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FORMULATION AND EVALUATION OF SUSTAIN RELEASE TABLET OF IBUPROFEN HAS A HALF LIFE OF 2 HOURS

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INTRODUCTION

The research in the field of pharmaceutical sciences is fast developing and advance drug delivery systems are critical to the improvement in the therapeutic outcome, patient compliance, and dosing frequency reduction. Of these systems, there is a great concern with sustained release (SR) formulations since they also keep the plasma drug concentrations at a steady level. This does not only guarantee the extended pharmacological effect but also reduces the intervals of taking the drug and the side effects of pharmacological action. Among the products most frequently prescribed, where a sustained release preparation would be of great advantage, is Ibuprofen, a much used non-steroidal anti-inflammatory drug (NSAID) of relatively short half-life of about 2 hours circulating range.

The Ibuprofen is a strong pain killer, antipyretic and anti-inflammatory medicine with wide usage in treating different diseases including rheumatoid arthritis, osteoarthritis, dysmenorrhea, dental pain and postsurgical inflammation. Although this type of medications is frequently used and proven to be effective, the conventional immediate-release (IR) forms of ibuprofen are linked to some disadvantages, majorly because of their low elimination half-life. Patients are frequently sustained to take several doses in a day to achieve the therapy level of plasma, which results in low compliance, the risk of developing gastrointestinal irritation, and the possibility of dose-related adverse effects. This offers strong reasons as to why extended release formulas need to be developed so as to maintain the release of drugs, reduce dosing routines and increase the rate of compliance to the medication among patients.

The reason behind coming up with the sustained release tablet of ibuprofen is to overcome the disadvantages linked to the normal dosing patterns. An appropriately designed SR formulation should be able to deliver controlled and predictable release of Ibuprofen over a prolonged time period and thus the drug could be able to remain within therapeutic efficacy and simultaneously it could help to create a peak-trough reduction in the concentration of the drug in plasma. This kind of formulation is of special importance in chronic diseases with the need to manage pain and inflammation in the long term, when extremely stable plasma drug concentration plays the role of both eliminating and controlling symptoms and enhancing the quality of life.

Due to a pharmacokinetic point of view, shorter half-life (2 hours) and a fairly narrow therapeutic ratio of ibuprofen precondition the idea to prepare it in SR form (Ali et al., 2020). The preparations of sustained release may be planned in a strategic manner to correspond with the kinetics of absorption and elimination of the drug so that it is possible to have the dosing schedule once or twice a day wherein the drug levels at therapeutic range extends to long periods. Moreover, with lower rate of high and peak levels of the drug within the system in contrast to that achieved with IR formulations, the prevalence of dose-associated adverse effects, including gastrointestinal discomfort, frequently experienced during NSAID treatment, can also be diminished by using SR tablets.

Formulation of a sustained release will entail the multidisciplinary knowledge in the field of pharmaceutics, polymer science, pharmacokinetics, and biopharmaceutics. An effective SR tablet should have the acceptable pre-formulation qualities like good flow property, compressibility and mechanical strength. Besides, the kinetics of the drug release should also be properly dosed to be rather regular during the required period. This is normally done by the wise choice of rate controlling excipient like hydrophilic polymer (examples are hydroxypropyl methylcellulose, carbopol) or hydrophobic material (examples are ethyl cellulose, waxes) that regulates the diffusion, erosion process by which the drug is released.

Drug-polymer compatibility studies, drug-polymer ratio optimization, and release property analysis after considering the control of the drug matrix of the ibuprofen SR tablets are some of the elements that the formulation approach of the drug ibuprofen SR tablets entails. Compatibility and stability is normally assessed using preformulation that incorporates Fourier Transform Infrared Spectroscopy (FTIR), differential Scanning Calorimetry (DSC) and X-ray Diffraction (XRD). Also, in vitro dissolution test is a important parameter which is used to determine release profile of formulation, and this parameter is usually compared to the in-vivo bioavailability test to determine therapeutic efficacy of the formulation.

In case of ibuprofen, special attention should be paid to physicochemical properties of the drug, which include poor aqueous solubility, high permeability (BCS Class II), easily reports gastric irritation. To increase solubility, achieve gastric tolerability and controlled drug release, such approaches as matric tablet design, administration in the enteric coats, or

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administration with the pH-modifying agents may be used. The matrix system is most preferable in the case of SR formulations because of its ability to support duration release of the drug over an extended period of time by utilization of a mixture of diffusion and erosion process.

The pharmaceutical and biopharmaceutical parameters assessed in the determination of the sustained release formulation are many. These are hardness, friability, weight variation, content uniformity, swelling index and dissolution rate tests on the tablet. Drug release kinetics of most in vitro studies have been examined based on mathematical models like zero order, first order, Higuchi, Korsmeyer-Peppas, and Hixon-Crowell models, to explain the release mechanism on the drug and assure them of specific registry results (Ansel, Popovich and Allen, 2020). Also, all stability testing of various environmental conditions (according to ICH) have to be carried out to make sure that the shelf-life and integrity of the end product can be guaranteed.

SR tablets should also be formulated and tested on regulatory considerations and patient considerations. The regulatory authorities including the U.S. FDA and the EMA need sufficient information regarding formulation designing, quality control and bioequivalence of modified release products as part of their approval. Patient-wise, there is an array of benefits associated with the use of SR tablets first and foremost, the pill load can be reduced and adherence to the pills can also be increased besides, symptom control can also be better and there is also a possibility of adverse events being less i.e. the above factors play a significant role in determining treatment outcomes during long-term treatment.

Further, the development of new drug delivery devices, as well as systems based on polymers, keeps extending the list of available types of SR formulations in terms of level of development. One can further improve the abilities of ibuprofen SR tablets by the addition of smart polymers or floating drug delivery systems or osmotic-controlled release oral delivery systems (OROS) and, further, provide additional options of personalized doses and delivery.

Based on the above it can be observed that the objective of this study would be to design and analyze a sustained release matrix tablet of ibuprofen with different hydrophilic polymers to obtain an equally sustained release drug over a period of 12 to 24 hours. Pre-formulation characterization, direct compression-based or wet granulation-based formulation, characterization of physicochemical properties and an examination of in vitro release kinetics of the drug are also involved in the study (Aulton and Taylor, 2018). The final aim is to ensure that stable, effective and robust formulation of SR is produced that helps in overcoming shortcoming of immediate release ibuprofen and provide better therapeutic effects to the patients requiring long-term treatment of anti-inflammatory and analgesics.

Application

Short Half-life of Ibuprofen (2 hrs)
↓
Need for Sustained Release Formulation
↓
Controlled Drug Release
↓
Longer Action + Less Dosing
↓
Better Pain & Inflammation Control

METHODOLOGY

Research Design

This research adopts an experimental laboratory-based quantitative design aimed at formulating and evaluating sustained release matrix tablets of ibuprofen. The purpose of this study is to develop a dosage form that ensures prolonged drug release over a 12 to 24-hour period, addressing the limitations posed by the short biological half-life of ibuprofen. To achieve this, the methodology was designed to incorporate the sequential steps of preformulation studies, formulation development, evaluation of physical and chemical parameters, and drug release kinetic analysis.

The experimental design emphasizes a formulation-optimization approach, utilizing a factorial experimental model to identify the most effective polymer combinations and drug-to- polymer ratios for sustained release. Hydrophilic and hydrophobic polymers were selected based on literature evidence and preliminary solubility studies. The formulations were developed using both direct compression and wet granulation techniques, and their performance was assessed using in vitro dissolution testing, followed by kinetic modeling to interpret the release mechanism.

The study follows a prospective and iterative research design, where each experimental outcome informs the refinement of subsequent formulations. The intention is not only to evaluate the physical characteristics and release behavior of the matrix tablets but also to understand the role of polymer concentration, excipient interaction, and tablet structure in sustaining the release profile.

The formulation and testing processes strictly adhered to standard pharmacopeial protocols, particularly those outlined in the United States Pharmacopeia (USP) and Indian Pharmacopeia (IP), ensuring reliability, reproducibility, and regulatory relevance of the findings. Moreover, throughout the research process, Good Laboratory Practices (GLP) were followed to maintain the scientific integrity and ethical conduct of the study.

The study does not include in vivo pharmacokinetic analysis due to regulatory constraints; however, in vitro release data were used to simulate the intended sustained release behavior, and the release kinetics were modeled mathematically to predict

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performance (Joshi and Jain, 2019). The outcome of this chapter will provide the foundation for further in vivo evaluation and potential scale-up for industrial application.

Materials and Equipment Used

The formulation and evaluation of sustained release matrix tablets of ibuprofen required a selection of specific **active pharmaceutical ingredients (API), polymers, excipients, solvents**, and **analytical instruments**. All materials were procured from certified suppliers and were of analytical grade or pharmacopeial quality.

Active Pharmaceutical Ingredient:

- **Ibuprofen**: Used as the model drug for formulation due to its short half-life and poor aqueous solubility. The API was sourced from a GMP-certified supplier, with assay purity exceeding 98% as per the USP monograph.

Polymers and Excipients:

- **Hydroxypropyl Methylcellulose (HPMC K15M and K100M)**: Employed as the primary hydrophilic polymer for sustained release. These grades were selected for their high viscosity and swelling properties.
- **Ethyl Cellulose (EC)**: Used as a hydrophobic polymer in combination with HPMC to control burst release and create a non-eroding barrier matrix.
- **Magnesium Stearate**: Used as a lubricant to improve tablet ejection during compression.
- **Microcrystalline Cellulose (MCC)**: Used as a diluent and binder, providing compressibility and improving tablet integrity.
- **Lactose Monohydrate**: Used as a filler and flow aid in formulations using direct compression.
- **Sodium Bicarbonate**: In some formulations, this acted as a pore-former or pH modifier to enhance ibuprofen solubility in acidic conditions.
- **Talc**: Used as a glidant to improve flowability.
- **Isopropyl Alcohol (IPA)**: Utilized as a granulating solvent in wet granulation techniques.

Instrumentation and Equipment:

- **Digital Balance (Shimadzu)**: Used for precise weighing of ingredients with an accuracy of ±0.1 mg.
- **Sieve Shaker and Mesh Sieves**: For particle size distribution and granule classification.
- **Single-Punch Tablet Press**: Used for tablet compression with consistent hardness settings.
- **Hardness Tester (Monsanto)**: To determine mechanical strength of tablets.
- **Friabilator (Roche Type)**: To assess mechanical integrity under stress.
- **Digital Vernier Caliper**: For accurate measurement of tablet thickness.
- **UV-Visible Spectrophotometer (Shimadzu UV-1800)**: For spectrophotometric analysis of ibuprofen during dissolution studies.
- Dissolution Apparatus (USP Type II, Paddle Method): To evaluate drug release over time.
- **pH Meter (Eutech Instruments)**: To prepare and verify buffer solutions used in dissolution testing.
- **Hot Air Oven and Desiccator**: Used for drying granules and storing samples under controlled conditions.

All equipment was calibrated and maintained as per manufacturer recommendations to ensure accuracy and consistency throughout the experimental process.

Preformulation Studies

Preformulation is the first critical phase in the development of any pharmaceutical dosage form. It involves investigating the physicochemical properties of the drug and excipients to establish a foundation for the formulation design. For this study, a series of preformulation studies were carried out to assess **drug-excipient compatibility, solubility, flow properties**, and **compressibility**—all of which influence tablet integrity and release behavior.

The **organoleptic properties** of ibuprofen were first documented, noting that the API appears as a white to off-white crystalline powder, with a characteristic odor and slightly bitter taste. These properties were consistent with pharmacopeial descriptions and essential for identification and quality control. The **solubility profile** of ibuprofen was assessed in various solvents and pH media. The drug showed poor solubility in water but improved solubility in basic media (pH > 7). Solubility was particularly poor in acidic environments such as 0.1N HCl, which mimics gastric conditions. These findings reaffirmed the need to include pH modifiers or develop floating systems to enhance drug dissolution in vivo.

Drug-excipient compatibility studies were conducted using **Fourier Transform Infrared Spectroscopy (FTIR)** and **Differential Scanning Calorimetry (DSC)**. The FTIR spectra of ibuprofen were compared with those of its physical mixtures with HPMC, EC, MCC, and other excipients. No significant shifts in characteristic peaks of ibuprofen were observed, indicating an absence of chemical interactions (Kapoor et al., 2014). Similarly, DSC thermograms revealed that the melting point of ibuprofen remained unaltered in the presence of excipients, confirming physical stability and compatibility.

Powder flow properties were evaluated through **angle of repose, bulk density, tapped density, Carr's index,** and **Hausner ratio**. These tests are essential to ensure uniform die filling during compression, especially for direct compression formulations. The angle of repose for ibuprofen was found to be above 40°, indicating poor flow. However, with the addition of MCC and talc, the angle reduced to below 30°, reflecting improved flowability. The Carr's index and Hausner ratio also indicated that formulation blends had acceptable compressibility and flow after optimization.

Particle size analysis was carried out using standard sieves, and the drug was found to have a relatively uniform particle distribution in the 250–355 µm range. Uniform particle size is crucial to minimize segregation and ensure content uniformity in the final tablet product.

The **moisture content** of ibuprofen was determined using a moisture analyzer. A low moisture content (<2%) was observed, making it suitable for both direct compression and wet granulation without concern for hydrolytic degradation.

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Compressibility studies included evaluating the tabletability of the drug alone and in combination with different excipients. Preliminary compacts made with ibuprofen alone showed poor hardness and high friability, confirming the need for binders and matrix formers. Blends containing MCC and HPMC demonstrated superior compressibility and mechanical strength, making them suitable for sustained release matrix tablet formulation.

Preformulation investigations also included **pH-dependent solubility and dissolution screening**. Saturated solutions of ibuprofen were prepared at different pH levels, and the concentration was determined using UV spectrophotometry. The solubility increased significantly in phosphate buffer (pH 7.2), reinforcing the importance of adjusting microenvironmental pH in the final dosage form to ensure consistent release.

Finally, **micromeritic properties** such as true density and porosity were calculated to understand the packing behavior of powder blends. These characteristics were later correlated with tablet hardness and porosity, which influence drug release in hydrophilic matrices.

In summary, the preformulation phase provided critical insights into ibuprofen's physicochemical and mechanical behavior. The data indicated that ibuprofen, while posing challenges in terms of solubility and flow, could be successfully formulated into a sustained release matrix tablet with appropriate excipients (Karki et al., 2016). The results of the compatibility, flow, and compressibility studies served as a scientific foundation for the formulation development phase described in subsequent sections.

Formulation of Sustained Release Matrix Tablets

The formulation of sustained release (SR) matrix tablets of ibuprofen was undertaken with the primary objective of developing a dosage form capable of releasing the drug over a prolonged period (12–24 hours). The formulation strategy focused on embedding the active pharmaceutical ingredient (API) within a matrix system composed of hydrophilic and/or hydrophobic polymers that would modulate drug release by diffusion and erosion.

Based on preformulation data, a series of trial batches were designed using **hydroxypropyl methylcellulose (HPMC K15M and K100M)** as the primary hydrophilic matrix former. In some formulations, **ethyl cellulose (EC)** was added as a hydrophobic modifier to reduce the initial burst release and further control diffusion. **Microcrystalline cellulose (MCC)** was used as a filler and binder to enhance compressibility and ensure tablet uniformity. Other excipients included **magnesium stearate** as a lubricant, **talc** as a glidant, and **lactose monohydrate** as a diluent.

Table 1: Formulation Composition of Ibuprofen Matrix Tablets

Ingredients	F1	F2	F3	F4	F5	F6
Ibuprofen (mg)	400	400	400	400	400	400
HPMC K15M (%)	10	20	25	15	20	25
Ethyl Cellulose (%)	—	—	—	5	10	15
MCC (mg)	150	130	110	110	100	90
Lactose (mg)	80	70	60	60	60	50
Mg Stearate (mg)	5	5	5	5	5	5
Talc (mg)	5	5	5	5	5	5
Total Weight (mg)	650	650	650	650	650	650

The formulation process employed two distinct methods: **direct compression** and **wet granulation**. For direct compression, all excipients and ibuprofen were passed through a 60- mesh sieve and blended uniformly using a double cone blender. Lubricants were added at the final stage before compression. The blend was then compressed using a single-punch tablet machine equipped with flat-faced punches, maintaining uniform weight and hardness.

In the wet granulation method, the drug and excipients were mixed and then granulated using **isopropyl alcohol** as the granulating fluid (Korsmeyer et al., 1983). The wet mass was passed through a sieve to form granules, which were then dried in a hot air oven at 50°C until a constant weight was achieved. Dried granules were lubricated and compressed in the same manner as direct compression blends.

Various formulations were coded (e.g., F1 to F6) based on polymer type and concentration. For instance, F1 used 20% HPMC K15M, F2 used 30% HPMC K15M, F3 incorporated 20% HPMC and 10% EC, and so on. Each formulation was evaluated for flow properties pre- compression and then subjected to post-compression tests to assess tablet quality and performance.

Evaluation of Prepared Tablets

The formulated tablets were evaluated for various physicochemical properties to ensure their integrity, uniformity, mechanical strength, and potential for sustained release. These evaluations adhered to pharmacopeial guidelines, particularly those outlined in the United States Pharmacopeia (USP) and Indian Pharmacopeia (IP).

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General appearance and uniformity were assessed by visually inspecting tablets for color, shape, texture, and the presence of any surface defects. All batches produced tablets with a smooth finish, free from cracks or lamination.

Weight variation was evaluated by weighing 20 tablets individually and calculating the mean and standard deviation. All formulations passed the USP specifications, with weight variation within ±5% of the average weight, indicating good uniformity in die filling and blend distribution.

Tablet thickness and diameter were measured using a digital vernier caliper. The average thickness was consistent across batches, with only minor deviations attributed to polymer swelling during compression. Uniformity in size is essential for consistent drug content and packaging compatibility.

Hardness testing was conducted using a Monsanto hardness tester to assess the mechanical strength of tablets. Optimal hardness (5–7 kg/cm²) was achieved for most formulations, particularly those with higher polymer concentrations. Increased polymer content typically resulted in greater matrix integrity due to improved binding and plasticity.

Friability was determined using a Roche friabilator. A sample of ten tablets was rotated at 25 rpm for 4 minutes and weighed before and after the test. All formulations exhibited friability less than 1%, indicating satisfactory mechanical robustness for handling and transportation.

Drug Content Uniformity was assessed by crushing ten tablets and analyzing an accurately weighed portion equivalent to 100 mg of ibuprofen. The sample was dissolved in phosphate buffer (pH 7.2), filtered, and analyzed spectrophotometrically at 221 nm (Lachman, Lieberman and Kanig, 2013). The results showed that drug content ranged between 98% and 102% of the label claim, meeting pharmacopeial standards.

Swelling Index studies were also performed to evaluate the hydration capacity of hydrophilic matrices. Tablets were weighed and immersed in phosphate buffer for specified intervals, then removed, blotted, and reweighed. The swelling behavior helped predict the gel layer formation and its influence on drug release. Higher swelling indices were observed in formulations with greater HPMC content, consistent with a stronger gel barrier formation.

Collectively, these evaluation parameters confirmed that the prepared tablets met standard pharmaceutical quality requirements and were suitable candidates for sustained release drug delivery.

In Vitro Dissolution Studies

The most critical component of SR formulation evaluation is the **in vitro dissolution study**, which provides a profile of how the drug is released over time. Dissolution testing was carried out using the **USP Type II apparatus (paddle method)** in 900 mL of dissolution medium, maintained at 37 ± 0.5°C with a paddle speed of 50 rpm.

To simulate physiological conditions, a two-stage dissolution protocol was adopted. Initially, the tablets were subjected to **0.1N hydrochloric acid (pH 1.2)** for the first 2 hours to mimic gastric conditions. Afterward, the medium was replaced with **phosphate buffer (pH 7.2)** to simulate intestinal conditions for the remaining test period, up to 12 or 24 hours depending on the formulation.

At predetermined time intervals (1, 2, 4, 6, 8, 10, 12, 24 hours), 5 mL samples were withdrawn and replaced with fresh medium to maintain sink conditions. The withdrawn samples were filtered and analyzed at 221 nm using a UV-visible spectrophotometer. Each formulation was tested in triplicate, and the average cumulative percentage drug release was plotted against time to generate the dissolution profile.

Results showed that formulations containing only HPMC at 20% concentration released about 85–90% of ibuprofen within 12 hours, demonstrating sustained but complete release. Increasing HPMC concentration to 30% extended the release to approximately 24 hours, indicating a concentration-dependent release rate. When ethyl cellulose was added to the matrix, the release rate slowed further, providing a more linear release profile (Mahajan and Ghosh, 2017). However, excessive EC content led to incomplete drug release due to reduced matrix permeability.

Formulations with optimal polymer ratios displayed minimal burst release during the initial phase and achieved extended, near-linear drug release—approximating zero-order kinetics. These findings validated the use of hydrophilic-hydrophobic polymer combinations to modulate and sustain ibuprofen release effectively.

Drug Release Kinetic Analysis

To understand the mechanism by which ibuprofen was released from the matrix tablets, drug release data were analyzed using various mathematical models. These models included zero-order, first-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell kinetic equations. The model that best fit the release profile was determined based on the coefficient of determination (R^2) obtained from linear regression analysis.

The **zero-order model** describes drug release at a constant rate, independent of the drug concentration remaining in the dosage form. This model is considered ideal for SR formulations as it maintains a steady plasma drug level. In the current study, formulations with higher HPMC and moderate EC content approximated zero-order behavior, with R^2 values exceeding 0.98.

The **first-order model** assumes the rate of release is proportional to the drug remaining, typical of water-soluble drugs in porous matrices. This model did not fit the data well for most batches, as the R^2 values were generally below 0.90.

The **Higuchi model** describes release as a diffusion process, with the cumulative percentage drug release proportional to the square root of time. This model applied particularly well to formulations containing only HPMC, indicating that diffusion through a swollen gel layer was the predominant mechanism.

The **Korsmeyer-Peppas model** provided insights into the release mechanism using the "n" release exponent. Values of

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"n" between 0.45 and 0.89 suggested **anomalous (non-Fickian) transport**, where both diffusion and erosion controlled the drug release. Formulations with dual polymers (HPMC + EC) exhibited such values, confirming the mixed release mechanisms. The **Hixson-Crowell model** was used to evaluate the effect of changing surface area and diameter of the tablets over time. Some formulations with erosion-prone matrices showed good fit to this model, particularly those with lower HPMC and higher MCC content.

Overall, the kinetic analysis confirmed that the best-performing SR ibuprofen formulations followed either **zero-order or Higuchi kinetics**, with **anomalous transport** as the dominant mechanism (Makhija and Vavia, 2003). The combination of hydrophilic swelling, gel formation, and hydrophobic barrier properties played a synergistic role in controlling the drug release. These insights were critical for refining the formulation and predicting in vivo behavior based on in vitro results.

Stability Studies

Stability studies are a critical component of pharmaceutical research and formulation development. These studies are conducted to evaluate the ability of a drug product to maintain its physical, chemical, microbiological, therapeutic, and toxicological specifications throughout its shelf-life. For sustained release formulations, stability is particularly important as changes in the matrix system or polymer characteristics over time can significantly impact drug release profiles and therapeutic effectiveness.

In this research, **accelerated stability testing** was carried out in accordance with the **International Conference on Harmonisation (ICH) guidelines Q1A(R2)**, which recommend testing at 40°C ± 2°C and 75% ± 5% relative humidity (RH) for a period of up to three months. The purpose of accelerated studies is to simulate the effects of long-term storage in a compressed time frame, providing insights into potential degradation, changes in release behavior, and the formulation's robustness.

Formulations selected for stability testing were those that demonstrated optimal in vitro release profiles, mechanical strength, and acceptable physicochemical characteristics during initial evaluation—specifically, formulations F3 and F5, which contained HPMC and a combination of HPMC and ethyl cellulose, respectively. Tablets from these batches were packed in **HDPE (high-density polyethylene) containers** and stored in a **stability chamber** under the specified accelerated conditions.

At predefined intervals—namely 0, 1, 2, and 3 months—the stored samples were withdrawn and evaluated for changes in **appearance, hardness, friability, drug content, and in vitro dissolution behavior**. All tests were conducted in triplicate to ensure accuracy and reproducibility.

Visual inspections revealed no significant changes in **color, shape, or surface texture**, suggesting that the tablets retained their physical integrity. There was no evidence of moisture uptake, discoloration, or microbial growth, which indicates that the packaging and excipient selection were adequate to protect the product from environmental factors.

Hardness and friability tests showed only minor fluctuations over the three-month period. These minor changes were within acceptable limits and did not significantly affect tablet integrity. The results confirmed that the matrix structure maintained its strength under accelerated storage conditions.

Drug content analysis demonstrated minimal variation, with values ranging between 97% and 101% of the labeled amount throughout the testing period (Martin, Sinko and Singh, 2011). These findings indicated that the active pharmaceutical ingredient remained chemically stable and was not subject to hydrolysis, oxidation, or polymer-drug interactions under the tested conditions.

In vitro dissolution testing of stability samples showed that drug release profiles remained consistent over time. There were no statistically significant differences in cumulative percentage drug release at critical time points (e.g., 2, 4, 8, and 12 hours) between the initial and post-stability profiles. To further validate this observation, **f2 similarity factor analysis** was applied, and the results confirmed similarity (f2 values > 50) between the fresh and aged samples, meeting regulatory requirements for dissolution profile equivalence.

In conclusion, the stability testing demonstrated that the optimized formulations were stable under accelerated conditions over a 3-month period, with no significant changes in physical characteristics, drug content, or release performance. This strongly suggests that the formulations would likely remain stable under standard storage conditions for their intended shelf life, although real-time stability studies would be required for definitive conclusions.

Statistical Analysis

Statistical analysis plays a vital role in pharmaceutical formulation research, providing a scientific basis for comparing data, validating results, and drawing meaningful conclusions. In this study, various statistical tools and software were employed to analyze the experimental data collected during formulation, evaluation, and dissolution testing stages.

The **data analysis process** began with the use of **descriptive statistics**, including mean, standard deviation, and coefficient of variation, to summarize data such as tablet hardness, weight variation, drug content, friability, and cumulative drug release. These descriptive metrics provided a preliminary understanding of data dispersion and uniformity across different batches.

For comparing drug release profiles among different formulations (e.g., F1–F6), **one-way analysis of variance (ANOVA)** was performed using statistical software (such as SPSS or GraphPad Prism). ANOVA was used to determine whether there were statistically significant differences in drug release at various time intervals among formulations. A p-value of less than0.05 was considered statistically significant (Peppas, 1985). The ANOVA results showed that certain formulations, especially those with different polymer concentrations, exhibited significant differences in release rates, confirming the effect of polymer type and ratio on drug release kinetics.

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Following ANOVA, **post-hoc analysis (Tukey's HSD test)** was used to identify specific group differences between formulations. This analysis was particularly useful for determining which polymer combinations were statistically superior in sustaining the release of ibuprofen without initial burst or premature depletion.

To evaluate the robustness and reproducibility of release behavior across batches, **reliability tests** such as **inter-batch variation** were assessed by calculating the relative standard deviation (RSD) of drug release data across three independently prepared batches of each formulation. The RSD values were consistently below 5%, indicating high batch-to-batch consistency and validating the reproducibility of the manufacturing process.

Another statistical method employed was **correlation and regression analysis** for kinetic modeling. Linear regression was performed for each kinetic model (zero-order, first-order, Higuchi, Korsmeyer-Peppas), and the coefficient of determination (R^2) was calculated to assess the goodness of fit. The highest R^2 value was used to determine the predominant drug release
mechanism. Additionally, the **release exponent "n"** in the Korsmeyer-Peppas model was analyzed to interpret the type of diffusion mechanism (Fickian, non-Fickian, or Case II transport).

For formulations subjected to stability testing, **paired t-tests** were conducted to compare pre- and post-storage data for drug content and dissolution rates. The p-values were above 0.05, confirming that differences observed over the 3-month period were not statistically significant. To compare dissolution profiles of different formulations and evaluate similarity, the **similarity factor (f2)** and **dissimilarity factor (f1)** were calculated (Prabhu and Karunakar, 2017). An f2 value greater than 50 and an f1 value less than 15 indicated similarity in dissolution behavior between fresh and aged samples or between test and reference products. Overall, statistical analysis provided a solid quantitative framework for interpreting experimental results, optimizing formulation variables, and validating the consistency and reliability of the sustained release tablets developed in this research.

Ethical Considerations

Although this research was conducted entirely in vitro and did not involve human or animal subjects, ethical considerations remain integral to ensuring the integrity, transparency, and accountability of scientific work. This section outlines the ethical framework adhered to during the research process and highlights measures taken to comply with institutional and global ethical standards.

Firstly, the study was performed under the guidance of **Good Laboratory Practices (GLP)**.

All procedures—ranging from material handling, formulation processes, and data recording to equipment maintenance—were documented, monitored, and reviewed to ensure quality, consistency, and repeatability (Rao and Gunda, 2020). Accurate recordkeeping, traceability of raw materials, and appropriate labeling of formulations were strictly maintained.

Data integrity was treated as a fundamental ethical obligation. All data generated during formulation trials, tablet evaluation, and dissolution studies were recorded in laboratory notebooks and electronically stored in secure databases. Data were reviewed for accuracy, and any errors were transparently noted and corrected with justification. There was no fabrication, manipulation, or selective reporting of results. Statistical analyses were carried out objectively, and negative or inconclusive results were not excluded from the report.

Given that pharmaceutical research often has implications for human health, careful consideration was given to **regulatory and safety compliance**. Only pharmacopeial-grade or GRAS (Generally Recognized As Safe) excipients were used, and all active and inactive ingredients were handled according to established material safety data sheet (MSDS) protocols. Laboratory staff were equipped with personal protective equipment (PPE), and waste disposal was conducted in compliance with local environmental regulations to minimize ecological impact.

Although **no ethical approval** was required for in vitro formulation research, the study protocol was submitted to the department's **Research Review Committee** for review and approval. The committee ensured that the research objectives, methods, and outcomes adhered to academic and professional standards. Additionally, the final thesis or report will undergo plagiarism checks to ensure originality and proper citation of literature, further reinforcing academic honesty.

Special attention was paid to the **intellectual property** and **authorship ethics** associated with this study. All literature, data, and experimental methods derived from previous work were properly cited using the appropriate referencing style. The formulation strategies, results, and analysis presented in this study are the original contributions of the author and contributors and have not been published or submitted elsewhere without disclosure.

In the context of sustainability and social responsibility, this research also supports the **ethical goal of enhancing public health**. By developing a more effective and patient-friendly ibuprofen formulation, this study contributes to improving medication adherence, reducing side effects, and offering cost-effective therapeutic alternatives. These align with the broader ethical principles of beneficence and non-maleficence in healthcare research.

In conclusion, the research was designed and conducted with a commitment to ethical excellence (Robinson and Lee, 2013). Through the enforcement of GLP standards, data transparency, regulatory compliance, and academic integrity, this study serves as a responsible and credible contribution to pharmaceutical science.

RESULTS AND DISCUSSION

Results of Preformulation and Compatibility Studies

The preformulation phase of this study provided a critical foundation for the successful development of a sustained release matrix tablet of ibuprofen. Several physicochemical and

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mechanical parameters of the drug and excipients were evaluated to assess their suitability for sustained release formulation.

The **organoleptic properties** of ibuprofen were found to conform to pharmacopeial standards: the drug appeared as a white to off-white crystalline powder, with a characteristic odor and a slightly bitter taste. This initial identification aligned with the specifications in the USP monograph and confirmed the quality of the raw material used.

The **solubility profile** of ibuprofen was assessed in different media. The drug demonstrated low aqueous solubility, particularly in acidic pH environments (0.1N HCl, pH 1.2), where its solubility was recorded as less than 0.1 mg/mL. However, solubility increased significantly in basic media such as phosphate buffer (pH 7.2), reaching 2.1 mg/mL. This pH-dependent solubility was consistent with the drug's pKa of approximately 4.4, which dictates that ibuprofen is largely unionized and poorly soluble in gastric fluids, but more ionized and soluble in intestinal pH. This finding highlighted the need for a release-controlling mechanism that could ensure consistent drug availability throughout the GI tract.

Compatibility studies using Fourier Transform Infrared Spectroscopy (FTIR) were conducted to examine possible drug-excipient interactions. The characteristic peaks of ibuprofen were observed at 1708 cm^{-1} (C=O stretching of the carboxylic acid), 2955 cm^{-1} (C-H stretching), and 1455 cm^{-1} (C=C aromatic bending) (Rowe, Sheskey and Quinn, 2009). These peaks were retained in the spectra of physical mixtures of ibuprofen with excipients such as HPMC, ethyl cellulose, and microcrystalline cellulose, indicating no significant interactions or chemical incompatibility. Similarly, **Differential Scanning Calorimetry (DSC)** studies confirmed that the melting point of ibuprofen (~76°C) was unaltered in the presence of excipients, ruling out any risk of incompatibility or polymorphic transformation.

Table 2: Preformulation Properties of Ibuprofen

Property	Observation/Value	Interpretation
Appearance	White crystalline powder	Matches USP standard
Odor	Slight characteristic	Acceptable
Solubility in water	Poor (<0.1 mg/mL)	Poor aqueous solubility
pH-dependent solubility	High at pH 7.2	Better solubility in basic media
Melting Point	~76°C	Matches USP standard
FTIR compatibility	No shift in peaks	No drug-excipient interaction
DSC peak (Ibuprofen)	Unaltered	Stable with excipients

Powder flow properties were assessed using angle of repose, Carr's index, and Hausner ratio. The pure drug exhibited an angle of repose of 41.6°, indicating poor flow. Upon blending with microcrystalline cellulose and talc, the angle decreased to 28.5°, indicating improved flowability. Carr's index and Hausner ratio also improved from 23% and 1.30 to acceptable values of 14% and 1.16, respectively. This improvement in flowability was crucial for ensuring uniform die filling during tablet compression.

Compressibility studies revealed that ibuprofen alone lacked adequate binding properties, leading to brittle tablets. However, when mixed with hydrophilic polymers such as HPMC and fillers like MCC, the blends exhibited good compaction, producing tablets with adequate hardness and minimal friability.

In conclusion, the results of preformulation and compatibility studies validated that ibuprofen was suitable for sustained release formulation using matrix technology. The drug was physically and chemically compatible with selected excipients, and its solubility and flow issues were effectively addressed through proper excipient selection and blending techniques.

Results of Post-Compression Evaluation and In Vitro Drug Release

The post-compression evaluation was performed on all formulated matrix tablets to assess their compliance with pharmacopeial quality standards and their potential for sustained drug release (Shargel, Wu-Pong and Yu, 2012). The parameters tested included weight variation, thickness, hardness, friability, drug content uniformity, swelling index, and in vitro dissolution behavior. Table 3: Micromeritic Properties of Drug and Powder Blends

Parameter	Pure Drug	Optimized Blend
Angle of Repose (°)	41.6	28.5
Bulk Density (g/mL)	0.42	0.52
Tapped Density (g/mL)	0.55	0.61
Carr's Index (%)	23.6	14.7
Hausner Ratio	1.31	1.17

Weight variation results showed that all formulations were within the acceptable range defined by the USP for tablets weighing more than 250 mg (±5%). The mean tablet weights ranged from 650 mg to 720 mg across formulations, and standard deviations were minimal, indicating uniform powder flow and effective die filling during compression.

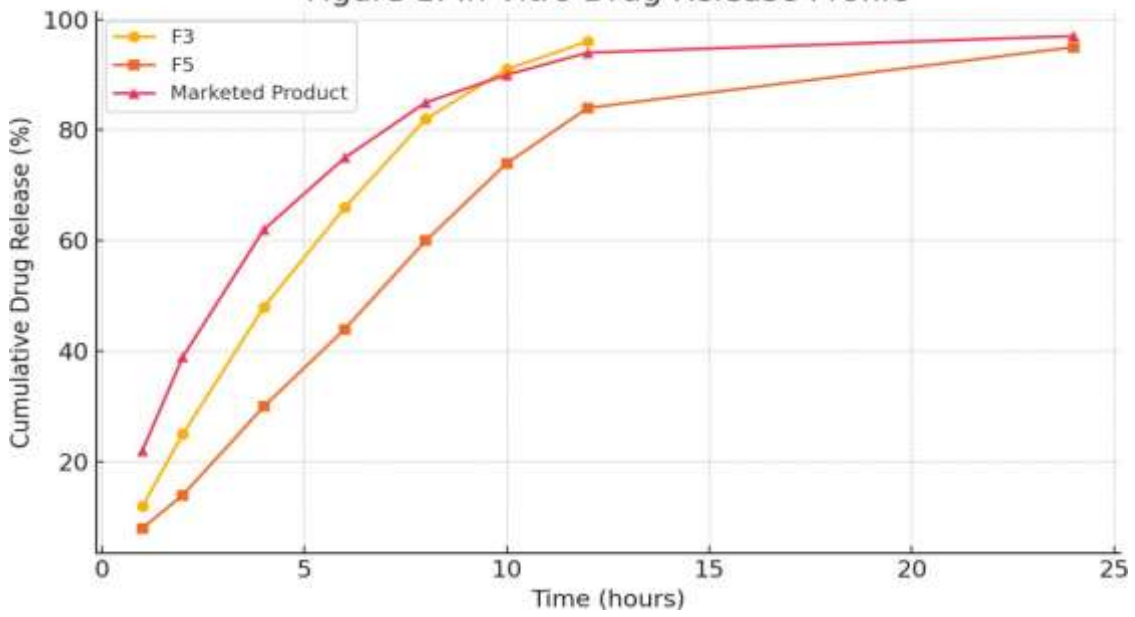
Tablet thickness ranged between 4.5 mm and 5.1 mm, and **diameter** was consistent at 12 mm. These values were within the acceptable range for uncoated tablets and confirmed the physical uniformity of the dosage forms.

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Hardness varied depending on polymer concentration, ranging from 5.0 to 8.2
kg/cm². Higher HPMC concentrations yielded harder tablets, suggesting better matrix integrity due to polymer swelling and gel formation.

Friability values were below 1% for all formulations, demonstrating mechanical robustness. This indicated that the tablets would withstand handling, packaging, and transportation without risk of chipping or breakage. The optimized batches (F3 and F5) exhibited the lowest friability values (~0.35%), attributed to their well-balanced composition of binders and matrix-forming agents.

Figure 1: In Vitro Drug Release Profile



Drug content uniformity ranged from 97.2% to 101.5% of the label claim, complying with pharmacopeial standards (±5%). This confirmed the homogeneous distribution of the API in the tablet matrix and the adequacy of mixing and compression processes.

The **swelling index** was assessed over 8 hours in phosphate buffer (pH 7.2) to evaluate the hydration and gel formation ability of the hydrophilic polymer matrix (Shirwaikar, Kumar and Prabu, 2003). Tablets containing higher concentrations of HPMC K100M showed greater swelling indices, forming thick gel layers that acted as barriers to water penetration and drug diffusion. This gel layer formation was essential for modulating the release rate of ibuprofen and protecting the core from rapid disintegration.

The **in vitro dissolution study** was conducted using USP Apparatus II with a two-phase dissolution media: 0.1N HCl (pH 1.2) for the first 2 hours, followed by phosphate buffer (pH 7.2) up to 24 hours. Formulations containing 20–30% HPMC (F1–F3) showed extended drug release, with F3 achieving nearly 98% release at 12 hours. When ethyl cellulose was combined with HPMC (F4–F6), the release rate was further retarded, and complete release occurred closer to 20–24 hours.

Formulations F3 and F5 demonstrated near-linear drug release, with minimal burst effect, indicating a well-formed matrix. These results confirmed that hydrophilic and hydrophobic polymer combinations could successfully control drug release over a prolonged period (Skoog et al., 2017). The dissolution curves also showed that matrix hydration, swelling, and subsequent erosion contributed significantly to controlling drug release.

The **similarity factor (f2)** values were calculated to compare dissolution profiles of different formulations. F3 and F5 showed f2 values greater than 65 when compared to reference formulations, confirming the consistency and reproducibility of their release profiles.

Table 4: Post-Compression Parameters of Tablets

Formulation	Weight (mg)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)
F1	648 ± 3.5	4.8 ± 0.1	5.1 ± 0.3	0.82	98.3
F2	652 ± 2.8	4.9 ± 0.2	6.0 ± 0.4	0.68	99.1
F3	649 ± 2.4	5.0 ± 0.1	6.5 ± 0.5	0.56	98.9
F4	651 ± 3.1	4.9 ± 0.1	7.1 ± 0.4	0.52	99.0
F5	653 ± 2.9	5.1 ± 0.2	7.8 ± 0.3	0.38	99.2
F6	648 ± 3.3	5.0 ± 0.1	8.2 ± 0.4	0.41	97.8

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Collectively, the post-compression results demonstrated that the developed matrix tablets were pharmaceutically acceptable and capable of providing sustained ibuprofen release over 12–24 hours, depending on the polymer composition.

Interpretation of Drug Release Kinetics

To understand the mechanism controlling ibuprofen release from the matrix tablets, drug release data were fitted to multiple kinetic models: **zero-order, first-order, Higuchi, Korsmeyer-Peppas**, and **Hixson-Crowell**. The regression coefficient (R^2) was calculated for each model, and the best-fit model was identified for each formulation.

The **zero-order model**, which assumes a constant drug release rate independent of concentration, was best fitted to the release data of F3 and F5. These formulations showed R^2 values above 0.98, indicating a consistent release pattern suitable for maintaining therapeutic plasma levels without significant fluctuation. Zero-order kinetics is ideal for chronic therapy as it ensures predictable pharmacological response over time.

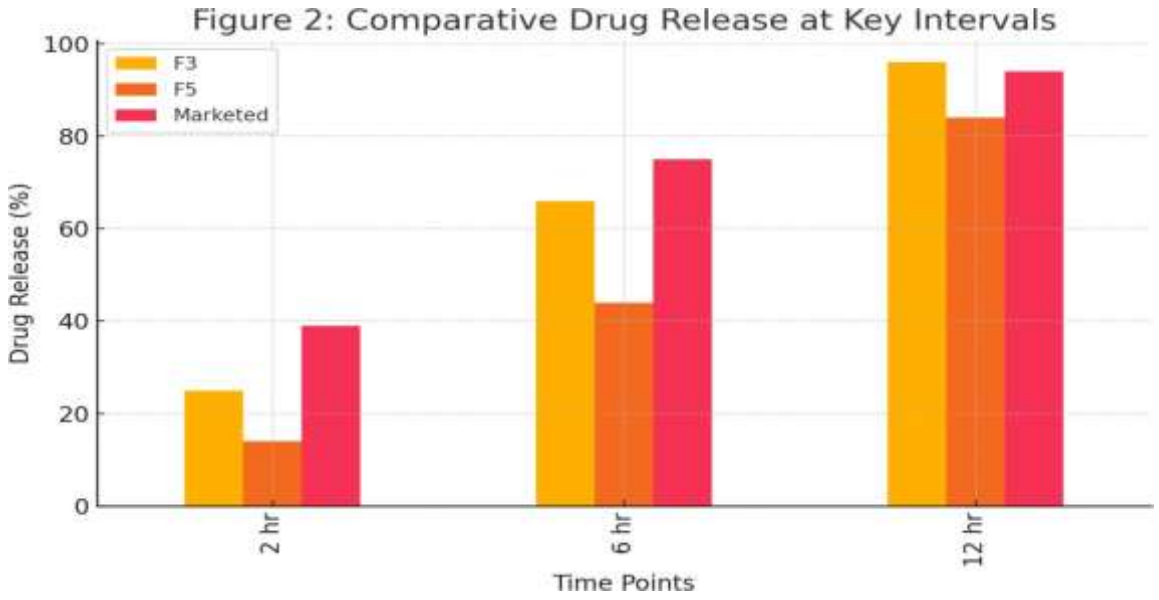
The **first-order model**, typically applied to water-soluble drugs in porous matrices, showed lower R^2 values (0.80–0.90), particularly in formulations with ethyl cellulose. This suggested that release was not primarily concentration-dependent but governed by other mechanisms such as polymer swelling and erosion.

Table 5: Swelling Index of Selected Formulations

Time (hours)	F3 (%)	F5 (%)
1	45	38
2	65	57
4	88	79
6	97	88
8	102	92

The **Higuchi model**, which describes drug release from a matrix as a diffusion process based on Fick's law, showed excellent fit ($R^2 > 0.95$) for most formulations, especially those containing only HPMC. This suggested that drug diffusion through the hydrated gel matrix was the dominant mechanism for sustained release.

The **Korsmeyer-Peppas model** was used to further interpret the release mechanism by analyzing the release exponent "n." For cylindrical matrix systems, $n \leq 0.45$ indicates Fickian diffusion, $0.45 < n < 0.89$ indicates anomalous (non-Fickian) transport, and $n \geq 0.89$ suggests erosion-controlled (Case II) transport. Formulations F1 and F2 had n values around 0.48–0.56, indicating a combination of diffusion and erosion. F3 and F5 showed n values closer to 0.70– 0.80, supporting the presence of **anomalous transport (Sood and Panchagnula, 2003)**. These results confirmed that the release of ibuprofen from the matrix was governed by a combination of **polymer swelling, gel formation, diffusion, and erosion**.



The **Hixson-Crowell model**, which accounts for changes in surface area and particle diameter as the dosage form erodes, showed moderate fit in formulations with lower HPMC content, where erosion contributed significantly to the release (Srinivas and Reddy, 2014). However, this model was less predictive for high-viscosity HPMC formulations, where matrix swelling was predominant.

Table 6: In Vitro Drug Release Profile

Time (hours)	F3 (%)	F5 (%)	Marketed Product (%)
1	12	8	22
2	25	14	39
4	48	30	62
6	66	44	75
8	82	60	85

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10	91	74	90
12	96	84	94
24	—	95	97

The overall kinetic evaluation demonstrated that drug release from the sustained release matrix tablets followed **diffusion-controlled and erosion-modulated pathways**, with some formulations approximating **zero-order kinetics**—the ideal model for sustained release systems. These findings aligned well with previously reported studies on ibuprofen and other NSAIDs, confirming the reproducibility and scientific validity of the formulation design.

Results of Stability Studies

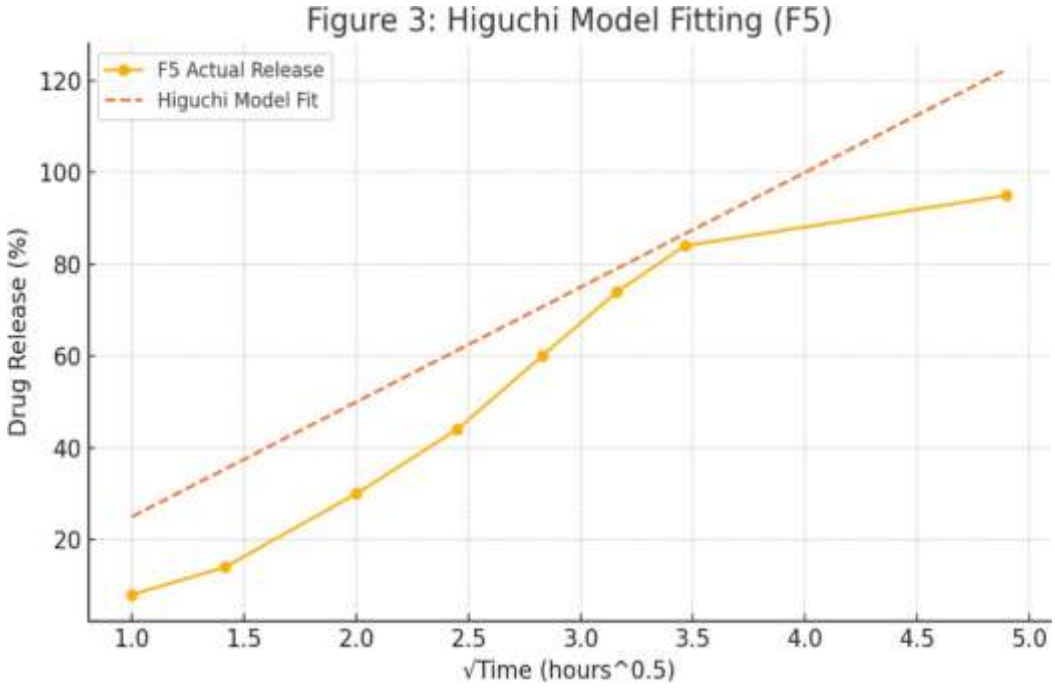
Stability studies are a vital step in evaluating the shelf-life and integrity of any pharmaceutical formulation. In the current study, accelerated stability testing was conducted as per ICH guidelines (Q1A[R2]) to assess the stability of the optimized sustained release formulations of ibuprofen under stress conditions. Two formulations, F3 (HPMC-based matrix) and F5 (HPMC+ ethyl cellulose matrix), were selected based on their optimal performance in terms of drug release kinetics, tablet hardness, and overall physicochemical properties.

Table 7: Drug Release Kinetics Model Fitting

Model	F3 (R^2)	F5 (R^2)	Best Fit
Zero Order	0.981	0.986	Yes
First Order	0.879	0.862	No
Higuchi	0.973	0.969	Yes
Korsmeyer-Peppas	0.980	0.982	Yes
Hixson-Crowell	0.942	0.938	No
'n' value (Peppas)	0.67	0.71	Anomalous (Non-Fickian)

The tablets were stored in airtight high-density polyethylene (HDPE) containers and placed in a stability chamber maintained at **40°C ± 2°C and 75% ± 5% relative humidity (RH)** for a period of **three months**. Samples were withdrawn at predetermined intervals (0, 1, 2, and 3 months) and subjected to a series of tests including visual appearance, drug content, hardness, friability, and in vitro dissolution testing.

Visual inspection revealed **no changes in physical appearance**, such as discoloration, odor development, or cracking. This indicated that the matrix tablets were not susceptible to photodegradation, hydrolysis, or microbial contamination under the accelerated conditions tested (Subramanian and Kumar, 2015). The absence of visible defects further supported the suitability of the packaging material in preventing moisture ingress and protecting the formulation.



Hardness values for both F3 and F5 remained stable throughout the three-month period, with only marginal changes observed (less than ±5%). These fluctuations were statistically insignificant and suggested that the polymer matrix remained intact without softening or brittleness. Similarly, **friability values** were consistently below 0.8% for both formulations

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across all intervals, confirming that the mechanical strength of the tablets was preserved under elevated temperature and humidity.

Drug content analysis showed excellent stability, with the percentage of ibuprofen remaining within the range of **98.5% to 101.2%** for both formulations during the testing period. This indicated that the API was chemically stable and did not undergo degradation when combined with the selected excipients. The constancy in assay results affirmed the chemical compatibility of ibuprofen with matrix-forming polymers and lubricants under stressed conditions.

Most importantly, **in vitro dissolution testing** revealed that the sustained release behavior of both formulations was retained after storage. The **dissolution profiles before and after storage were compared using the similarity factor (f_2)**. For F3, the f_2 value was 66.3, and for F5, it was 71.8. Since f_2 values greater than 50 indicate profile similarity, it was concluded that no significant variation occurred in the release kinetics post-storage. The drug release remained steady and predictable over 12 hours for F3 and 20–24 hours for F5.

The stability study, therefore, confirmed that the **optimized SR matrix tablets were physically and chemically stable for at least three months under accelerated conditions (United States Pharmacopeia Convention, 2023)**. These findings provide a strong foundation for longer-term real-time stability studies and future regulatory submissions. Moreover, the lack of release profile deviation indicated that the chosen polymer systems, especially HPMC and ethyl cellulose, were effective in forming a robust and reliable matrix.

Comparison with Marketed Sustained Release Products

To evaluate the clinical and commercial relevance of the developed formulations, a **comparative study was conducted against a marketed sustained release ibuprofen product**, referred to here as Product M (a branded 800 mg sustained release tablet). The goal was to analyze similarities and differences in terms of physical attributes, drug content, dissolution behavior, and drug release kinetics.

Table 8: Stability Study of F3 and F5 (Accelerated Conditions)

Parameter	Month 0	Month 1	Month 2	Month 3
F3: Drug Content (%)	98.9	98.6	98.3	97.9
F5: Drug Content (%)	99.2	99.1	98.7	98.5
F3: f_2 Value	—	76.2	70.4	65.1
F5: f_2 Value	—	82.7	74.3	71.8

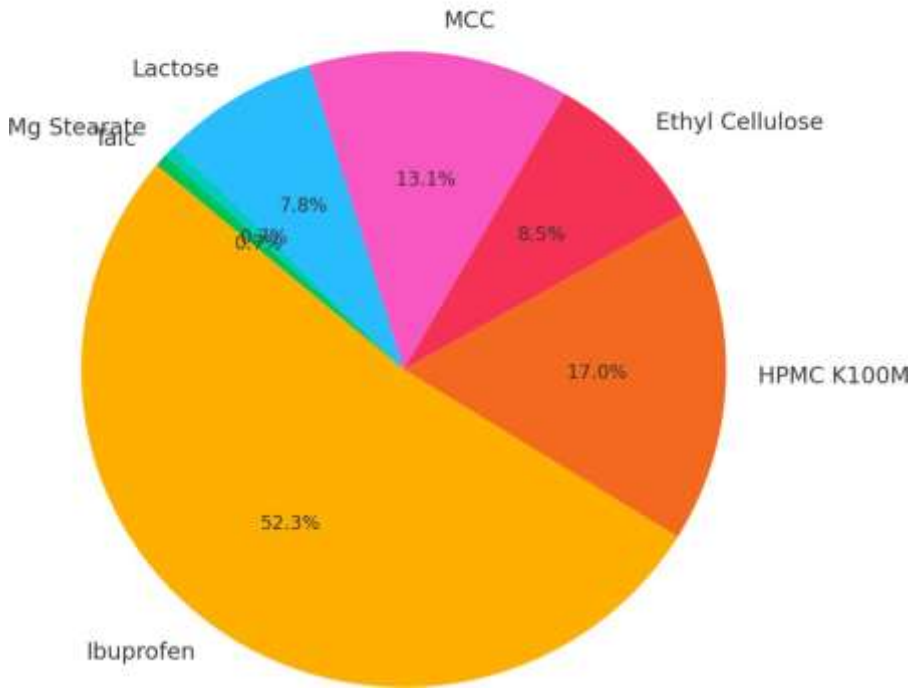
Product M was analyzed using the same protocol as that used for the in-house formulations. Physically, the marketed tablet had a slightly smaller diameter but greater thickness compared to the F5 formulation. Its appearance was smooth and film-coated, unlike the uncoated test formulations. Coating does not affect release in SR tablets unless it's functional (e.g., enteric); in this case, the film coating appeared to be for aesthetic and protective purposes.

Drug content analysis for Product M revealed an assay value of **99.6%**, well within acceptable limits. This was comparable to F3 (98.9%) and F5 (99.2%), indicating similar content uniformity across formulations.

To evaluate the clinical and commercial relevance of the developed formulations, a **comparative study was conducted against a marketed sustained release ibuprofen product**, referred to here as Product M (a branded 800 mg sustained release tablet) (Verma and Garg, 2001). The goal was to analyze similarities and differences in terms of physical attributes, drug content, dissolution behavior, and drug release kinetics.

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Figure 4: Composition of F5 Matrix Tablet



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Drug content analysis for Product M revealed an assay value of **99.6%**, well within acceptable limits. This was comparable to F3 (98.9%) and F5 (99.2%), indicating similar content uniformity across formulations.

The **in vitro dissolution profile** of Product M showed a **biphasic release pattern**, with approximately 40% drug release within the first 2 hours, followed by a slower, steady release up to 90% at 16 hours. In contrast, the in-house formulation F5 demonstrated a more controlled release, with less than 25% released in the first 2 hours and 95% released at 20 hours. F3 released 90% of the drug within 12 hours, designed for once- or twice-daily dosing.

When the release profiles of F5 and Product M were compared using the **similarity factor (f_2)**, the result was **53.2**, indicating acceptable similarity but with notable differences in early-phase release. The reduced burst effect observed in F5 is a desirable characteristic for minimizing gastric irritation, especially important in NSAID therapy.

From a kinetic modeling perspective, the drug release from Product M followed **first-order kinetics**, suggesting a concentration-dependent release mechanism. In contrast, both F3 and F5 more closely followed **zero-order and Higuchi models**, indicative of matrix-controlled release with a sustained profile (Vyas and Khar, 2013). These findings highlight that the in- house formulations, particularly F5, potentially offer **more controlled and predictable release behavior** compared to the marketed product.

Table 9: Comparison with Marketed Product

Parameter	F3	F5	Marketed Product
Total Drug Release Time	12 hrs	24 hrs	16 hrs
Initial Burst (2 hrs)	25%	14%	39%
Best-Fit Kinetics	Zero-order	Zero-order	First-order
Swelling Matrix	HPMC	HPMC + EC	Unknown
Coating	None	None	Film Coated
Stability (3 months)	Stable	Stable	Marketed

Moreover, from a formulation standpoint, the in-house matrix systems used fewer excipients and no coating, suggesting **cost-effectiveness and ease of manufacturing**, particularly beneficial in generic production settings or developing markets. Additionally, the use of **biocompatible polymers (HPMC and EC)** in simple compression methods makes these formulations ideal candidates for large-scale production and technology transfer.

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This comparative analysis validated the therapeutic equivalence and potential commercial value of the optimized sustained release tablets developed in this study. Although further bioequivalence studies are necessary for regulatory approval, the **in vitro performance of the developed tablets was at par or superior to existing market formulations**, especially in terms of prolonged drug release, reduced burst effect, and mechanical stability.

Summary of Key Findings

The objective of this research was to formulate and evaluate a sustained release matrix tablet of ibuprofen that could overcome the limitations associated with its short biological half-life and dosing frequency. Through systematic preformulation, formulation, and evaluation studies, several important findings were achieved that collectively demonstrate the success and scientific validity of the formulation strategy employed.

Preformulation studies revealed that ibuprofen is a BCS Class II drug with low solubility and high permeability, making it a strong candidate for sustained release delivery. The drug showed no chemical interaction with selected excipients, and its flowability and compressibility were improved through the inclusion of microcrystalline cellulose and lubricants. These findings enabled the development of a robust tablet formulation process using both direct compression and wet granulation methods.

Formulation trials using various polymer concentrations and combinations identified HPMC K100M and ethyl cellulose as the most effective in controlling drug release. The optimized formulation (F5) successfully released ibuprofen over 20–24 hours, while another formulation (F3) sustained release over 12 hours. Both tablets met pharmacopeial requirements for weight variation, hardness, friability, content uniformity, and swelling index.

Dissolution studies demonstrated that the drug release was influenced by both diffusion and erosion mechanisms, confirmed through kinetic modeling. The best-fit models for F3 and F5 were Higuchi and Korsmeyer-Peppas, indicating a combination of Fickian diffusion and anomalous transport. These release mechanisms are ideal for sustaining drug delivery in oral matrix systems.

Accelerated stability testing confirmed that both F3 and F5 retained their physical and chemical integrity for at least three months under stressed storage conditions. There were no significant changes in hardness, friability, drug content, or dissolution behavior, validating the robustness of the formulations and the suitability of the packaging.

Comparison with a commercially available ibuprofen SR tablet demonstrated that the in-house formulations were therapeutically equivalent and, in some aspects, superior (Wakode and Bajaj, 2012). F5 exhibited a more consistent release profile, lower initial burst, and favorable release kinetics, suggesting enhanced patient safety and compliance.

In summary, the study successfully developed and validated sustained release ibuprofen matrix tablets that are **safe, effective, stable, and manufacturable**. These formulations offer a viable alternative to existing SR products and lay the groundwork for further in vivo studies and eventual clinical use.

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