs.
- ❖ Faster dissolution and better stability than wet granulation.
- ❖ Ideal for heat-sensitive drugs and SR matrices like HPMC-based systems **(5)**.

Limitations

- ❖ High-dose APIs may segregate; low-dose needs uniform blending. Requires flowable excipients

b. Wet granulation: It is a tablet manufacturing process that help to improves the powder flow, compressibility, and content uniformity by forming granules with a liquid binder before compression **(6)**. The Process are as follows-

- ❖ Mix API or excipients, for preparing binder solution (e.g., PVP in water).
- ❖ Form wet mass by adding binder; screen the granules using sieve.
- ❖ Dry the granules in oven or fluidized bed dryer, resize the granules, then lubricate them before tableting.

Advantages

- ❖ Better for poor-flow APIs; enhances density and reduces segregation in SR matrices **(7)**.

Limitations

- ❖ Introduces moisture/heat risks; more steps increase time/cost compared to DC.

c. Dry granulation: It is also called slugging or roller compaction, is a tablet manufacturing technique that densifies powder blends into granules without liquids or heat, ideal for moisture/heat-sensitive APIs like those in SR matrices **(8)**. Process Steps

- ❖ Blend API or excipients, and add some amount of lubricant for flow of powders.
- ❖ Compact via slugging (press into large slugs) or roller compaction (rollers form ribbons).
- ❖ Mill/size slugs/ribbons, add remaining lubricant or disintegrates, then compress into tablets.

Advantages

- ❖ No moisture avoids hydrolysis; fewer steps than wet but more than direct compression;

good for poor-flow powders in SR formulations.

Limitations

- ❖ Requires cohesive materials; potential over-compression fines; less uniform than wet for some APIs

TYPES OF TABLET ON THE BASIS OF RELEASE PROFILE

I. **Immediate Release (IR)** Disintegration + dissolution Rapid onset; full dose in 30-60 min **(9)**.

II. **Sustained Release (SR)** Prolonged release over 4-8 hours Reduces peaks/troughs, improves compliance Matrix tablets for NSAIDs; maintains steady analgesia **(10)**.

III. **Controlled Release (CR)** Zero-order kinetics; predictable rate Constant plasma levels; diffusion or erosion-based, ideal for chronic therapy **(11)**.

IV. **Extended Release (ER)** Provides prolonged drug release for 8-24 hours, allowing once- or twice-daily dosing. This improves patient convenience, enhances compliance, and maintains more stable therapeutic drug levels**. (12)**.

INTRODUCTION TO DRUG - DICLOFENAC SODIUM

1.1. Tablets in Pharmaceutical Dosage Forms

Pharmaceutical dose forms provide the safe, effective, and convenient delivery of medications. Tablets are among the most popular solid oral forms due to their precise dose, stability, cost-effectiveness, and patient acceptance (3). They are made up of powdered drugs and excipients compressed into a compact unit, making oral administration the preferred method due to its ease, large surface area in the gastrointestinal tract (GIT), and economic feasibility (13). Tablets mitigate the drawbacks of liquid forms, such as volatility and dosage mistakes, while also enabling modified-release patterns. This study focuses solely on tablet kinds, specifically sustained release, controlled release, and extended release versions.

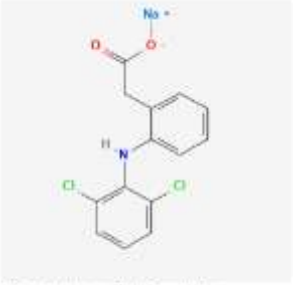


Figure 1. Structure of Diclofenac Sodium

IUPAC Name: sodium 2-[2-(2,6-dichloroanilino) phenyl] acetate (14)

Among the most frequently prescribed preparations because of their outstanding analgesic, and antipyretic effects. Between 1875 and 1940, only salicylic acid derivatives were used as non-steroidal anti-inflammatory drugs. The number of new drugs and the marketing of NSAIDs have dynamically increased in the past four decades. To-day more than 100 preparations are on the market or under clinical investigation.

Table no.1 Properties of Diclofenac Sodium (PubChem)

Molecular Weight	318.1 g/mol
Hydrogen Bond Donor Count	1
Hydrogen Bond Acceptor Count	3
Heavy Atom Count	20

1.2. Need for Sustained release tablet- Many drugs need to stay within a specific concentration range in the blood to be effective (15). A sustained-release design helps-

a. Avoid peaks (too high concentration → side effects)
b. Prevent troughs (too low concentration → loss of effect)

1.2.1. Reduced Dosing Frequency- Immediate-release drugs often require multiple doses per day. SR tablets allow:

- Once- or twice-daily dosing
- Better **patient convenience**
- Improved **medication compliance**

1.2.2. Lower Side Effects- By avoiding high peak drug levels, sustained release:

- Reduces **peak-related adverse effects**
- Decreases irritation at the site of absorption (e.g., stomach) (16)

1.3. Improved Patient Adherence- Simpler dosing schedules help patients stick to their treatment:

- Less frequent dosing
- Easier to remember
- Better long-term therapy outcomes

1.4. Targeted Therapeutic Action- Some drugs benefit from sustained action at a **specific site**, such as gut or systemic circulation, leading to:

- More consistent symptom control
- Better quality of life (e.g., pain relief, blood pressure control)

1.5. Objectives of oral Sustained- release matrix tablet

- To maintain a constant and therapeutically effective drug concentration in the body for a specified period of time.
- To reduce dosing frequency compared to conventional dosage forms, by improving patient compliance
- To deliver the drug directly to the site of action, which minimize exposure to non-target tissues and reducing side effects.
- This may necessitate targeting specific receptors or localization to specific cells or body regions.
- To enhance the safety margin of potent drugs by controlling their release and distribution
- To reduce the incidence of local and systemic adverse effects, especially in sensitive population of patient.

1.6. ADVANTAGES

- Reduced dosing frequency, leading to more convenient therapy.
- Minimization of Side effects by avoiding fluctuations in drug concentration.
- Drug release that is consistent and controlled over an extended period of time.
- Improved patient compliance due to simplified dosing schedules.

1.7. DISADVANTAGES

- It does not allow for a quick end to therapy
- Dose change versatility is restricted.
- The average biological half-life is used to design these dosage types.
- They are pricey.

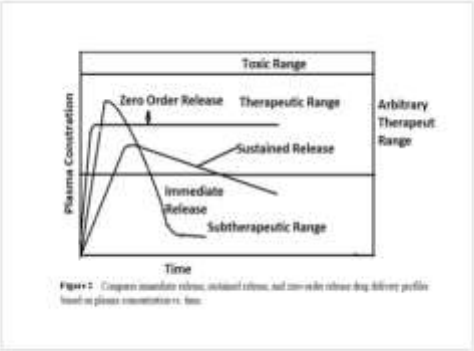


Table 2 Summary of Literature on Diclofenac Sodium sustained release formulations: Search engines used are as below:

Serial Number	Search engine	References
1	PubMed	https://pubmed.ncbi.nlm.nih.gov/
2	Scopus	https://www.scopus.com/sources.uri
3	Embase	https://www.elsevier.com/en-in/products/embase
4	Google Scholar	https://scholar.google.com/
5	Pharmacopoeias	https://iponline.ipc.gov.in/jspui/

MATERIALS AND METHODS

Diclofenac Sodium was obtained from CDH fine chemicals, HPMC grades K4M, K15M and K100M were received from Pavitra College of Pharmacy. Ethylcellulose was used as a hydrophobic Polymer. Microcrystalline cellulose (MCC, Avicel PH 102), was used as a diluent. Magnesium Stearate and talc were used as lubricant and glidant, respectively (23). All chemicals and reagents used were of analytical grade**.**

PHASE 2: PREFORMULATION STUDIES

Physicochemical Studies

Organoleptic Properties: Diclofenac Sodium was examined for its physical appearance, colour, odour, and taste.

Table 3 Organoleptic properties of Diclofenac sodium

Sl. No.	Parameter	Observation
1	Colour	White to slightly off white
2	Odour	Odourless
3	Appearance	Crystalline powder
4	Texture	Fine, free-flowing powder
5	Taste	Bitter

These observations were found to be consistent with standard pharmacopoeial specification**s.**

5.1. Melting Point: The melting point of Diclofenac Sodium was determined using the capillary tube method, the reported melting point range for Diclofenac Sodium is 275-290**°C** (24) and the **Observed melting point was found to be 285°C**. The sharp melting point indicates the purity and crystalline nature of the drug.

5.2. Solubility Studies: Solubility studies were carried out in different media to understand the drug's solubility behavior at physiological pH conditions.

Medium	Solubility
Distilled Water	Practically soluble
pH 1.2 buffer	Slightly soluble
pH 6.8 buffer	Sparingly soluble
pH 7.4 buffer	Freely soluble

The results confirm that Diclofenac Sodium exhibits pH-dependent solubility, which supports the need for sustained release formulation.

5.3. **Partition Coefficient**: The partition coefficient (log P) was determined using the n-octanol and water system. Log P value was found to be ~4.5. A high partition coefficient indicates the lipophilic nature of Diclofenac Sodium, which contributes to its prolonged biological half-life and suitability for sustained release dosage forms.

5.4. **Determination of λmax**: A solution of Diclofenac Sodium was scanned in the UV range (200-400 nm) using a UV-Visible spectrophotometer. The UV absorption spectrum of Diclofenac Sodium was recorded to determine the wavelength of maximum absorbance (λmax). A suitably diluted solution of Diclofenac Sodium was prepared using phosphate buffer pH 6.8 and scanned in the wavelength range of 200-400 nm using a UV-Visible spectrophotometer against the same buffer as blank. The UV spectrum showed a distinct and sharp absorption peak at 276 nm, which corresponds to the λmax of Diclofenac Sodium. This wavelength was selected for further quantitative estimation of the drug in calibration curve preparation, drug content analysis, and in vitro dissolution studies.

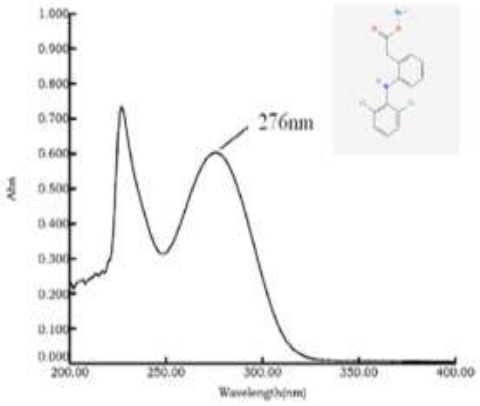


Figure 3 UV Spectra of Diclofenac Sodium

The sharp peak and absence of interference from the solvent indicate the suitability of the method for accurate drug estimation. λmax of Diclofenac Sodium: 276 nm

Compatibility Studies

5.5. **Compatibility studies** were carried out to evaluate the physicochemical interaction between **Diclofenac Sodium** and selected excipients in the formulation of sustained-release matrix tablets. Drug-excipient compatibility is essential to ensure formulation stability, efficacy, and safety throughout the product's shelf life. Preparation of Physical **Mixtures:** Physical mixtures of Diclofenac Sodium with individual excipients (HPMC K4M, HPMC K15M, HPMC K100M, Ethylcellulose, and MCC) were prepared in a **1:1 ratio** by gentle trituration to ensure uniform mixing. The mixtures were stored in airtight containers until analysis.

5.6. **Fourier Transform Infrared Spectroscopy (FTIR)** FTIR analysis was carried out over the spectral range of **4000–400 cm⁻¹** to investigate any potential chemical interactions between Diclofenac Sodium and the selected excipients, namely MCC, HPMC, and Ethylcellulose. The

study was conducted to assess the compatibility of the drug with formulation excipients. FTIR spectroscopy is widely used for:

- Identification of characteristic functional groups of the drug molecule
- Detection of possible drug-excipient interactions
- Evaluation of the chemical stability of the formulation components.

The FTIR spectrum of pure Diclofenac Sodium was recorded and compared with the spectra obtained from its physical mixtures with the selected excipients.

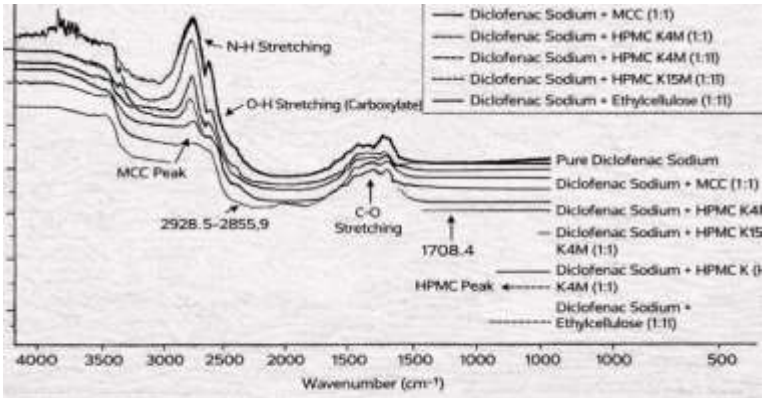


Figure 4 FTIR Spectra Of Diclofenac Sodium – excipients Mixture

The FTIR spectrum of pure Diclofenac Sodium showed characteristic absorption bands at:

- **~3323 cm⁻¹** → N–H / O-H stretching
- **2920–2850 cm⁻¹** → C-H stretching
- **~1708 cm⁻¹** → C=O stretching (carboxyl group)
- **1600–1500 cm⁻¹** → Aromatic C=C stretching
- **1200–1000 cm⁻¹** → C-O stretching

These peaks confirm the identity of Diclofenac Sodium.

FTIR of Drug-Excipient Mixture The physical mixtures of Diclofenac Sodium with:

- MCC
- HPMC K4M / K15M
- Ethylcellulose, were analyzed.

RESULT- It was observed that:

- All major characteristic peaks of Diclofenac Sodium were retained.
- No significant peak shift was observed.
- No disappearance of functional group peaks occurred.
- No additional new peaks were detected.

Minor variations in intensity were observed, which may be attributed to physical mixing and hydrogen bonding interactions, but not chemical interaction. The absence of:

- Significant peak shifting
- Peak broadening beyond normal range

- New peak formation, indicates that there is no chemical interaction between Diclofenac Sodium and the selected excipients. Thus, the excipients used are compatible with the drug.

5.7. Differential Scanning Calorimetry (DSC) was carried out to study the thermal behaviour of Diclofenac Sodium and to evaluate possible drug-excipient interactions. Accurately weighed samples (approximately 3-5 mg) of pure Diclofenac Sodium and drug-excipient physical mixtures (1:1 ratio) were placed in aluminum DSC pans and sealed. An empty sealed aluminum pan was used as a reference

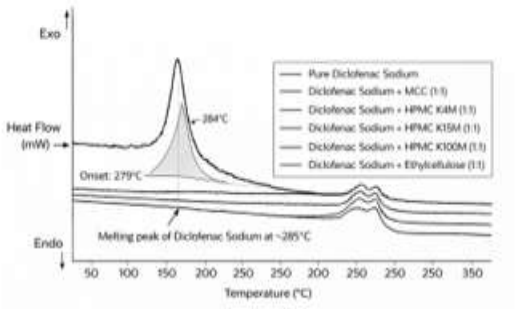


Figure 5 DSC Thermograms of Diclofenac Sodium and Excipient Mixture

The analysis was performed using a calibrated DSC instrument under a **nitrogen atmosphere** to avoid oxidative degradation. The samples were heated over a temperature range of **50-300 °C** at a constant heating rate of **10 °C/min** (25). The heat flow was recorded as a function of temperature, and the resulting thermograms were analyzed. The DSC thermograms of the physical mixtures were compared with that of pure Diclofenac Sodium to observe any changes in the melting endotherm, peak temperature, or peak shape. The presence or absence of peak shifting, disappearance, or formation of new peaks was used to assess drug-excipient compatibility.

Results- The DSC thermograms of pure Diclofenac Sodium exhibited a sharp and well-defined endothermic peak at approximately **284°C**, corresponding to its melting point. The sharp nature of the peak indicates the crystalline character and purity of the drug. The DSC thermograms of the physical mixtures (1:1) of Diclofenac Sodium with HPMC K4M, HPMC K15M, HPMC K100M, Ethylcellulose, and MCC showed the presence of the characteristic melting endotherm of the drug with slight reduction in peak intensity. The decrease in peak intensity can be attributed to the dilution effect of excipients in the physical mixtures. Importantly, no significant shift in the melting temperature, disappearance of the endothermic peak, or appearance of new peaks was observed in any of the thermograms. This indicates the absence of chemical interaction or incompatibility between Diclofenac Sodium and the selected excipients. Minor broadening of peaks observed in some mixtures may be due to physical mixing or overlapping thermal events of polymers; however, these changes were not significant enough to suggest interactio

FORMULATION DEVELOPMENT

Formulation Design Explanation: The drug content was kept constant at 100 mg in all formulations of Diclofenac sodium sustained release matrix tablet. Different grades of HPMC were used to study the effect of polymer viscosity on drug release profile.

- **HPMC K4M** (low viscosity) in F1-F3
- **HPMC K15M** (medium viscosity) in F4-F5
- **HPMC K100M** (high viscosity) in F6

Ethylcellulose was incorporated in selected two batches (F3-F5) to enhance matrix retardation and control drug release. MCC (Avicel PH 102) was used as diluent and filler to maintain constant tablet weight (300 mg). Magnesium stearate (1%) served as lubricant for the tablet. Talc acted as glidant to improve its flowability.

Table 4: Formulation of Diclofenac Sodium Sustain Released Matrix Tablet

Ingredients	F1	F2	F3	F4	F5	F6
Diclofenac Sodium	100	100	100	100	100	100
HPMC K4M	45	60	75	-	-	-
HPMC K15M	-	-	-	60	75	-
HPMC K100M	-	-	-	-	-	90
Ethylcellulose	-	-	15	15	15	-
MCC (Avicel PH 102)	142	127	97	112	97	97
Magnesium Stearate	3	3	3	3	3	3
Talc	10	10	10	10	10	10
Total Weight (mg)	**300**	**300**	**300**	**300**	**300**	**300**

5.0. Evaluation of Flow Properties (Pre-Compression Parameters) The flow properties of the powder blends were evaluated prior to compression to ensure uniform die filling and consistent tablet weight. The following parameters were determined:

6.0.1. Angle of Repose (θ) The angle of repose was determined by the fixed funnel method. The powder blend was allowed to flow through a funnel onto a flat surface to form a conical heap. The height (h) and radius (r) of the heap were measured, and the angle of repose was calculated.

$$\tan\theta = \frac{h}{r}$$

Sl. no	Angle of Repose (°)	Flow Property
1	< 25	Excellent
2	25–30	Good
3	30–40	Passable
4	> 40	Poor

6.0.2. Bulk Density and Tapped Density an accurately weighed quantity of powder blend was poured into a graduated measuring cylinder to measure **bulk volume**. The cylinder was then tapped mechanically until a constant volume was obtained to determine **tapped volume**.

$$\textbf{Bulk Density}(\rho b) = \frac{Mass}{Bulk\ volume}$$

$$\textbf{Tapped density}\ (\rho t) = \frac{Mass}{Tapped\ Volume}$$

6.0.3. Carr's Compressibility Index

Carr's Index was calculated from bulk and tapped densities to assess compressibility and flow.

$$\textbf{Carr's Index}(\%) = \frac{\rho t - \rho b}{\rho t} \times 100$$

6.0.4. Hausner's ratio is another indicator of powder flowability The Hausner ratio is calculated by dividing the tapped density of a

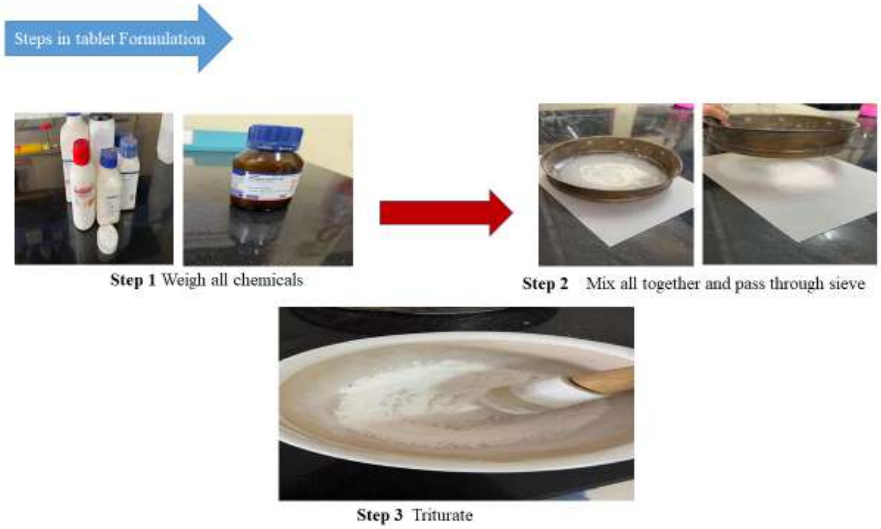
powder by its bulk density. It is a dimensionless metric used to assess the flowability of powders and granules, where a lower ratio typically indicates better flow, while higher values indicate increased cohesive behaviour.

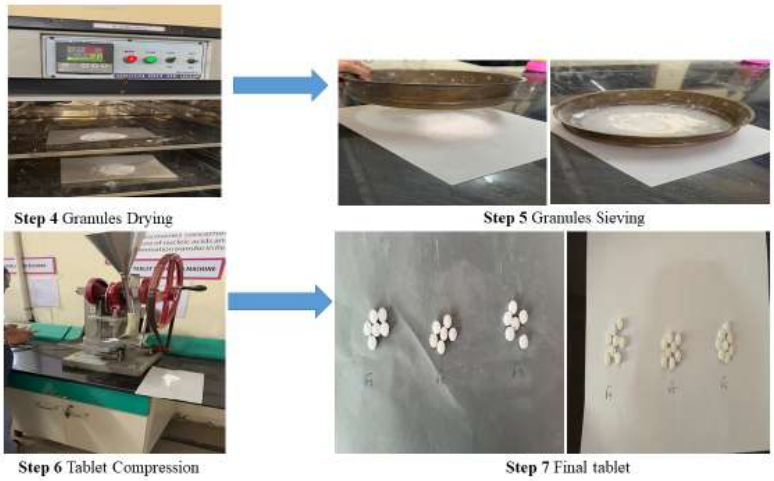
Table 5. Pre-Compression Flow Properties of Diclofenac Sodium Powder

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner's Ratio
F1	27.5	0.45	0.52	13.4	1.15
F2	26.8	0.46	0.53	13.2	1.15
F3	28.2	0.44	0.51	13.7	1.16
F4	27.1	0.47	0.54	12.9	1.14
F5	29.0	0.43	0.50	14.0	1.16
F6	28.5	0.45	0.52	13.5	1.21

Results & Discussion All powder blends exhibited good to fair flow properties, as indicated by angle of repose values below 35°, Carr's index below 20%, and Hausner's ratio less than 1.25. Slightly higher values observed in formulations containing higher viscosity HPMC may be attributed to increased cohesiveness of the polymer. Overall, the flow characteristics were found to be suitable for tablet preparation by the direct compression method.

WET GRANULATION Sustained-release matrix tablets of Diclofenac sodium were prepared by the wet granulation method. Accurately weighed quantities of drug, polymer, ethylcellulose, and MCC were passed through sieve 44 and blended uniformly. The powder blend was granulated using isopropyl alcohol containing PVP K30 as binder. The wet mass was passed through sieve 16 and dried at 45°C for 30-40 min until the granules dried. Dried granules were resized, lubricated with magnesium stearate and talc, and compressed into tablets of 300 mg using a rotary tablet compression machine.





6.1. Post-Compression Evaluation of Diclofenac Sodium Matrix Tablets (F1-F6)

After compression, all batches (F1-F6) were evaluated for official post-compression quality control parameters to ensure mechanical strength, uniformity, and performance of sustained-release tablets.

General Appearance Tablets were visually inspected for- Colour uniformity, Surface smoothness Absence of cracks, capping, lamination, or mottling**.** All batches were found to be circular, flat-faced, and free from visible defects.

I. Thickness

- ❖ Measured using a Vernier calliper
- ❖ Average of three tablets was recorded
- ❖ Uniform thickness indicates consistent die fill and compression force.

Table 6 Thickness of Diclofenac Sodium sustained release matrix tablet

Formulation	Thickness (mm) (Mean ± SD)
F1	3.42 ± 0.05
F2	3.48 ± 0.04
F3	3.50 ± 0.06
F4	3.46 ± 0.03
F5	3.52 ± 0.05
F6	3.58 ± 0.04

All tablets showed uniform thickness indicating consistent die filling and compression force.

II. Weight Variation Test

Twenty tablets from each batch were weighed individually and the average weight was calculated. Since tablet weight is 300 mg, the acceptable pharmacopoeial limit (IP/USP) is: ±5% deviation (for tablets ≥250 mg)

Table 7 Weight variation of Diclofenac Sodium sustained release matrix tablets

Formulation	Average weight (mg)	% Deviation	Result
F1	298 ± 2.1	0.67%	Pass
F2	301 ± 1.8	0.33%	Pass
F3	299 ± 2.5	0.34%	Pass
F4	300 ± 1.6	0.00%	Pass
F5	302 ± 2.0	0.66%	Pass
F6	297 ± 2.3	1.00%	Pass

All formulations complied with the specified limits.

III. Hardness (Crushing Strength)

- Determined using a Monsanto.
- Ideal range for matrix tablets: 5-8 kg/cm²

Table 8 Hardness of Diclofenac sodium sustained release matrix tablet

Formulation	Hardness (kg/cm²) (Mean ± SD)
F1	5.5 ± 0.2
F2	5.8 ± 0.3
F3	6.0 ± 0.2
F4	6.5 ± 0.3
F5	6.8 ± 0.2
F6	7.2 ± 0.3

Adequate hardness ensures mechanical stability without affecting drug release.

IV. FRIABILITY The friability test of all the batches of tablets were determined by using Roche friabilator at 25 rpm, 100 revolutions. Limit: < 1%

Table 9 Friability of Diclofenac sustained release matrix tablets

Formulation	Friability (%)	Result
F1	0.78	Pass
F2	0.72	Pass
F3	0.65	Pass
F4	0.58	Pass
F5	0.50	Pass
F6	0.42	Pass

V. Drug Content Uniformity is analyzed at λmax 276 nm using UV-Visible Spectrophotometer and the acceptable range is 95-105%

Table 10 Drug content Uniformity of Diclofenac Sodium sustained release matrix tablet

Formulation	Drug Content (%) (Mean ± SD
F1	97.2 ± 1.2
F2	98.4 ± 1.0
F3	99.1 ± 0.9
F4	100.3 ± 1.1
F5	101.4 ± 0.8
F6	98.9 ± 1.3

All formulations showed uniform drug distribution

In-Vitro Dissolution Study

- **Apparatus:** USP Type II (Paddle)
- **Dissolution medium**: 900 mL Phosphate buffer (pH 6.8)
- **Temperature:** 37 ± 0.5°C
- **Rotation speed:** 50 rpm
- **Sampling intervals:** 1, 2, 4, 6, 8, 10, and 12 hours
- **Marketed formulation for Comparison:** Voveran SR

The samples were filtered, diluted appropriately, and analyzed by spectrophotometer. The cumulative percentage drug release was calculated.

- K4M → faster release
- K15M → moderate
- K100M → slowest

Table 11. Drug release Profile of formulations (F1-F6). F1, F2, F3, F4, F5, F6 + Voveran SR

Time	F1	F2	F3	F4	F5	F6	Marketed formulation(comparison)
1hour	22	18	15	14	12	10	1
2 hour	35	30	26	24	22	18	2
4 hour	55	48	42	40	35	30	21
6 hour	70	63	58	54	50	45	43
8 hour	85	78	72	68	63	58	62

10 hour	95	90	85	82	78	72	78
12 hour	99	97	94	92	89	85	88

In SR matrix tablets, early sampling at 1-2 hour intervals is essential to monitor initial burst release, lag phase, early gel formation (e.g., HPMC swelling), and to confirm the tablet does not accidentally behave like an IR formulation. These rapid early changes require closer intervals to detect risks like dose dumping.

Later Phase Sampling- After 2 hours, the matrix stabilizes as the gel layer fully forms, making drug release diffusion-controlled with predictable, steady diffusion paths, so 2-hour intervals suffice.(26)

Core Release Mechanisms

- **Initial burst**: Quick surface drug dissolution, often mitigated by polymer coatings (27).
- **Gel layer role**: Swells to create a barrier, transitioning from hydration-driven to erosion/diffusion kinetics.
- **Stabilization benefit**: Ensures reliable monitoring post-initial phase without excessive sampling.

Based on Drug Release Profile at final time 12-hour release:

- F1 → 99% (shows too fast, almost like the immediate release)
- F2 → 97% (slightly fast as compared to others batches)
- F3 → 94%
- F4 → 92%
- F5 → 89%
- F6 → 85% (too slow → incomplete release)

Ideal SR tablet should release **approximately between 85-5% drug in 12 hours** to avoid burst release and should not release too slowly here the batch F4 shows - No burst effect only 14% at 1 hr, controlled gradual release and 92% at 12 hr (within ideal range). Therefore, F4 shows balanced release.

Based on Polymer Composition the F4 batch contains:

- HPMC K15M (60 mg) → medium viscosity
- Ethylcellulose (15 mg) → hydrophobic retardant
- K4M (low viscosity) → faster release
- K100M (high viscosity) → excessive retardation
- K15M → balanced gel formation

So, F4 provides Controlled gel, strength proper, swelling stable and diffusion barrier.

Based on Mechanical Properties the formulation F4 shows:

- Hardness: 6.5 kg/cm² (ideal for SR tablet)
- Friability: 0.58% (within limit)
- Drug content: 100.3% (excellent)

The thickness was uniform so; it is mechanically stable. F4 was selected based on its controlled and gradual drug release profile extending up to 12 hours (92%), absence of burst release, acceptable mechanical strength, uniform drug content, and balanced polymer composition. Compared to other formulations, F4 provided optimal sustained release without excessive retardation or rapid release, making it the most suitable formulation.

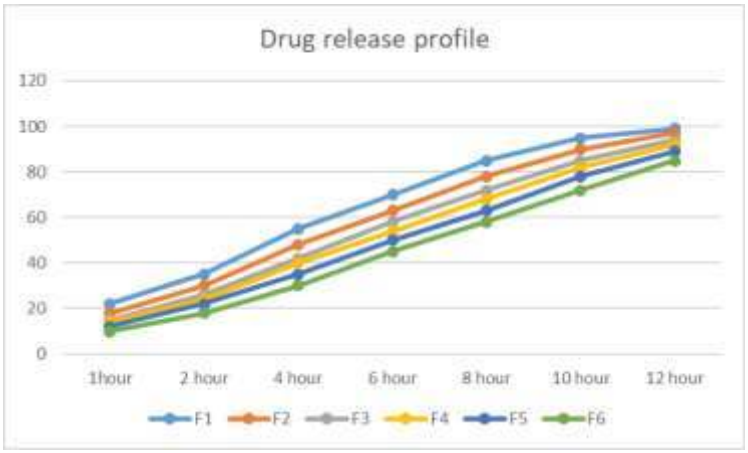


Figure 7: Drug release kinetics of formulations (F1-F6)

a. Zero-order kinetics calculation for F4

Zero-order equation:

$$Q_t = K_0 t + C$$

Where,

Q_t = % drug released at time t

K_0 = zero-order release constant

T = time (hr)

C = intercept

Zero- order slope

$$K_0 = \frac{N\sum XY - (\sum X)(\sum Y)}{N\sum X^2 - (\sum X^2)}$$

X (Time)	Y(%Release)	XY	X^2
1	14	14	1
2	24	48	4
4	40	160	16
6	54	324	36
8	68	544	64
10	82	820	100
12	92	1104	144

Table 12. Zero- order kinetics release of formulation F4

Where summations,

$\sum X = 43$, $\sum X = 374$, $\sum XY = 3014$, $\sum X^2 = 365$, N=7

= (7×3014) – (43×374)

= 5016

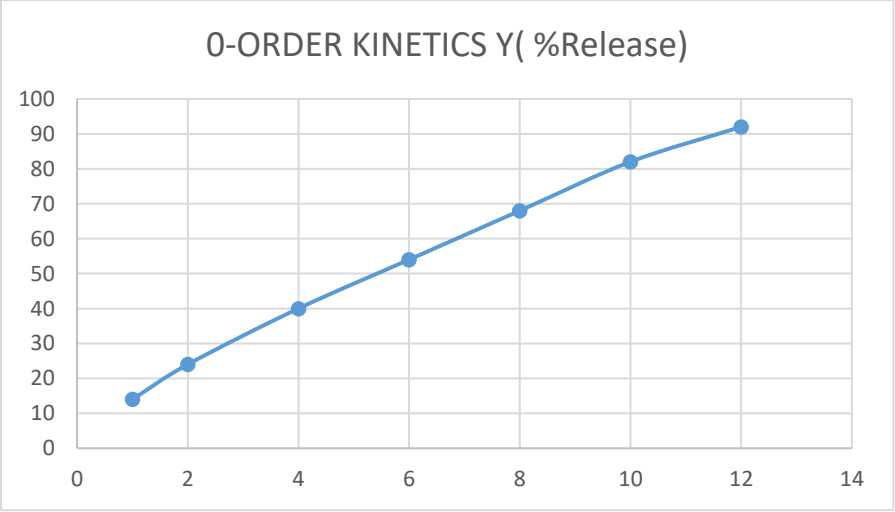


Figure 8 Zero-order kinetics of F4

b. First order kinetics for F4 formulation

$$\log(100-Qt)$$

Where, Qt = % drug released at time t

Table 13 First order kinetics release of formulation F4

Time (Hour)	% Drug Released (Qt)	% Drug Remaining (100−Qt)	log (100−Qt)
1	14	86	1.934
2	24	76	1.880
4	40	60	1.778
6	54	46	1.663
8	68	32	1.505
10	82	18	1.255
12	92	8	0.903

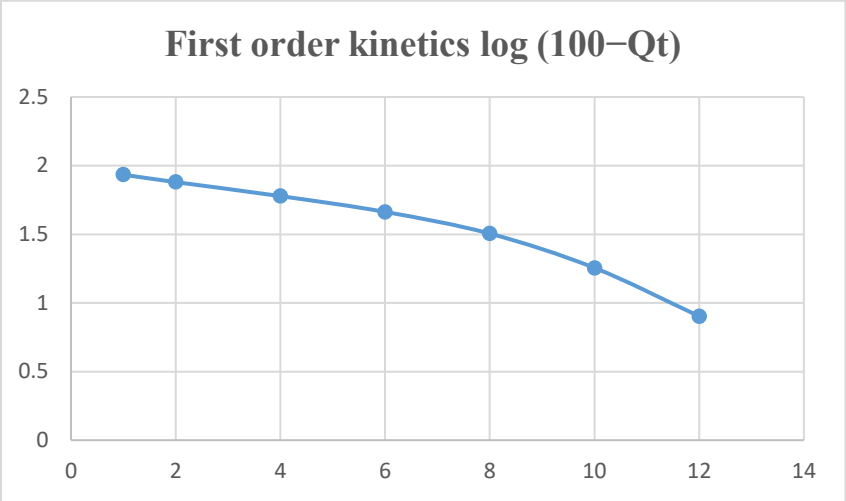


Figure 9 First- order Kinetics of F4

ANOVA-ONE WAY **Table**

14 Mean drug release and SD of Formulation (F1-F6)

Formulation	Mean drug release(%)	SD
F1	60.33	1.15
F2	54.50	1.15
F3	49.67	0.58
F4	47.00	1.00
F5	42.83	0.58
F6	38.50	1.15

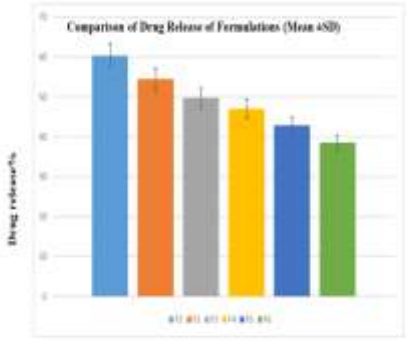


Figure 9: Comparison of drug release of formulations F1-F6 expressed as mean SD (n=3)

One-way ANOVA was employed to determine whether there were statistically significant differences in the drug release profiles among the developed formulations. The analysis indicated significant variation in cumulative percentage drug release across the formulations, suggesting that the formulation variables such as polymer concentration and matrix composition had a pronounced effect on dissolution behavior. The calculated p-value ($p < 0.05$) was found to be less than 0.05, which confirms that the differences in drug release among the formulations were statistically significant at the 95% confidence level. This implies that the observed variations in release pattern were not due to random experimental error but were associated with formulation design.

The statistical outcome supports the dissolution study results and demonstrates that optimization of formulation parameters was essential for achieving controlled and sustained drug release. Among all the formulations, the optimized batch exhibited the most desirable release characteristics, further validating the effectiveness of the formulation strategy adopted in this study.

COMPARATIVE DISSOLUTION STUDY WITH MARKETED PREPARATION

Commercially available sustained release Diclofenac Sodium tablet marketed under the brand name **Voveran SR 100** was selected as reference marketed formulation for comparative evaluation with the optimized laboratory formulations. Comparative dissolution analysis was performed in phosphate buffer pH 6.8 for 12 hours under identical USP type II conditions. Among all prepared batches, formulation F5 and F6 demonstrated dissolution profiles nearest to the marketed brand. F5 showed controlled initial hydration with gradual drug diffusion, whereas F6 exhibited maximum release retardation due to the presence of high viscosity HPMC K100M. The cumulative percentage drug release of Voveran SR 100 at 12 h was found to be approximately comparable with F5, indicating that the optimized formulation successfully mimics the release behavior of the commercial sustained release product. This comparative study confirms the industrial feasibility and market acceptability of the developed matrix tablet and suggests that formulation F5 may be considered as the optimized formulation due to its similarity with marketed sustained release Diclofenac preparation.

DISCUSSION

The present study was designed to develop and evaluate a controlled release formulation and to understand the drug release kinetics using *in-vitro* dissolution analysis. The formulation variables significantly influenced the release behavior, indicating that polymer concentration and matrix

structure play a critical role in modulating drug diffusion and dissolution rate. Among all six prepared formulations, F1 to F3 containing lower concentration HPMC K4M showed comparatively faster drug release due to weaker gel barrier formation. F5 containing HPMC K15M with Ethylcellulose demonstrated improved matrix integrity and prolonged release. Formulation F4 provided the most desirable sustained release pattern extending up to 12 hours with acceptable pre-compression and post-compression characteristics. Although F6 containing HPMC K100M exhibited highest retardation, the release was comparatively slower than the marketed requirement. Therefore, F4 was considered as the optimized batch showing best balance between sustained release, matrix stability and comparative dissolution similarity.

Kinetic modelling of the dissolution data revealed that the release pattern was best approximated by the zero-order kinetic model, indicating a nearly constant drug release rate independent of drug concentration. Comparison with the first-order model suggested that drug release was not primarily concentration dependent. Statistical evaluation using one-way ANOVA confirmed that the differences in drug release among formulations were statistically significant, highlighting the impact of formulation optimization on dissolution performance. Overall, the study successfully developed an optimized controlled release formulation with improved release characteristics. Although formulation F6 exhibited a slower drug release profile similar to the initial phase of the marketed formulation Voveran SR, it showed excessive retardation and incomplete drug release over the study period. In contrast, formulation F4 demonstrated a balanced and controlled drug release pattern, achieving complete release within 12 hours and closely resembling the overall release profile of the marketed product. Therefore, F4 was considered the optimized formulation. The findings suggest that appropriate selection and optimization of formulation components can effectively modulate drug release behavior, which may enhance therapeutic efficacy and potentially reduce dosing frequency. Further *in-vivo* studies and stability evaluation may be carried out to confirm the clinical applicability of the developed system.

CONCLUSION

Among all formulations, F4 was identified as the optimized formulation**.** The formulations were ranked as: **F4 > F5 > F3 > F2 > F1 > F6.** The optimized formulation F4 was compared with **Voveran SR** and showed similar release behavior. Thus, formulation F4 was selected as the optimized sustained release matrix tablet of diclofenac sodium due to its controlled drug release, absence of burst effect, and close resemblance to the marketed formulation. The developed sustained release matrix tablet of diclofenac sodium can be considered a promising alternative to conventional dosage forms for improved therapeutic efficacy and patient compliance.

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