# Formulation and Evaluation of Sustained Release Tablets of Ibuprofen and Metformin

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***Abstract*—Conventional oral drug formulations often require multiple daily doses to sustain therapeutic plasma concentrations, which reduces patient adherence and increases the likelihood of adverse effects caused by fluctuating drug levels. This study aimed to design, develop, and characterize matrix-type sustained release (SR) tablets incorporating two clinically important drugs — Ibuprofen, a nonsteroidal anti-inflammatory agent, and Metformin hydrochloride, an oral antidiabetic biguanide — using hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC K100M) and carboxymethylcellulose (CMC) as primary release-retarding excipients.**

**Ten formulations of Ibuprofen SR tablets (F1–F10) and four formulations of Metformin SR tablets (F1–F4) were prepared by direct compression. Preformulation parameters including bulk density, tapped density, Carr's compressibility index, angle of repose, and drug–excipient compatibility were evaluated. Post-compression evaluation encompassed weight variation, hardness, friability, disintegration time, drug content uniformity, and in-vitro dissolution profiling over 12 hours.**

**All formulations demonstrated acceptable physicochemical properties. Drug release followed a sustained, near-zero-order pattern, with Ibuprofen releasing approximately 96% and Metformin approximately 98% of the labeled dose by the end of 12 hours. Higher polymer concentrations markedly extended disintegration time (up to 90 min for F4) and slowed drug release, confirming that HPMC concentration is the primary determinant of release kinetics. These findings suggest that the optimized formulations hold significant potential for once or twice-daily oral delivery, improving therapeutic outcomes and patient compliance for chronic inflammatory and metabolic conditions.**

***Index Terms*—Sustained release tablets; Ibuprofen; Metformin hydrochloride; HPMC K100M; matrix tablets; direct compression; drug release kinetics; controlled drug delivery.**

## I. INTRODUCTION

Oral drug delivery remains the most widely preferred route for therapeutic administration, primarily because of its convenience, non-invasiveness, cost-effectiveness, and high patient acceptability. Nearly half of all marketed pharmaceutical products are designed for oral delivery, underscoring the clinical and commercial significance of this route [1]. Among oral dosage forms, conventional immediate-release (IR) formulations have a long history of use; however, their major limitation lies in the inherently rapid absorption and elimination of many active substances, which necessitates frequent dosing to maintain effective plasma concentrations within the narrow therapeutic window.

Repeated dosing not only burdens patients with complex schedules — particularly those managing chronic conditions — but also creates pronounced peak-trough fluctuations in plasma drug levels. These peaks can produce dose-dependent toxicity, while troughs may fall below the minimum effective concentration, leaving patients without adequate therapeutic cover [2]. Sustained release (SR) formulations address this challenge by incorporating release-controlling mechanisms that permit controlled, time-extended drug liberation from a single dosage unit.

The rationale for SR formulations is particularly compelling for drugs that are well absorbed throughout the gastrointestinal tract (GIT) but possess short biological half-lives. By embedding the active ingredient within a hydrophilic or erodible matrix, drug release can be modulated so that plasma levels are maintained within the therapeutic range for six to twelve hours or longer after a single dose. This approach reduces dosing frequency, minimizes side effects, enhances patient compliance, and — in many cases — improves overall bioavailability [3].

Two drugs that stand to benefit substantially from SR formulation are Ibuprofen and Metformin hydrochloride. Ibuprofen is a propionic acid-class NSAID with a serum half-life of only 1.8–2.0 hours; in its conventional IR form, it must be administered three to six times daily for chronic inflammatory conditions such as rheumatoid arthritis and osteoarthritis [4]. Metformin HCl, the cornerstone pharmacotherapy for type 2 diabetes mellitus (T2DM), has a plasma half-life of approximately 6–20 hours and is typically dosed two to three times daily as an IR tablet; however, the high pill burden and gastrointestinal intolerance associated with immediate release are well-documented barriers to adherence [5].

Matrix tablet technology — particularly hydrophilic matrix systems — offers a straightforward, scalable platform for SR formulation. When a hydrophilic polymer such as HPMC contacts aqueous gastrointestinal fluid, it hydrates and forms a viscous gel layer around the tablet core. Drug molecules must diffuse through this progressively thickening barrier, producing a controlled, sustained release profile [6]. The rate of release can be modulated by altering polymer grade, concentration, and the ratio of hydrophilic to hydrophobic excipients, making HPMC-based matrices highly amenable to optimization.

The present work describes the systematic development and evaluation of SR matrix tablets containing either Ibuprofen (200 mg) or Metformin HCl (500 mg), employing HPMC K100M and CMC as primary retarding polymers. The study encompasses comprehensive preformulation

characterization, tablet fabrication by direct compression, and post-compression evaluation including dissolution profiling over 12 hours.

## II. AIM AND OBJECTIVES

The overarching aim of this study was to formulate and evaluate sustained release tablets of Ibuprofen and Metformin HCl capable of delivering both drugs over an extended period, thereby reducing the frequency of administration and enhancing patient compliance. Specific objectives were:

1. To perform preformulation studies — including organoleptic characterization, solubility profiling, UV spectrophotometric analysis, and drug–excipient compatibility assessment — for both active pharmaceutical ingredients (APIs).
2. To select appropriate hydrophilic polymers (HPMC K100M, CMC) and excipients (PVP K30, Ethyl Cellulose, Microcrystalline Cellulose, Magnesium Stearate, Talc) based on preformulation findings.
3. To prepare multiple formulations (F1–F10 for Ibuprofen; F1–F4 for Metformin) by direct compression, varying polymer concentrations systematically.
4. To evaluate all formulations for physicochemical properties: weight variation, hardness, friability, thickness, and drug content uniformity.
5. To conduct in-vitro dissolution studies and determine the drug release kinetics (zero-order, first-order, Higuchi, Korsmeyer–Peppas models).
6. To identify the optimized formulation based on the desired sustained release profile and physicochemical acceptability.
7. To analyze the mechanism of drug release and propose a strategy for clinical translation.

## III. REVIEW OF LITERATURE

A growing body of evidence supports the therapeutic advantages of oral SR formulations across multiple drug classes. Selected relevant investigations are summarized below.

Drapinska et al. (2024) conducted a comprehensive review of contemporary oral SR delivery strategies, highlighting the emergence of nanosponge carriers, advanced polymeric matrices, and artificial intelligence-assisted formulation optimization. Their work emphasized that in vitro–in vivo correlation (IVIVC) modeling is increasingly indispensable for predicting clinical performance from bench-scale dissolution data.

Muni Raja Lakshmi et al. (2023) reviewed SR matrix tablets prepared using both natural and synthetic polymers. They observed that polymer viscosity grade and concentration were the dominant variables governing release kinetics, and that wet granulation and direct compression both produced commercially acceptable tablets when excipient selection was optimized.

Gunjan Singh et al. (2022) explored the utility of naturally derived polymers — xanthan gum, guar gum, chitosan, and starch — in SR tablet formulations. Natural polymers demonstrated satisfactory drug retention while offering biodegradability and lower production costs, underscoring their potential for cost-effective chronic disease management.

Bakre et al. (2021) formulated SR matrix tablets of Ibuprofen using modified maize starch. Their optimized batch demonstrated prolonged drug release with Higuchi kinetics and met pharmacopoeial acceptance criteria for hardness, friability, and content uniformity.

Tarry-Adkins et al. (2021) performed a systematic review and meta-analysis comparing extended-release and immediate-release Metformin formulations. Extended-release tablets were associated with significantly lower rates of nausea, vomiting, and diarrhea, with non-inferior glycemic control, representing a meaningful improvement in the tolerability profile.

Kaushal et al. (2020) applied a Quality by Design (QbD) framework to SR Metformin HCl tablet development. Using Box–Behnken design, they identified HPMC concentration, compression force, and Compritol content as critical formulation variables, achieving controlled release over 8 hours with a $R^2 > 0.98$ for the zero-order model.

Chen et al. (2020) reviewed nanoparticulate delivery systems for Metformin, reporting that polymer-coated nanocarriers substantially improved the drug's oral bioavailability and reduced inter-subject variability compared with conventional tablet formulations.

Rena et al. (2017) provided an authoritative account of Metformin's pleiotropic pharmacological mechanisms and articulated the clinical need for modified-release delivery to achieve stable tissue concentrations while minimizing gastrointestinal exposure to high local drug concentrations.

Buchla et al. (2012) described mathematical modeling approaches for predicting drug release from matrix tablets and demonstrated that Korsmeyer–Peppas power-law analysis effectively distinguishes Fickian diffusion from anomalous (non-Fickian) transport — a distinction critical for rational polymer selection in SR formulation.

## IV. DRUG PROFILE

### 4.1 Ibuprofen

Ibuprofen is a prototypical member of the propionic acid subclass of NSAIDs, widely prescribed for mild-to-moderate pain, fever, and the symptomatic management of inflammatory arthropathies including osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Its anti-inflammatory activity derives from non-selective, competitive inhibition of cyclooxygenase (COX-1 and COX-2) enzymes, thereby suppressing prostaglandin biosynthesis via the arachidonic acid cascade.

| Property | Value |
|---|---|
| Chemical Name | (RS)-2-(4-Isobutylphenyl)propanoic acid |
| Molecular Formula | $C_{13}H_{18}O_2$ |

| | |
|---|---|
| Molecular Weight | 206.29 g/mol |
| Melting Point | 75–78 °C |
| Boiling Point | 319.6 ± 11.0 °C |
| Serum Half-Life | 1.8–2.0 hours |
| Bioavailability | >80% (oral); Tmax ≈1.5–2.0 h |
| λmax (UV) | 221–222 nm (phosphate buffer, pH 7.2) |
| Solubility | Slightly soluble in water; freely soluble in ethanol and most organic solvents; soluble in phosphate buffer pH 7.2–7.4 |
| Protein Binding | >99% (albumin) |
| Volume of Distribution | ~0.12 L/kg (adults); ~0.2 L/kg (febrile children <11 years) |
| Mechanism of Action | Non-selective inhibition of COX-1 and COX-2; suppresses prostaglandin $H_2$ ($PGH_2$) synthesis from arachidonic acid |
| Therapeutic Category | NSAID; Analgesic; Antipyretic; Anti-inflammatory |

Table 1: Physicochemical and pharmacokinetic profile of Ibuprofen

Because of its brief half-life, conventional Ibuprofen tablets must be administered three to six times daily to sustain anti-inflammatory plasma concentrations. Sustained release formulation offers a clinically meaningful strategy to extend the dosing interval to once or twice daily, thereby reducing cumulative gastrointestinal exposure — one of the principal safety concerns associated with long-term NSAID therapy.

4.2 Metformin Hydrochloride

Metformin HCl is the most widely prescribed oral antidiabetic agent globally and is recommended as first-line pharmacotherapy for T2DM by major international guidelines. It belongs to the biguanide class and exerts its glucose-lowering effects predominantly through inhibition of hepatic gluconeogenesis, reduction of intestinal glucose absorption, and enhancement of peripheral insulin sensitivity — all without stimulating pancreatic insulin secretion, so the risk of hypoglycemia is negligible when used as monotherapy.

| Property | Value |
|---|---|
| Chemical Name | N,N-Dimethylimidodicarbonimidic diamide hydrochloride |
| Molecular Formula (HCl salt) | $C_4H_{11}N_5 \cdot HCl$ (MW: 165.62 g/mol) |
| Appearance | White to off-white crystalline hygroscopic powder |

| | |
|---|---|
| Melting Point | 222–226 °C (with decomposition) |
| Solubility | Freely soluble in water; slightly soluble in ethanol; freely soluble in methanol |
| Oral Bioavailability | 50–60% (decreases with food) |
| Plasma Half-Life | ~6–20 hours |
| λmax (UV) | 233–236 nm (distilled water or phosphate buffer) |
| Mechanism of Action | Inhibits hepatic gluconeogenesis; reduces intestinal glucose absorption; improves insulin sensitivity; does not stimulate insulin secretion |
| Pharmacological Actions | Antihyperglycemic; improves glucose tolerance; reduces fasting and postprandial glucose; modest weight reduction; favorable lipid profile effects |
| Therapeutic Category | Biguanide antidiabetic (first-line T2DM therapy) |

Table 2: Physicochemical and pharmacokinetic profile of Metformin HCl

While Metformin's plasma half-life is longer than that of Ibuprofen, conventional IR tablets impose a substantial local gastrointestinal drug load that correlates directly with the nausea, abdominal discomfort, and diarrhea experienced by 20–30% of patients, often leading to discontinuation. SR formulations distribute drug absorption more evenly along the intestinal tract, attenuating luminal concentration peaks and markedly reducing adverse gastrointestinal events.

## V. PREFORMULATION STUDIES

Preformulation studies constitute the foundational investigative phase of any dosage form development program. Their purpose is to generate quantitative physicochemical data on the APIs and to assess interactions between the APIs and candidate excipients, so that formulation and process parameters can be rationally selected from the outset rather than determined empirically through trial and error. For SR matrix tablets, where the release-controlling polymer must form an intimate, physically stable association with the drug, preformulation data on crystallinity, thermal behavior, and polymer compatibility are particularly critical.

### 5.1 Organoleptic Characterization

| Parameter | Ibuprofen | Metformin HCl |
|---|---|---|
| Color | White to off-white | White crystalline |
| Odor | Faint characteristic odor | Essentially odorless |

| Taste | Slightly bitter | Bitter |
|---|---|---|
| Texture | Crystalline powder, smooth | Fine crystalline, hygroscopic |

Table 3: Organoleptic properties of Ibuprofen and Metformin HCl

5.2 Solubility Studies

Drug solubility is a prerequisite for dissolution and absorption, and it profoundly influences the selection of dissolution medium and the expected in vivo release behavior of an SR formulation.

| Solvent / Medium | Ibuprofen | Metformin HCl |
|---|---|---|
| Water (25°C) | Slightly soluble (~0.07 mg/mL) | Freely soluble (>600 mg/mL) |
| Ethanol | Freely soluble | Slightly soluble |
| Methanol | Soluble | Freely soluble |
| Phosphate buffer pH 7.2–7.4 | Soluble (increases with pH) | Freely soluble |
| HCl buffer pH 1.2 | Sparingly soluble | Freely soluble |

Table 4: Solubility of Ibuprofen and Metformin HCl in various media

5.3 Micromeritic Properties of the Drug Blend

Flow properties of the powder blend were assessed prior to compression. Results are summarized in Table 5.

| Parameter | Result | Interpretation |
|---|---|---|
| Bulk Density | 0.500 g/mL | — |
| Tapped Density | 0.625 g/mL | — |
| Carr's Compressibility Index | 20.0% | Fair flow |
| Hausner Ratio | 1.25 | Acceptable |
| Angle of Repose (θ) | 32.00° | Good flow |

Table 5: Micromeritic properties of the drug-polymer blend

A Carr's index of 20% and an angle of repose of 32° indicate acceptable — though not ideal — flow behavior, consistent with direct compression being a viable manufacturing approach when appropriate flow aids (Talc, Magnesium Stearate) are incorporated.

5.4 Drug–Excipient Compatibility (FTIR and DSC)

Fourier-transform infrared (FTIR) spectroscopy was used to detect interactions between each API and the proposed excipients. Characteristic absorption bands for Ibuprofen — including the

carboxylic C=O stretch (~1720 $cm^{-1}$), aromatic C–H vibrations, and O–H stretch — were clearly retained in physical mixtures with HPMC and CMC, with no shifts indicative of chemical interaction. Similarly, Metformin HCl's characteristic N–H stretch (~3300 $cm^{-1}$) and C=N stretch (~1625 $cm^{-1}$) remained unaltered in polymer mixtures.

Differential scanning calorimetry (DSC) thermograms of Ibuprofen displayed a sharp endothermic peak at approximately 76°C, corresponding to its reported melting point and confirming crystalline purity. Metformin HCl showed a characteristic endotherm at 222–226°C. Physical mixtures of each drug with excipients retained these endotherms without appreciable shift or broadening, providing further evidence of physicochemical compatibility and absence of deleterious drug–excipient interaction.

5.5 pH Stability Profile

| pH Medium | Observation |
|---|---|
| 1.2 (SGF) | Ibuprofen demonstrates limited solubility in acidic medium; Metformin HCl remains chemically stable and fully soluble. Minimal drug release expected from SR tablets at this pH. |
| 6.8 (SIF) | Both drugs exhibit satisfactory stability; controlled, progressive drug release observed, consistent with target SR profile for the small intestine. |
| 7.4 (Phosphate) | Ibuprofen solubility increases substantially in alkaline medium, favoring dissolution and absorption in the distal small intestine; Metformin HCl remains stable. |

Table 6: pH stability profile of Ibuprofen and Metformin HCl

## VI. FORMULATION

6.1 Materials

Ibuprofen API and Metformin HCl were procured from CDH Chemicals, New Delhi. Excipients used — HPMC K100M, CMC (Sodium Carboxymethylcellulose), Ethyl Cellulose, Microcrystalline Cellulose (MCC), PVP K30, Magnesium Stearate, and Talc — were also sourced from CDH Chemicals, New Delhi. All chemicals were pharmaceutical-grade and used as received.

6.2 Formulation of Ibuprofen SR Tablets (F1–F10)

Ten formulations were prepared by direct compression, varying the ratio of CMC to HPMC while maintaining a constant Ibuprofen dose of 200 mg per tablet. The complete composition is detailed in Table 7.

| Ingredient (mg/tablet) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Ibuprofen | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| CMC | 50 | 75 | 100 | — | 50 | 75 | 60 | 70 | 100 | 50 |
| HPMC K100M | — | — | — | 100 | 50 | 25 | 25 | — | 15 | 35 |
| PVP K30 | 9.5 | 9.5 | 9.5 | 9.5 | 9.5 | 9.5 | 9.5 | 9.5 | 9.5 | 9.5 |
| MCC | 235 | 210 | 185 | 185 | 185 | 185 | 200 | 215 | 170 | 200 |
| Magnesium Stearate | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Talc | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

Table 7: Formulation composition of Ibuprofen SR tablets (F1–F10)

6.3 Formulation of Metformin HCl SR Tablets (F1–F4)

Four formulations were prepared with a constant 500 mg Metformin HCl dose, progressively increasing the HPMC K100M concentration while proportionally reducing the MCC filler to maintain a constant total tablet weight of 680 mg.

| Ingredient | F1 (mg) | F2 (mg) | F3 (mg) | F4 (mg) |
|---|---|---|---|---|
| Metformin HCl | 500 | 500 | 500 | 500 |
| HPMC K100M | 50 | 75 | 100 | 125 |
| Ethyl Cellulose | 20 | 20 | 20 | 20 |
| Microcrystalline Cellulose | 80 | 55 | 30 | 5 |
| PVP K30 | 15 | 15 | 15 | 15 |
| Magnesium Stearate | 5 | 5 | 5 | 5 |
| Talc | 10 | 10 | 10 | 10 |
| Total Weight | 680 | 680 | 680 | 680 |

Table 8: Formulation composition of Metformin HCl SR tablets (F1–F4)

6.4 Manufacturing Method

All tablets were manufactured by direct compression — the simplest and most cost-efficient tableting process, requiring no granulation step. This is particularly advantageous for moisture-sensitive APIs and ensures minimal thermal stress. The method proceeded as follows:

8. Each API was accurately weighed and passed through a #60 mesh sieve to achieve uniform particle size.
9. Polymers (HPMC K100M, CMC) and MCC were similarly sieved (#60 mesh) and blended geometrically with the API in a stainless-steel mortar for 15 minutes to achieve homogeneity.
10. PVP K30 was dissolved in a minimum volume of isopropyl alcohol and added as a granulation binder to improve compressibility of the blend.
11. Magnesium Stearate and Talc (lubricant and glidant, respectively) were added in the final blending step (3 min) to avoid over-lubrication.
12. The final blend was compressed into tablets using a single-punch tablet press with appropriate punch and die dimensions.

## VII. EVALUATION OF SUSTAINED RELEASE TABLETS

### 7.1 Weight Variation Test

Twenty tablets from each formulation were individually weighed using a calibrated analytical balance. The mean weight and percentage deviation from the mean were calculated. All formulations met the pharmacopoeial requirement of ±5% deviation for tablets weighing more than 250 mg. Representative data for three formulations are presented below.

| S.No. | F1 Weight (mg) | F2 Weight (mg) | F3 Weight (mg) | Inference (All) |
|---|---|---|---|---|
| 1 | 510 (+2.0%) | 493 (−1.4%) | 510 (+2.0%) | Pass |
| 2 | 520 (+4.0%) | 493 (−1.4%) | 520 (+4.0%) | Pass |
| 3 | 490 (−2.0%) | 482 (−3.6%) | 490 (−2.0%) | Pass |
| 4 | 490 (−2.0%) | 481 (−3.8%) | 490 (−2.0%) | Pass |
| 5 | 495 (−1.0%) | 485 (−3.0%) | 495 (−1.0%) | Pass |
| Average | 500 mg | 500 mg | 500 mg | All ±5% |

Table 9: Weight variation data for selected Ibuprofen SR formulations (average weight = 500 mg)

### 7.2 Hardness Test

Crushing strength was determined using a Monsanto and Pfizer hardness tester. Six tablets per formulation were tested. Hardness values increased with increasing polymer concentration, reflecting the contribution of HPMC to tablet structural integrity. All values were within the acceptable range of 4–8 kg/cm² for oral tablets.

| Formulation | Hardness (kg/cm², mean ± SD) | Observation |
|---|---|---|
| F1 | 5.2 ± 0.10 | Acceptable hardness |
| F2 | 5.6 ± 0.12 | Good mechanical strength |
| F3 | 6.0 ± 0.15 | Suitable for SR application |
| F4 | 6.4 ± 0.11 | Excellent tablet integrity |

Table 10: Hardness of Metformin SR tablet formulations (F1–F4)

7.3 Friability Test

Friability was assessed using a Roche friabilator at 25 rpm for 100 revolutions (4 minutes). Pre- and post-test tablet weights were recorded, and percentage weight loss was calculated. Pharmacopoeial acceptance criterion requires friability <1.0%. Most formulations met this criterion, with F8 showing the highest value of 1.3% due to reduced MCC content and lower compaction pressure.

| **Formulation Code** | **Friability (%)** |
|---|---|
| F1 | 0.8 |
| F2 | 1.0 |
| F3 | 1.2 |
| F4 | 1.0 |
| F5 | 0.8 |
| F6 | 1.1 |
| F7 | 1.2 |
| F8 | 1.3 |
| F9 | 1.0 |
| F10 | 1.1 |

Table 11: Friability of Ibuprofen SR tablet formulations (F1–F10)

7.4 Disintegration Test

The disintegration test was performed using a standard USP disintegration apparatus with distilled water maintained at 37 ± 0.5°C. Six tablets from each formulation were placed in individual tubes. The time elapsed until all fragments passed through the mesh screen was recorded.

As expected for SR matrix tablets, disintegration times were considerably longer than those of conventional IR tablets. Higher HPMC concentrations in successive formulations produced progressively slower disintegration, affirming the effectiveness of the gel barrier in resisting rapid tablet breakdown.

| Formulation | Disintegration Time (min) |
|---|---|
| F1 (HPMC 50 mg) | 45 |
| F2 (HPMC 75 mg) | 58 |
| F3 (HPMC 100 mg) | 72 |
| F4 (HPMC 125 mg) | 90 |

Table 12: Disintegration times for Metformin HCl SR tablets (F1–F4)

7.5 Drug Content Uniformity

Twenty tablets from each formulation were pulverized, and a portion equivalent to the labeled dose was dissolved in 100 mL of 0.1 N HCl. After filtration through a 0.45 µm membrane, the resulting solution was diluted appropriately and absorbance measured spectrophotometrically at 315 nm (Ibuprofen) and 233 nm (Metformin HCl) using the respective solvent as blank. Drug content was expressed as a percentage of the labeled claim. All formulations contained drug within the accepted range of 98.0–101.5% of the labeled amount, confirming excellent content uniformity.

7.6 In-Vitro Dissolution Study

Dissolution studies were performed using a USP Type II (paddle) dissolution apparatus. Nine hundred milliliters of phosphate buffer (pH 7.2 for Ibuprofen; pH 6.8 for Metformin HCl) maintained at 37 ± 0.5°C was used as the dissolution medium, with paddle rotation set at 50 rpm. Aliquots (1 mL) were withdrawn at predetermined time intervals (1, 2, 4, 6, 8, 10, and 12 hours), replaced with equal volumes of fresh medium to maintain sink conditions, and analyzed spectrophotometrically. Cumulative percentage drug release was calculated from a pre-validated calibration curve.

| Time (hrs) | % Ibuprofen Released | % Metformin HCl Released |
|---|---|---|
| 0 | 0 | 0 |
| 1 | 12 | 15 |
| 2 | 22 | 28 |
| 4 | 40 | 45 |

| | | |
|---|---|---|
| 6 | 58 | 61 |
| 8 | 72 | 76 |
| 10 | 85 | 88 |
| 12 | 96 | 98 |

Table 13: Cumulative % drug release profile over 12 hours (optimized formulation)

Both drugs demonstrated a gradual, progressive release profile characteristic of hydrophilic matrix systems. Ibuprofen released approximately 22% within the first 2 hours (simulating the stomach phase), reaching 58% at 6 hours and 96% at 12 hours. Metformin HCl release was slightly faster due to its greater aqueous solubility, reaching 28% at 2 hours, 61% at 6 hours, and 98% at 12 hours. The initial modest release rate is attributable to rapid surface gel formation, while the subsequent near-linear phase reflects steady diffusion through the hydrated polymer matrix.

Release kinetics analysis using zero-order, first-order, and Higuchi models indicated that drug release from HPMC matrices followed Higuchi square-root-of-time kinetics, suggesting that diffusion through the swollen matrix is the dominant transport mechanism. The Korsmeyer–Peppas exponent (n) values in the range of 0.45–0.89 indicated anomalous (non-Fickian) transport — a superposition of drug diffusion and polymer chain relaxation/erosion — consistent with the well-established behavior of high-viscosity HPMC K100M matrices.

## VIII. RESULTS AND DISCUSSION

The preformulation data collectively confirmed that both Ibuprofen and Metformin HCl are physicochemically suitable candidates for matrix-type SR tablet formulation. FTIR and DSC compatibility studies provided no evidence of detrimental drug–excipient interactions, validating the selection of HPMC K100M, CMC, and Ethyl Cellulose as safe and compatible release-controlling polymers.

Direct compression was selected as the manufacturing method because it avoids the risk of drug degradation from moisture or elevated temperatures that can occur during wet granulation, and because the micromeritic properties of the blend (Carr's index 20%, angle of repose 32°) — while at the lower end of acceptable flow — were sufficiently manageable with the inclusion of talc and magnesium stearate as flow aids.

Post-compression evaluation revealed that all ten Ibuprofen and four Metformin formulations complied with pharmacopoeial specifications for weight uniformity and drug content. Hardness values across formulations (5.2–6.4 kg/cm²) were within the range recommended for oral tablets, with hardness trending upward as polymer concentration increased. This relationship is mechanistically consistent: higher HPMC content produces a denser, more cohesive tablet matrix.

Friability data showed that most formulations met the <1.0% criterion, with only F3 (1.2%) and F8 (1.3%) marginally exceeding the threshold. These slight exceedances are attributed to the

reduced MCC content in high-polymer formulations. Future optimization might increase MCC or compression force in these batches to bring friability within specification.

The disintegration data clearly illustrated the inverse relationship between HPMC concentration and tablet disintegration rate: F1 (50 mg HPMC) disintegrated in 45 minutes, whereas F4 (125 mg HPMC) required 90 minutes. This 2-fold increase in disintegration time with a 2.5-fold increase in polymer concentration highlights the non-linear, concentration-dependent swelling kinetics of HPMC–water systems, and underscores HPMC's effectiveness as a release-retarding excipient at the concentrations studied.

The dissolution results were the most clinically informative outcome of this study. Achieving approximately 96–98% cumulative drug release over 12 hours, with a near-linear release profile between 2 and 10 hours, is precisely the kinetic target for a twice-daily oral SR formulation. This profile is contrasted with conventional Ibuprofen IR tablets, which typically release >80% of their drug content within 30–60 minutes. The SR formulations developed here would be expected to maintain plasma Ibuprofen concentrations within the therapeutic range for 6–8 hours after a single dose, potentially halving the required daily dosing frequency.

For Metformin, the sustained release profile addresses the root cause of its principal adverse effect: GI intolerance arises primarily from high luminal drug concentrations that occur after rapid dissolution of conventional IR tablets in the proximal small intestine. By distributing drug release across the entire intestinal transit time, the SR matrix reduces peak luminal concentrations and their associated mucosal irritation, which aligns with published clinical data showing superior tolerability of extended-release Metformin formulations.

## IX. CONCLUSION

This investigation successfully demonstrated that sustained release matrix tablets of Ibuprofen (200 mg) and Metformin HCl (500 mg) can be reliably manufactured by direct compression using HPMC K100M and CMC as hydrophilic release-retarding polymers. All formulations met established pharmacopoeial criteria for weight uniformity, hardness, and drug content. In-vitro dissolution profiles confirmed sustained, near-linear drug release over 12 hours for both APIs, with release following anomalous (non-Fickian) diffusion kinetics mediated by simultaneous polymer swelling, drug diffusion, and matrix erosion.

Higher HPMC concentrations produced harder tablets with significantly extended disintegration times and slower drug release rates, providing a rational basis for fine-tuning the release profile to meet target pharmacokinetic requirements. The optimized formulations — characterized by ~96% Ibuprofen release and ~98% Metformin HCl release at 12 hours — represent clinically viable candidates for once or twice-daily oral administration. If translated to clinical practice, such formulations could meaningfully reduce pill burden, minimize GI adverse effects, maintain stable therapeutic plasma concentrations, and ultimately improve adherence and outcomes in patients with chronic inflammatory or metabolic conditions.

Future work should explore in vivo pharmacokinetic studies in appropriate animal models, stability testing under ICH-recommended accelerated conditions, and scale-up feasibility to validate the formulation's commercial potential.

Declarations

Conflict of Interest: The authors declare no conflict of interest.

Funding: This study received no external funding. All experimental work was conducted as part of the B.Pharm final-year project at Bansal College of Pharmacy, Bhopal, India.

Ethical Approval: Not applicable (in-vitro study; no human participants or animals).

Acknowledgements: The authors gratefully acknowledge the support of the faculty and laboratory staff of the Department of Pharmacy, Bansal College of Pharmacy, Bhopal.

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