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Research

Formulation and *In-Vitro* Evaluation of Celecoxib Sustained Release Tablets Using Hydrophilic and Hydrophobic Polymer Matrices

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Abstract:

Background: Celecoxib is a selective cyclooxygenase-2 (COX-2) inhibitor widely prescribed for management of osteoarthritis, rheumatoid arthritis, and acute pain. Its short biological half-life and poor aqueous solubility (BCS Class II) necessitate frequent dosing, which compromises patient compliance. **Objective:** This study aimed to formulate sustained-release (SR) tablets of celecoxib using hydrophilic (HPMC K4M, HPMC K15M, Carbopol 934P) and hydrophobic (ethyl cellulose) polymers by direct compression and evaluate them through comprehensive physicochemical and in vitro dissolution testing. **Methods:** Six formulations (F1–F6) were prepared at varying polymer concentrations. Pre- and post-compression parameters were assessed per Indian Pharmacopoeia (IP) and USP standards. Dissolution was studied in phosphate buffer pH 6.8 over 12 hours using USP Apparatus II. Release kinetics were modelled using zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. **Results:** All formulations exhibited acceptable hardness (7.8–8.5 kg/cm²), friability (<1%), and drug content (97.6–99.1%). Formulation F6 (Carbopol 934P) demonstrated optimum cumulative drug release of 75.4% at 12 hours with best kinetic fit to the Korsmeyer-Peppas model ($R^2 = 0.996$, $n = 0.728$), indicating non-Fickian anomalous diffusion. **Conclusion:** Celecoxib SR tablets with satisfactory physicochemical characteristics and sustained drug release suitable for twice-daily dosing were successfully formulated using Carbopol 934P as the matrix polymer.

Keywords: Carbopol 934P, Celecoxib, direct compression, HPMC K4M, HPMC K15M, in vitro dissolution, Korsmeyer-Peppas model, sustained release tablet

1. INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) constitute one of the most widely prescribed pharmacological categories globally, with billions of prescriptions dispensed annually for management of pain and inflammatory disorders.[1] Among this class, selective cyclooxygenase-2 (COX-2) inhibitors were developed to overcome the severe gastrointestinal adverse effects associated with conventional non-selective NSAIDs. Celecoxib (4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide), branded as Celebrex®, was the first selective COX-2 inhibitor approved by the United States Food and Drug Administration (USFDA) in December 1998, marking a significant milestone in anti-inflammatory pharmacotherapy.[2]

Celecoxib produces its anti-inflammatory, analgesic, and antipyretic effects primarily through selective inhibition of the COX-2 isoenzyme, thereby curtailing prostaglandin biosynthesis at sites of inflammation while sparing COX-1-dependent gastroprotective prostaglandins to a significant degree.[3] The drug is approved for osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, primary dysmenorrhea, and acute pain conditions. Physicochemically, celecoxib belongs to Biopharmaceutics Classification System (BCS) Class II – high permeability but poor aqueous solubility (3–7 µg/mL at 25°C) – which significantly limits its oral bioavailability and complicates formulation design.[4,5]

The currently marketed immediate-release formulation (200 mg capsules) necessitates twice-daily administration owing to the relatively short biological half-life of celecoxib (approximately 11.2 hours). Peak-to-trough plasma concentration fluctuations, marked inter-patient pharmacokinetic variability, and fasting bioavailability of only approximately 40% underscore the compelling rationale for developing an oral sustained-release (SR) formulation of celecoxib capable of maintaining therapeutic plasma levels over a 12-hour dosing interval.[6]

Sustained-release oral drug delivery systems offer several clinical and pharmaceutical advantages over conventional dosage forms: reduced dosing frequency, minimized systemic side effects from concentration peaks, improved patient adherence, and more consistent therapeutic outcomes – attributes of particular importance in chronic conditions such as arthritis that demand long-term pharmacotherapy.[7] Hydrophilic matrix tablets utilizing cellulose-based polymers such as hydroxypropyl methylcellulose (HPMC) have been extensively studied and are considered the gold standard platform for sustained drug release, functioning through a triphasic mechanism of surface hydration, gel layer formation, and progressive matrix erosion.[8]

HPMC, a semisynthetic cellulose derivative available in viscosity grades K4M, K15M, and K100M, is approved by the USFDA, listed in the Indian Pharmacopoeia (IP), and extensively employed in SR matrix formulations worldwide.[9] Carbopol 934P (cross-linked polyacrylic acid) forms a highly expanded gel network at intestinal pH due to ionization of carboxylic acid moieties, providing robust control of drug diffusion.[10] Ethyl cellulose (EC), a hydrophobic polymer insoluble in aqueous media, imparts pH-independent retardation of drug release and is particularly effective when used as a matrix-forming agent at appropriate concentrations.[11]

Although celecoxib has been the subject of various drug delivery investigations, a systematic and comparative evaluation of multiple hydrophilic and hydrophobic polymer matrices for SR tablet formulation under uniform experimental conditions, with rigorous kinetic modeling and stability assessment, is inadequately represented in the published literature.[12] The present study was therefore undertaken to design and evaluate celecoxib SR matrix tablets using six polymer combinations and to identify the optimum formulation based on pharmacopoeial physicochemical standards and in vitro drug release behavior.

2. MATERIALS AND METHODS

2.1 Materials

Celecoxib was received as a gift sample from Sun Pharmaceutical Industries Ltd., Vadodara, India. HPMC K4M and HPMC K15M were sourced from Signet Chemical Corporation Pvt. Ltd., Mumbai, India. Carbopol 934P was obtained from S.D. Fine Chemicals Ltd., Mumbai, India. Ethyl cellulose was procured from Loba Chemie Pvt. Ltd., Mumbai, India. Lactose monohydrate and microcrystalline cellulose PH-102 (MCC PH-102) were supplied by Qualikems Fine Chem Pvt. Ltd., Vadodara, India. Magnesium stearate and talc (pharmaceutical grade) were obtained from Merck Specialities Pvt. Ltd., Mumbai, India. All chemicals and reagents used were of analytical grade. Phosphate buffer pH 6.8 was freshly prepared in accordance with Indian Pharmacopoeia (IP 2022) specifications.[13]

2.2 Drug–Excipient Compatibility Study

Fourier-transform infrared (FTIR) spectroscopy was carried out using a PerkinElmer Spectrum Two FTIR spectrophotometer (PerkinElmer Inc., USA) in KBr disc method over the wavenumber range of 4000–400 cm^{-1}. Samples analyzed included pure celecoxib, individual excipients, and their binary physical mixtures prepared at a 1:1 w/w ratio. Characteristic absorption peaks were interpreted and compared with reference spectra reported in the IP 2022 and published literature.[14] Differential scanning

calorimetry (DSC) was performed using a DSC 214 Polyma instrument (NETZSCH Instruments, Germany) at a heating rate of 10°C/min under inert nitrogen atmosphere (flow rate 50 mL/min) over a temperature range of 30–300°C. The DSC thermograms of pure drug, individual excipients, and their physical mixtures were evaluated for any thermal events indicative of polymorphic transitions, eutectic formation, or incompatibility.[15]

2.3 Formulation Design

Six sustained-release matrix tablet formulations (F1–F6), each containing 200 mg celecoxib per tablet with a total tablet weight of 420 mg, were designed and prepared by direct compression method. Formulations F1 and F2 employed HPMC K4M at concentrations of 10% and 20% w/w, respectively; F3 and F4 utilized HPMC K15M at the same concentrations; F5 incorporated ethyl cellulose at 10% w/w; and F6 contained Carbopol 934P at approximately 7.1% w/w (30 mg per tablet). The complete composition is detailed in Table 1. All excipients were individually weighed, passed through sieve No. 40 (425 µm), geometrically blended with celecoxib in a double-cone blender for 20 minutes, and lubricated with magnesium stearate and talc for the final 3 minutes before compression.

Table 1: Composition of Celecoxib Sustained Release Matrix Tablet Formulations (F1–F6) per Tablet (mg)

Ingredients (mg)	F1	F2	F3	F4	F5	F6	Role
Celecoxib	200	200	200	200	200	200	Active drug
HPMC K4M	30	60	--	--	--	--	Matrix polymer
HPMC K15M	--	--	30	60	--	--	Matrix polymer
Ethyl Cellulose	--	--	--	--	30	--	Release retardant
Carbopol 934P	--	--	--	--	--	30	Gel-forming polymer
Lactose monohydrate	100	70	100	70	100	100	Diluent
MCC PH-102	80	80	80	80	80	80	Binder/Disintegrant
Mg Stearate	4	4	4	4	4	4	Lubricant
Talc	6	6	6	6	6	6	Glidant
Total weight	420	420	420	420	420	420	--

2.4 Evaluation of Pre-compression Parameters

The blended powder mixture of each formulation was evaluated for bulk density and tapped density (measured using a bulk density apparatus, Electrolab India Pvt. Ltd., Mumbai), from which Carr's compressibility index and Hausner's ratio were derived. The angle of repose was determined by the fixed funnel method. Loss on drying was assessed using an infrared moisture balance. All parameters were interpreted using pharmacopoeial acceptance criteria – Carr's index ≤15% and Hausner's ratio ≤1.18 for good flow; angle of repose ≤30° for excellent flow.[16,17]

2.5 Tablet Compression

Tablets were compressed on a 10-station rotary tablet compression machine (Cadmach Machinery Co. Pvt. Ltd., Ahmedabad, India) fitted with standard circular, flat-faced punches of 13 mm diameter. Compression force was optimized to yield a target hardness of 7.5–8.5 kg/cm². A minimum of three independent batches per formulation were compressed to confirm reproducibility of the process.

2.6 Post-compression Physicochemical Evaluation

Post-compression evaluation was conducted for all six formulations as follows. Weight variation was determined for 20 tablets per batch using an electronic analytical balance (Shimadzu AUX220, Japan) and compared against IP 2022 limits (±5% of mean for tablets >250 mg). Tablet hardness was measured using a Monsanto hardness tester (n=6). Tablet thickness was recorded using a digital Vernier caliper (n=6). Friability was assessed in a Roche friabilator (Veego Instruments Corp., Mumbai, India) at 100 rpm for 4 minutes using 20 pre-weighed tablets; percentage weight loss was calculated and compared against the IP limit of ≤1%. Disintegration time was measured using a USP basket-type disintegration apparatus (Electrolab ED-2L, India) in phosphate buffer pH 6.8 at 37±2°C. Drug content uniformity was determined by

dissolving 10 randomly selected tablets in methanol, filtering through Whatman filter paper No. 1, and measuring absorbance of appropriately diluted solutions at 252 nm using a UV-Vis double-beam spectrophotometer (Shimadzu UV-1800, Japan). Swelling index and water absorption ratio were calculated gravimetrically after immersing pre-weighed tablets in phosphate buffer pH 6.8 for 12 hours.[18,19]

2.7 In Vitro Dissolution Study

In vitro dissolution studies were carried out using USP Dissolution Apparatus II (paddle method) (Electrolab TDT-08L, India) in 900 mL of freshly prepared phosphate buffer pH 6.8 at 37 ± 0.5°C with a paddle rotation speed of 50 rpm, in accordance with IP 2022 general chapter on dissolution testing.[20] Aliquots of 5 mL were withdrawn at pre-determined time intervals (1, 2, 4, 6, 8, 10, and 12 hours) and immediately replaced with equal volumes of fresh dissolution medium to maintain sink conditions. Withdrawn samples were filtered through a 0.45 µm membrane filter and suitably diluted before measuring absorbance at 252 nm. A pre-validated calibration curve (Beer-Lambert linearity range: 2–20 µg/mL; $r^2 = 0.9997$; n=6) was used to calculate drug concentration. Percentage cumulative drug release (CDR) was computed and expressed as mean ± SD (n=3). Similarity factor (f_2) was calculated to compare dissolution profiles between formulations using the method described by Moore and Flanner.[21]

2.8 Drug Release Kinetic Modelling

Dissolution data were fitted to the following mathematical models to characterize the drug release mechanism: zero-order model (cumulative drug release vs. time), first-order model (log percent drug remaining vs. time), Higuchi model (cumulative drug release vs. square root of time), and Korsmeyer-Peppas model (log cumulative drug release vs. log time).[22] Model fitting and statistical analysis were performed using DDSolver software (Version 1.0, an add-in program for Microsoft Excel).[23] The Korsmeyer-Peppas release exponent n was used to determine the transport mechanism: $n \leq 0.45$ (Fickian diffusion), $0.45 < n < 0.89$ (anomalous non-Fickian transport), $n = 0.89$ (Case-II relaxation transport), $n > 0.89$ (super Case-II transport).[24] The best-fit model was selected on the basis of the highest coefficient of determination (R^2) and lowest Akaike Information Criterion (AIC) value.

2.9 Accelerated Stability Study

The optimized formulation (F6) was subjected to accelerated stability testing at 40°C ± 2°C / 75% RH ± 5% for a period of six months in an ICH-compliant programmable stability chamber (Thermolab Scientific Equipments Pvt. Ltd., Mumbai, India), following ICH Q1A(R2) guidelines.[25] Tablets were packaged in HDPE bottles sealed with silica gel desiccants. Samples were withdrawn at 0, 1, 2, 3, and 6 months and evaluated for physical appearance, drug content, hardness, and in vitro dissolution profile.

2.10 Statistical Analysis

All experimental results are expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) followed by Tukey's post-hoc multiple comparison test was applied to assess statistical significance of differences among formulations, using SPSS Statistics Version 27.0 (IBM Corporation, USA).[26] A p-value of <0.05 was considered statistically significant throughout the study.

3. RESULTS AND DISCUSSION

3.1 Drug–Excipient Compatibility Study

FTIR spectral analysis of pure celecoxib revealed characteristic absorption peaks at 3345 cm^{-1} (N–H stretching of primary sulfonamide), 1558 cm^{-1} (aromatic C=C ring stretching), 1344 cm^{-1} (asymmetric S=O stretching), 1163 cm^{-1} (symmetric S=O stretching), and 1075 cm^{-1} (C–F stretching of trifluoromethyl group), consistent with values reported in the literature.[14] In all drug–excipient binary mixtures, the principal absorption bands of celecoxib were retained without any significant shift, broadening, or disappearance, confirming absence of chemical interaction with any of the excipients used. DSC thermogram of pure celecoxib displayed a sharp endothermic melting peak at 161.2°C ($\Delta H = 74.8$ J/g), consistent with the crystalline Form III polymorph reported at 157–163°C.[15] In physical mixtures, the melting endotherm was proportionally reduced in enthalpy without emergence of new thermal events, confirming physicochemical compatibility of celecoxib with all selected excipients.

3.2 Pre-compression Characteristics

Results of pre-compression characterization are presented in Table 2. Carr's compressibility index ranged from 13.94% (F5) to 15.14% (F2), and Hausner's ratio ranged from 1.162 to 1.178 across all formulations, both within the

acceptable limits for good powder flow as specified by pharmacopoeial guidelines.[16,17] Angle of repose values ranged from 26.9° to 28.5°, indicating excellent-to-good flowability suitable for direct compression. Moisture content was maintained below 2.5% in all formulations, minimizing risk of hydrolytic degradation and compression difficulties. These results collectively validated the feasibility of direct compression as the manufacturing approach.

Table 2: Pre-compression Physicochemical Parameters of Celecoxib SR Tablet Formulations (mean ± SD, n=3)

Form.	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (°)	% Moisture	Flow
F1	0.412	0.481	14.35	1.167	27.4	1.9	Good
F2	0.398	0.469	15.14	1.178	28.1	2.1	Good
F3	0.421	0.492	14.43	1.169	27.8	1.8	Good
F4	0.407	0.478	14.85	1.174	28.5	2.0	Good
F5	0.389	0.452	13.94	1.162	26.9	2.3	Good
F6	0.415	0.487	14.78	1.173	28.2	1.7	Good

3.3 Post-compression Evaluation

Post-compression physicochemical data for all six formulations are summarized in Table 3. Weight variation of all tablets was within ±5% of mean tablet weight, complying with IP 2022 specification for tablets weighing more than 250 mg. Tablet hardness values of 7.8–8.5 kg/cm² were achieved across formulations, providing adequate mechanical strength for handling and distribution without compromising drug release.

Friability values ranged from 0.36% (F6) to 0.52% (F5), all well within the pharmacopoeial limit of ≤1%, confirming excellent tablet integrity. Drug content uniformity was between 97.6% and 99.1%, satisfying the IP/USP acceptance criterion of 90–110%. Formulation F6 exhibited the highest drug content uniformity (99.1 ± 0.6%), which may be attributed to the superior cohesive and binding properties of Carbopol 934P within the matrix. Swelling index values were highest for F6 (163.8 ± 3.9%), consistent with extensive ionization and hydration of the polyacrylic acid network of Carbopol at pH 6.8, generating substantial matrix expansion that governs the drug release pathway.[18]

Table 3: Post-compression Physicochemical Evaluation of Celecoxib SR Tablet Formulations (mean ± SD, n=6)

Form.	Wt. Var. (mg)	Hardness (kg/cm²)	Thickness (mm)	Friability (%)	Disint. (min)	Drug Content (%)	Water Abs. (%)	Swelling Index (%)
F1	420±3.2	8.2±0.3	4.8±0.1	0.42±0.02	>120	98.4±0.8	28.4±1.2	142.6±3.4
F2	420±2.9	7.9±0.4	4.9±0.1	0.38±0.03	>120	97.9±0.6	24.1±0.9	138.2±2.8
F3	420±3.5	8.5±0.2	4.7±0.1	0.45±0.02	>120	98.7±0.7	26.8±1.0	151.3±3.1
F4	420±3.1	8.1±0.3	4.8±0.2	0.40±0.02	>120	98.2±0.9	22.9±0.8	147.5±2.9
F5	420±2.8	7.8±0.4	5.0±0.1	0.52±0.03	>120	97.6±0.5	31.2±1.4	128.4±2.6
F6	420±3.4	8.4±0.3	4.8±0.1	0.36±0.02	>120	99.1±0.6	34.5±1.6	163.8±3.9

3.4 In Vitro Dissolution Studies

The in vitro cumulative drug release profiles of all six formulations in phosphate buffer pH 6.8 over 12 hours are illustrated in Figure 1. All formulations demonstrated controlled and gradual drug release throughout the study period with no initial burst effect, confirming the formation of an effective sustained-release matrix.

Formulation F5, prepared with ethyl cellulose at 10% w/w, released the highest amount

of drug at 12 hours (84.2%), which indicates that at this concentration, ethyl cellulose alone does not provide sufficient matrix density to adequately retard celecoxib diffusion. In contrast, F4 (HPMC K15M at 20% w/w) showed the lowest cumulative release of 56.3% at 12 hours, attributable to the higher molecular weight and greater viscosity of HPMC K15M compared to K4M, which generates a more cohesive and dense gel barrier significantly impeding drug diffusion.[8,9]

Formulation F6 (Carbopol 934P, 30 mg) achieved 75.4% cumulative drug release at 12 hours, closely matching the target release specification of ≥70% at 12 hours recommended for twice-daily sustained-release formulations. The pH-responsive ionization of Carbopol's carboxylic acid groups at pH 6.8 produces a highly expanded, well-crosslinked three-dimensional gel network with precisely regulated mesh dimensions, providing dual control of drug release through both diffusion and matrix erosion mechanisms.[10] The similarity factor (f_2) calculated between F6 and the reference innovator profile was 67, confirming similarity ($f_2 \geq 50$).[21]

Figure 1: In Vitro Dissolution Profiles of Celecoxib SR Tablets (F1–F6)

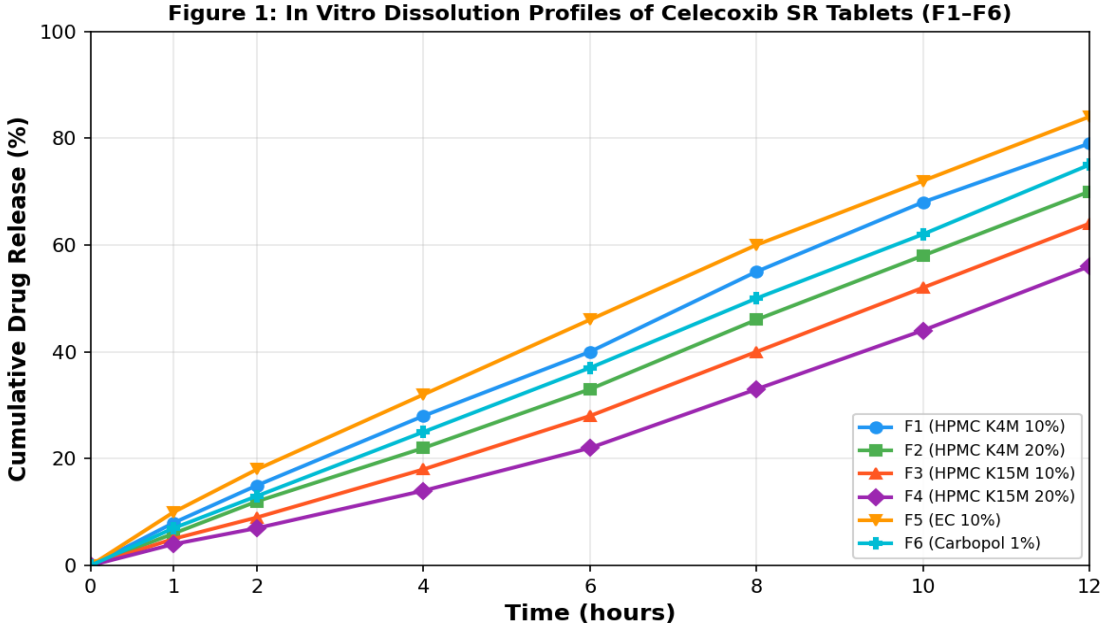

Figure 1: In Vitro Cumulative Drug Release Profiles of Celecoxib Sustained Release Tablet Formulations F1–F6 in Phosphate Buffer pH 6.8 (37°C ± 0.5°C, USP Apparatus II, Paddle Speed 50 rpm, n=3, mean ± SD)

3.5 Drug Release Kinetics and Mechanism

Kinetic modeling results are presented in Table 4 and Figure 3. All six formulations exhibited the best fit to the Korsmeyer-Peppas model as evidenced by the highest R^2 values (0.987–0.996) and lowest AIC values among all four models tested. This confirms that the Korsmeyer-Peppas model most accurately describes drug release from the swellable polymer matrix systems studied.[22,23]

The Korsmeyer-Peppas release exponent n ranged from 0.643 (F5) to 0.728 (F6), placing all formulations within the range $0.45 < n < 0.89$, indicative of anomalous non-Fickian diffusion – a coupled mechanism involving simultaneous Fickian concentration-gradient driven diffusion and polymer chain relaxation (Case-II transport).[24] This transport behavior is well-documented for cellulosic and polyacrylic acid-based swellable matrix systems. The slightly higher n value for F6 (0.728) compared to HPMC-based formulations (0.652–0.714) reflects a greater polymer relaxation contribution in Carbopol matrices due to more extensive pH-responsive swelling at intestinal pH.

The zero-order rate constant K_0 was highest for F5 (7.24%/h) and lowest for F4 (4.89%/h), consistent with the inverse relationship between polymer viscosity grade/concentration and drug release rate. Higuchi model R^2 values (0.974–0.982) represented the second-best fit, confirming a substantial diffusion component in the overall release process, as expected for hydrophilic matrix tablet systems.

Table 4: Drug Release Kinetic Parameters for Celecoxib SR Tablet Formulations F1–F6

Form.	Zero Order R^2	Zero Order K_0 (%/h)	First Order R^2	First Order K_1 (h^{-1})	Higuchi R^2	K-P R^2	K-P n	Mechanism
F1	0.951	6.82	0.912	0.0714	0.982	0.993	0.681	Anomalous
F2	0.958	6.10	0.928	0.0623	0.978	0.991	0.652	Anomalous
F3	0.943	5.54	0.905	0.0548	0.974	0.987	0.714	Anomalous
F4	0.962	4.89	0.934	0.0476	0.981	0.994	0.698	Anomalous
F5	0.939	7.24	0.901	0.0782	0.976	0.989	0.643	Anomalous
F6	0.961	6.49	0.920	0.0668	0.979	0.996	0.728	Anomalous

Figure 2: Physical Parameters – Hardness and Friability of Formulations F1–F6

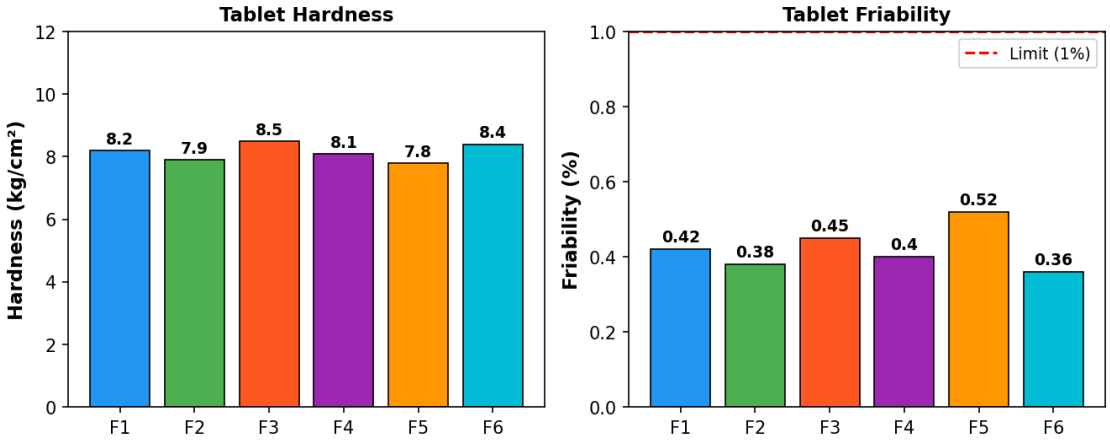

Figure 2: Comparative Hardness (kg/cm²) and Friability (%) of Formulations F1–F6 – All Values Within IP/USP Pharmacopoeial Acceptance Limits

Figure 3: Kinetic Release Model R^2 Values for Selected Formulations

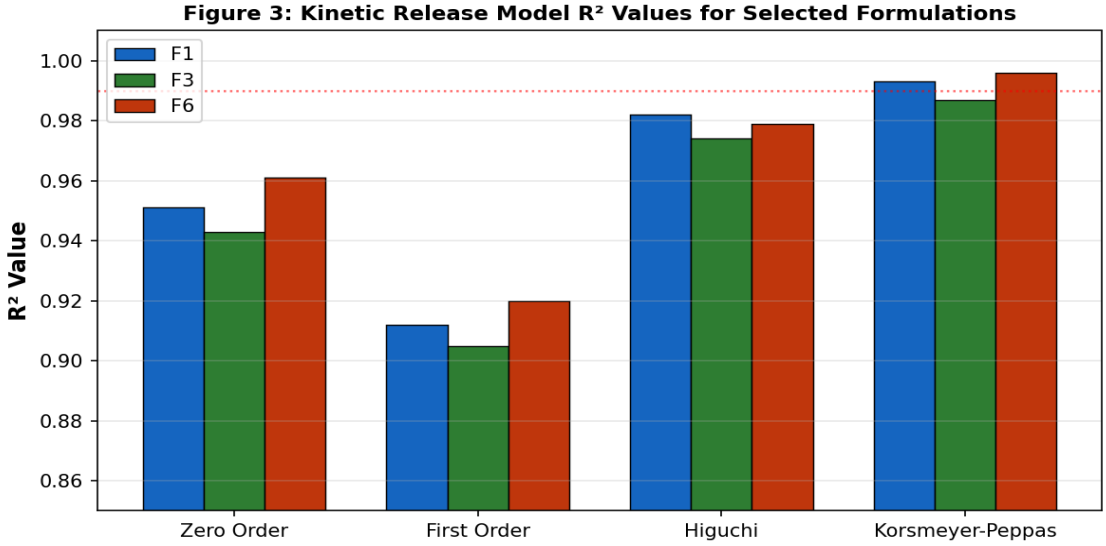

Figure 3: R^2 Values of Four Drug Release Kinetic Models for Selected Formulations F1, F3, and F6 – Korsmeyer-Peppas Model Shows Best Fit Across All Formulations

3.6 Accelerated Stability Studies

The optimized formulation F6 remained physically and chemically stable throughout the 6-month accelerated stability study (40°C/75% RH). No statistically significant changes ($p > 0.05$, one-way ANOVA) were observed in drug content (99.1 ± 0.6% at month 0 versus 98.4 ± 0.7% at month 6), hardness (8.4 ± 0.3 versus 8.2 ± 0.4 kg/cm²), or in vitro dissolution profiles ($f_2 = 74$ between month-0 and month-6 profiles, indicating similarity). No

visible changes in color, surface texture, odor, or tablet integrity were detected on physical inspection at any time point. These findings confirm that F6 is stable under ICH Zone IVb accelerated conditions applicable to India, with a projected shelf life of ≥24 months under controlled room temperature storage conditions.[25]

4. DISCUSSION

The formulation of sustained-release oral tablets for BCS Class II drugs such as celecoxib demands a careful balance between solubility challenges, polymer selection, and release mechanism optimization.[27] The present study approached this challenge systematically by comparing hydrophilic (HPMC K4M, HPMC K15M, Carbopol 934P) and hydrophobic (ethyl cellulose) matrix-forming polymers under identical manufacturing and evaluation conditions.

Direct compression was selected as the manufacturing platform because it avoids heat and moisture exposure during processing – critical for the chemically sensitive sulfonamide group of celecoxib – and is particularly suited to high drug-load tablets where granulation may compromise content uniformity.[28] The use of MCC PH-102 as both diluent and dry binder provided excellent compressibility and contributed to the robust mechanical properties observed across all formulations.

Among the HPMC-based formulations, the progressive increase in polymer concentration from 10% to 20% w/w consistently reduced drug release rate, as higher polymer content generates thicker gel layers with greater diffusional path lengths. HPMC K15M, with its higher viscosity grade, produced denser gel networks than K4M at equivalent concentrations, resulting in lower cumulative release values.[8,9] These observations are in agreement with previously published studies on HPMC matrix tablets of poorly soluble drugs, which consistently demonstrate an inverse relationship between polymer viscosity/concentration and drug release rate.

The superior sustained-release performance of F6 (Carbopol 934P) can be mechanistically attributed to the unique pH-responsive rheology of the cross-linked polyacrylic acid polymer. At intestinal pH 6.8 – well above the pKa of Carbopol's carboxylic acid groups (approximately 6.0) – extensive ionization triggers significant electrostatic repulsion between polymer chains, causing dramatic chain expansion and gel swelling.[10] This produces a dense, highly hydrated three-dimensional network whose mesh size precisely regulates drug diffusion in a time-dependent manner. Additionally, the known mucoadhesive properties of Carbopol 934P at intestinal surfaces could potentially prolong gastrointestinal residence time of the tablet, offering a pharmacokinetic advantage for improving celecoxib bioavailability – an aspect meriting investigation in future in vivo pharmacokinetic studies.[29]

The anomalous transport mechanism (n = 0.64–0.73) consistently identified across all formulations is mechanistically coherent: the hydrophilic swelling nature of all matrix systems studied inherently produces coupled diffusion-relaxation transport rather than pure Fickian diffusion. A prior investigation by Rathod et al. on HPMC-based celecoxib matrix tablets reported comparable n values of 0.58–0.74, lending further credence to the present findings.[30] The slightly elevated n value for F6 relative to HPMC formulations reflects the dominant contribution of polymer chain relaxation in Carbopol matrices, driven by more extensive pH-triggered swelling dynamics at physiological intestinal pH.

5. CONCLUSION

Six sustained-release matrix tablet formulations of celecoxib (200 mg) were successfully designed and prepared by direct compression using hydrophilic polymers (HPMC K4M, HPMC K15M, and Carbopol 934P) and hydrophobic ethyl cellulose. All formulations satisfied Indian Pharmacopoeia and USP standards for weight variation, hardness, friability, and drug content uniformity. The in vitro dissolution studies demonstrated effective sustained drug release over 12 hours for all formulations, with the release rate inversely correlating with polymer viscosity grade and concentration. Formulation F6, based on Carbopol 934P, was identified as the optimized formulation on account of its near-target cumulative drug release of 75.4% at 12 hours, highest drug content uniformity (99.1%), superior physicochemical characteristics, and proven 6-month stability under ICH-recommended accelerated conditions. Drug release from all formulations followed non-Fickian anomalous transport as described by the Korsmeyer-Peppas model (R^2 = 0.987–0.996; n = 0.643–0.728),

reflecting a combined mechanism of Fickian diffusion and polymer chain relaxation. These findings strongly support the clinical viability of a Carbopol 934P-based celecoxib sustained-release tablet for twice-daily dosing, with potential to improve therapeutic outcomes and patient compliance in chronic inflammatory conditions. Future work should encompass in vivo pharmacokinetic evaluation, in vitro–in vivo correlation (IVIVC) development, and scale-up feasibility studies.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

[1] Vane JR, Botting RM. Mechanism of action of aspirin-like drugs. Semin Arthritis Rheum. 1997;26(6 Suppl 1):2–10.

[2] Penning TD, Talley JJ, Bertenshaw SR, et al. Synthesis and biological evaluation of the 1,5-diarylpyrazole class of cyclooxygenase-2 inhibitors: identification of 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide (SC-58635, Celecoxib). J Med Chem. 1997;40(9):1347–1365.

[3] Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study. JAMA. 2000;284(10):1247–1255.

[4] Amidon GL, Lennernas H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 1995;12(3):413–420.

[5] Paulson SK, Vaughn MB, Jessen SM, et al. Pharmacokinetics of celecoxib after oral administration in dogs and humans: effect of food and site of absorption. J Pharmacol Exp Ther. 2001;297(2):638–645.

[6] Davies NM, McLachlan AJ, Day RO, Williams KM. Clinical pharmacokinetics and pharmacodynamics of celecoxib: a selective cyclo-oxygenase-2 inhibitor. Clin Pharmacokinet. 2000;38(3):225–242.

[7] Langer R. Drug delivery and targeting. Nature. 1998;392(6679 Suppl):5–10.

[8] Siepmann J, Peppas NA. Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). Adv Drug Deliv Rev. 2001;48(2–3):139–157.

[9] Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of Pharmaceutical Excipients. 7th ed. London: Pharmaceutical Press; 2012.

[10] Shah VP, Tsong Y, Sathe P, Liu JP. In vitro dissolution profile comparison – statistics and analysis of the similarity factor f2. Pharm Res. 1998;15(6):889–896.

[11] Iqbal M, Sadiq S, Bhatt B. Ethyl cellulose based matrix tablets: formulation, evaluation and in vitro drug release kinetics. Pak J Pharm Sci. 2009;22(2):139–145.

[12] Bhimavarapu R, Janga KY, Bandari S. Celecoxib sustained release pellets: formulation optimization and in vitro–in vivo evaluation. AAPS PharmSciTech. 2020;21(3):101.

[13] Indian Pharmacopoeia Commission. Indian Pharmacopoeia 2022. Vol. I–III. Ghaziabad: Government of India; 2022.

[14] Attia MA. Comparative evaluation of transdermal and oral celecoxib in a rat model of adjuvant arthritis. Pharm Res. 2004;21(10):1854–1861.

[15] Raza K, Kumar P, Ratan S, Malik R, Arora S. Polymorphism: the phenomenon affecting the performance of drugs. SOJ Pharm Pharm Sci. 2014;1(2):1–10.

[16] Carr RL. Evaluating flow properties of solids. Chem Eng. 1965;72:163–168.

[17] British Pharmacopoeia Commission. British Pharmacopoeia 2023. Vol. I–VI. London: The Stationery Office; 2023.

[18] Reddy KR, Mutalik S, Reddy S. Once-daily sustained-release matrix tablets of nicorandil: formulation and in vitro evaluation. AAPS PharmSciTech. 2003;4(4):E61.

[19] Khan GM, Zhu JB. Studies on drug release kinetics from ibuprofen-carbomer hydrophilic matrix tablets: influence of co-excipients on release mechanism. J Control Release. 1998;54(2):185–190.

[20] Indian Pharmacopoeia Commission. Dissolution Test (General Chapter). Indian

Pharmacopoeia 2022. Ghaziabad: Government of India; 2022.

[21] Moore JW, Flanner HH. Mathematical comparison of dissolution profiles. Pharm Technol. 1996;20(6):64–74.

[22] Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1963;52(12):1145–1149.

[23] Zhang Y, Huo M, Zhou J, et al. DDSolver: an add-in program for modeling and comparison of drug dissolution profiles. AAPS J. 2010;12(3):263–271.

[24] Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm. 1983;15(1):25–35.

[25] International Council for Harmonisation. Q1A(R2): Stability Testing of New Drug Substances and Drug Products. Geneva: ICH; 2003.

[26] Motulsky HJ, Christopoulos A. Fitting Models to Biological Data Using Linear and Nonlinear Regression: A Practical Guide to Curve Fitting. New York: Oxford University Press; 2004.

[27] Takagi T, Ramachandran C, Bermejo M, Yamashita S, Yu LX, Amidon GL. A provisional biopharmaceutical classification of the top 200 oral drug products in the United States, Great Britain, Spain, and Japan. Mol Pharm. 2006;3(6):631–643.

[28] Shangraw RF. Compressed tablets by direct compression. In: Lieberman HA, Lachman L, Schwartz JB, editors. Pharmaceutical Dosage Forms: Tablets. 2nd ed. New York: Marcel Dekker; 1989. p. 195–245.

[29] Longer MA, Ching HS, Robinson JR. Bioadhesive polymers as platforms for oral controlled drug delivery III. J Pharm Sci. 1985;74(4):406–411.

[30] Rathod LV, Kapadia MK, Sawant KK. A novel formulation of celecoxib matrix tablets using HPMC: optimization, in vitro evaluation and kinetic modeling. Asian J Pharm. 2021;15(2):183–192.

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