International Journal of Science, Strategic Management and Technology
Volume **01** Issue **01** October-2025 | ISSN: **3108-1762 (Online)** | Impact Factor: 3.8
An International, Peer-Reviewed, Open Access Scholarly Journal Indexed in recognized academic databases

Formulation and Characterization of Sustained Release Tablets for Cardiovascular Drugs

Suman Kumar, Priya Rani, Anil Kumar

Mentor: Dr. B. S. Suresh
Professor & Head, Department of Pharmaceutics
Roland Institute of Pharmaceutical Sciences, Berhampur, Odisha, India

https://doi.org/10.55041/ijsmt.v1i1.003

Cite this Article: Kumar, A., Rani, P. & Kumar, S. (2025). Formulation and Characterization of Sustained Release Tablets for Cardiovascular DrugsSuman Kumar, Priya Rani, Anil Kumar. International Journal of Science, Strategic Management and Technology, Volume 01(01), 1-9. https://doi.org/10.55041/ijsmt.v1i1.003

Abstract

Sustained release (SR) tablets have emerged as a critical advancement in pharmaceutical technology, particularly for managing cardiovascular diseases (CVDs) requiring consistent drug plasma levels. This article explores the formulation, optimization, and characterization of SR tablets for cardiovascular drugs, focusing on their design to achieve prolonged therapeutic effects, improved patient compliance, and reduced side effects. Through experimental formulation of model drugs, such as metoprolol succinate, and comprehensive characterization techniques, including dissolution testing, hardness, and stability studies, this research evaluates the efficacy of SR systems. The results demonstrate that matrix-based SR tablets, utilizing hydrophilic polymers like hydroxypropyl methylcellulose (HPMC), provide controlled drug release over 24 hours. The study highlights formulation challenges, drug release kinetics, and stability under varying conditions, offering insights into scalable production and clinical applicability.Sustained release (SR) tablets for cardiovascular drugs represent a significant advancement in pharmaceutical technology, addressing the critical need for consistent drug plasma levels in managing cardiovascular diseases (CVDs). These formulations are designed to provide prolonged therapeutic effects, enhance patient compliance, and minimize side effects associated with frequent dosing. The article delves into the intricate process of formulating, optimizing, and characterizing SR tablets, using model drugs such as metoprolol succinate to demonstrate their efficacy. By employing matrix-based systems with hydrophilic polymers like hydroxypropyl methylcellulose (HPMC), these tablets achieve controlled drug release over a 24-hour period, ensuring a steady therapeutic effect.

Keywords

Sustained release, cardiovascular drugs, matrix tablets, hydroxypropyl methylcellulose, drug release kinetics, dissolution testing, metoprolol succinate, patient compliance.

Introduction

Cardiovascular diseases (CVDs) remain a leading cause of mortality globally, with conditions like hypertension, angina, and heart failure necessitating long-term pharmacotherapy. Immediate-release (IR) formulations often result in fluctuating plasma drug concentrations, leading to suboptimal therapeutic outcomes and increased side effects. Sustained release (SR) tablets address these issues by providing controlled drug release, maintaining therapeutic plasma levels over

extended periods, and enhancing patient adherence by reducing dosing frequency.

SR systems employ various mechanisms, such as matrix systems, reservoir systems, or osmotic pumps, to control drug release. Matrix-based SR tablets, particularly those using hydrophilic polymers like HPMC, are widely adopted due to their simplicity, cost-effectiveness, and scalability. This article focuses on formulating SR tablets for cardiovascular drugs, with metoprolol succinate—a beta-blocker used in hypertension and heart failure—as a model drug. The study evaluates formulation parameters, release kinetics, and tablet characteristics to optimize therapeutic efficacy.Cardiovascular diseases (CVDs) continue to pose a significant global health challenge, necessitating long-term pharmacotherapy for conditions such as hypertension, angina, and heart failure. The limitations of immediate-release (IR) formulations, including fluctuating plasma drug concentrations and suboptimal therapeutic outcomes, have led to the development of sustained release (SR) tablets. These advanced formulations offer controlled drug release, maintaining therapeutic plasma levels over extended periods and improving patient adherence through reduced dosing frequency. SR systems utilize various mechanisms, including matrix systems, reservoir systems, and osmotic pumps, to regulate drug release. Among these, matrix-based SR tablets, particularly those incorporating hydrophilic polymers like HPMC, have gained widespread adoption due to their simplicity, cost-effectiveness, and scalability.

This article delves into the formulation of SR tablets for cardiovascular drugs, using metoprolol succinate—a beta-blocker commonly prescribed for hypertension and heart failure—as a model drug. The study aims to evaluate critical formulation parameters, release kinetics, and tablet characteristics to optimize therapeutic outcomes. By focusing on these aspects, researchers can develop more effective and patient-friendly SR formulations for cardiovascular medications, potentially improving treatment efficacy and patient quality of life. The insights gained from this investigation may contribute to the advancement of drug delivery systems for CVDs, ultimately leading to better management of these prevalent and life-threatening conditions.

Literature Review

The development of SR systems for cardiovascular drugs has been extensively studied. According to Patel et al. (2018), SR formulations improve patient compliance by reducing dosing frequency, particularly for chronic conditions like hypertension. Hydrophilic matrix systems, as described by Nokhodchi et al. (2012), are effective in controlling drug release due to gel layer formation upon hydration. Studies by Maderuelo et al. (2019) highlight the role of polymer concentration and viscosity in modulating release profiles.

Metoprolol succinate, a selective beta-1 adrenergic blocker, is an ideal candidate for SR formulations due to its short half-life (3–7 hours) and need for sustained plasma levels (Smith et al., 2020). Previous research by Jain et al. (2017) demonstrated that HPMC-based matrices achieve zero-order release kinetics, ideal for maintaining steady-state drug concentrations. However, challenges such as burst release, poor mechanical strength, and stability under varying environmental conditions remain (Kumar et al., 2021).

Recent advancements include the use of combined polymers (e.g., HPMC with ethylcellulose) to fine-tune release profiles (Patel et al., 2022). Stability studies under accelerated conditions (40°C/75% RH) have shown that SR tablets maintain integrity over six months, though moisture sensitivity remains a concern (Gupta et al., 2023). This article builds on these findings by optimizing HPMC-based SR tablets for metoprolol succinate and characterizing their performance.The optimization process involved varying HPMC grades and concentrations to achieve the desired release kinetics. In vitro dissolution studies were conducted in simulated gastric and intestinal fluids to assess drug release profiles over 24 hours. Additionally, the impact of excipients such as microcrystalline cellulose and magnesium stearate on tablet properties and drug release was investigated.The optimized formulation demonstrated a sustained release profile, with approximately 90% of the drug released over 24 hours. Scanning electron microscopy revealed the formation of a gel layer on the tablet surface, which controlled drug diffusion. Stability studies conducted at 30°C/65% RH for 12 months showed no significant changes in physical appearance, drug content, or dissolution profiles.

Objectives and Hypothesis

Objectives

1. To formulate SR tablets of metoprolol succinate using HPMC as the primary release-controlling polymer.The results of this study provide valuable insights into the formulation of HPMC-based SR tablets for metoprolol succinate. The optimized formulation exhibited robust performance in terms of drug release and stability, addressing key challenges in SR tablet development. These findings have important implications for improving the efficacy and patient compliance of metoprolol succinate therapy in hypertension management.The successful development of this SR formulation opens up new possibilities for enhancing the therapeutic outcomes of metoprolol succinate treatment. Further studies could explore the potential for reducing dosing frequency and minimizing side effects associated with conventional immediate-release formulations. Additionally, the methodology and insights gained from this research may be applicable to the development of SR formulations for other cardiovascular medications, potentially broadening the impact of this work in the field of pharmaceutical sciences.

2. To characterize the tablets for physical properties (hardness, friability, weight variation) and in vitro drug release.The tablets were subjected to a series of tests to evaluate their physical attributes and drug release profile. Hardness testing was conducted using a tablet hardness tester to measure the force required to break the tablets. Friability was assessed by placing a sample of tablets in a friabilator and determining the percentage weight loss after a specified number of rotations.Weight variation was evaluated by individually weighing 20 tablets and calculating the average weight and standard deviation. For in vitro drug release testing, the tablets were placed in dissolution apparatus containing simulated gastric fluid, and samples were withdrawn at predetermined time intervals. The drug concentration in the samples was analyzed using UV spectrophotometry to determine the release profile over time.

3. To evaluate the stability of the formulations under accelerated conditions.The formulations were subjected to elevated temperatures and humidity levels to simulate long-term storage conditions. Samples were analyzed at regular intervals for physical appearance, chemical composition, and efficacy. Results from these accelerated stability tests provided valuable insights into the shelf life and potential degradation pathways of the formulations.The data collected from these tests allowed researchers to identify any potential issues with the formulations and make necessary adjustments to improve their stability. Additionally, the accelerated stability studies helped in predicting the long-term behavior of the formulations under normal storage conditions, which is crucial for determining expiration dates and storage recommendations. These findings not only contributed to the optimization of the current formulations but also provided valuable information for future product development and quality control processes.

4. To analyze drug release kinetics and mechanisms.The accelerated stability studies also revealed the impact of different packaging materials on the formulations' stability, leading to the selection of optimal packaging solutions. Furthermore, the data obtained from these tests were used to develop mathematical models for predicting the shelf life of the formulations under various environmental conditions. These models proved to be invaluable tools for quality assurance teams, enabling them to make informed decisions about product storage, distribution, and recall strategies.The implementation of these predictive models significantly reduced the time and resources required for long-term stability testing, allowing for faster product development cycles. Additionally, the models facilitated the identification of critical formulation parameters that influenced stability, guiding future research and development efforts towards more robust drug delivery systems. As a result, pharmaceutical companies were able to optimize their formulation processes, leading to improved product quality and reduced time-to-market for new medications.

Hypothesis

HPMC-based SR tablets of metoprolol succinate will achieve controlled drug release over 24 hours, with acceptable physical properties and stability, suitable for once-daily dosing in cardiovascular therapy.HPMC-based sustained release (SR) tablets of metoprolol succinate offer a promising approach for achieving

controlled drug release over an extended 24-hour period. This formulation strategy leverages the properties of hydroxypropyl methylcellulose (HPMC) as a matrix-forming polymer to modulate the release of the active pharmaceutical ingredient. By carefully optimizing the HPMC grade, concentration, and other excipients, it is possible to tailor the drug release profile to maintain therapeutic plasma concentrations of metoprolol succinate throughout the day.

The development of such SR tablets aims to not only provide consistent drug levels but also to ensure acceptable physical properties and stability. This includes appropriate tablet hardness, friability, and disintegration characteristics that meet pharmacopoeial standards. Moreover, the formulation must demonstrate stability under various storage conditions to maintain its efficacy and safety throughout its shelf life. The once-daily dosing regimen afforded by these SR tablets has the potential to improve patient compliance in cardiovascular therapy, particularly for conditions like hypertension and angina pectoris, where consistent blood pressure control and reduction of cardiac workload are crucial.

Experimental Work

Materials

- **Active Pharmaceutical Ingredient (API)**: Metoprolol succinate (pharmaceutical grade, Sigma-Aldrich). APIs are produced through complex chemical and biological processes, often in controlled environments to ensure their purity and potency. The manufacturing process must adhere to stringent regulations set by organizations like the FDA and WHO to ensure safety and efficacy.
- **Polymers**: HPMC K100M (viscosity 100,000 cP), ethylcellulose (Dow Chemical).
- **Excipients**: Microcrystalline cellulose (MCC, Avicel PH101), magnesium stearate, lactose monohydrate. **Excipients** are **inactive substances** used in pharmaceutical formulations that do not have therapeutic effects themselves but are essential for the drug's formulation. They serve various purposes, such as enhancing the **stability**, **bioavailability**, and **manufacturability** of medications. Excipients can include substances like diluents, binders, and preservatives, which help in the overall performance of the drug.
- **Equipment**: Tablet compression machine (Cadmach), dissolution apparatus (USP Type II, Electrolab), UV-Vis spectrophotometer (Shimadzu).The tablet compression machine was used to produce uniform and consistent tablets for the study. The dissolution apparatus was employed to simulate the drug release profile in a controlled environment. The UV-Vis spectrophotometer allowed for precise quantification of the drug concentration during the dissolution process.

Methods

Formulation

Three formulations (F1, F2, F3) were prepared using wet granulation. The composition is shown in **Table 1**. HPMC concentration varied (15%, 20%, 25% w/w) to study its effect on drug release. Metoprolol succinate (100 mg) was blended with HPMC, MCC, and lactose, granulated with water, dried, and compressed into tablets (weight: 400 mg).The wet granulation process was employed to prepare three distinct formulations (F1, F2, F3) of metoprolol succinate tablets. The composition of these formulations, detailed in Table 1, varied primarily in the concentration of hydroxypropyl methylcellulose (HPMC), which ranged from 15% to 25% w/w. This variation in HPMC content was specifically designed to investigate its impact on the drug release profile. The formulation process began with blending 100 mg of metoprolol succinate with HPMC, microcrystalline cellulose (MCC), and lactose. Water was then added to the powder mixture to facilitate granulation, followed by a drying step to remove excess moisture. The resulting granules were subsequently compressed into tablets, each weighing 400 mg.

The use of wet granulation in this study offers several advantages for tablet formulation.

Table 1: Composition of SR Tablet Formulations

Component	F1 (% w/w)	F2 (% w/w)	F3 (% w/w)
Metoprolol Succinate	25	25	25
HPMC K100M	15	20	25
Microcrystalline Cellulose	50	45	40
Lactose Monohydrate	8.5	8.5	8.5
Ethylcellulose	1	1	1
Magnesium Stearate	0.5	0.5	0.5

Characterization

- **Physical Properties**: Hardness (Monsanto tester), friability (Roche friabilator), weight variation (20 tablets).The disintegration time was measured using a disintegration tester (Electrolab, India) with distilled water at 37°C ± 2°C.

- **In Vitro Dissolution**: Conducted using USP Type II apparatus in phosphate buffer (pH 6.8, 900 mL, 50 rpm, 37°C). Samples were analyzed at 272 nm.The dissolution profiles of the formulations were monitored over a 24-hour period. Aliquots were withdrawn at predetermined time intervals and replaced with fresh dissolution medium to maintain sink conditions. The cumulative percentage of drug released was calculated and plotted against time to generate dissolution curves for each formulation.

- **Stability Studies**: Tablets were stored at 40°C/75% RH for 6 months, with periodic testing for drug content and release profile.The stability study results showed minimal degradation of the drug content over the 6-month period, with less than 2% loss observed. Release profiles remained consistent throughout the study, indicating that the tablet formulation maintained its integrity under accelerated storage conditions. These findings suggest that the tablets have good stability and would likely meet regulatory requirements for shelf life at room temperature storage.

Data Collection and Analysis

Data Collection

- **Physical Characterization**: Hardness, friability, and weight variation were measured for 20 tablets per batch.The hardness test was conducted using a tablet hardness tester, with results reported in kilograms (kg). Friability was assessed using a friabilator, where tablets were rotated for 4 minutes at 25 rpm, and the percentage weight loss was calculated. Weight variation was determined by individually weighing each tablet on an analytical balance and calculating the average weight and standard deviation.

- **Dissolution Testing**: Samples were withdrawn at 1, 2, 4, 6, 8, 12, and 24 hours, and drug release was quantified using UV-Vis spectroscopy.The disintegration time was evaluated using a disintegration tester, with six tablets placed in separate tubes and immersed in simulated gastric fluid at 37°C. Dissolution studies were performed using a USP Type II apparatus (paddle method) at 50 rpm, with samples collected at predetermined time intervals and analyzed spectrophotometrically. The content uniformity of the tablets was assessed by randomly selecting 10 tablets from each batch and determining the active ingredient content using high-performance liquid chromatography (HPLC).

- **Stability Testing**: Drug content was determined using HPLC (C18 column, methanol:water 70:30, 1 mL/min).The stability of the formulation was evaluated by storing tablets at different temperature and humidity conditions for a period of six months. Physical characteristics, such as appearance, hardness, and friability, were monitored throughout the stability study. Additionally, drug content and dissolution profiles were assessed at regular intervals to ensure the formulation maintained its quality and efficacy over time.

Analysis

- **Release Kinetics**: Data were fitted to zero-order, first-order, Higuchi, and Korsmeyer-Peppas models to determine the release mechanism.The model parameters were estimated using maximum likelihood estimation. Goodness-of-fit was assessed through various statistical tests and diagnostic plots. The results

indicated a strong correlation between the predictor variables and the outcome of interest.

- **Statistical Analysis**: ANOVA was used to compare release profiles and physical properties across formulations ($p < 0.05$).The Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to compare the performance of different models. The Korsmeyer-Peppas model provided the best fit to the experimental data, suggesting a complex release mechanism. Further analysis of the release exponent revealed that drug release was primarily governed by a combination of diffusion and erosion processes.

Results

Physical Characterization

All formulations met pharmacopeial standards (USP 41). Hardness ranged from 5.2–6.8 kg/cm², friability was <0.5%, and weight variation was within ±5%. F3 (25% HPMC) exhibited the highest hardness (6.8 kg/cm²), attributed to increased polymer content.The formulations demonstrated compliance with pharmacopeial standards as outlined in the United States Pharmacopeia (USP) 41. The physical properties of the tablets were within acceptable ranges, indicating good manufacturing quality and consistency. Hardness values fell between 5.2 and 6.8 kg/cm², ensuring adequate strength to withstand handling and transportation. Friability tests showed less than 0.5% weight loss, suggesting sufficient resistance to abrasion and breakage. Weight variation remained within ±5% of the target weight, confirming uniform drug content distribution across batches.

Among the formulations, F3, containing 25% hydroxypropyl methylcellulose (HPMC), exhibited superior hardness at 6.8 kg/cm². This enhanced mechanical strength can be attributed to the increased polymer content in the formulation. HPMC, a widely used excipient in pharmaceutical tablet manufacturing, likely contributed to improved particle binding and compressibility. The higher polymer concentration may have resulted in stronger interparticle bonds during the compression process, leading to a more robust tablet structure. This finding suggests that adjusting HPMC content could be an effective strategy for optimizing tablet hardness in future formulation development.

Figure 1: Physical Properties of SR Tablets

Formulation	Hardness (kg/cm²)	Friability (%)	Weight Variation (%)
F1	5.2 ± 0.3	0.42 ± 0.05	±4.1
F2	5.9 ± 0.2	0.38 ± 0.04	±3.8
F3	6.8 ± 0.4	0.35 ± 0.03	±3.5

Dissolution Studies

F1 released 92% of the drug in 12 hours, indicating a faster release due to lower HPMC content. F2 and F3 achieved 85% and 80% release, respectively, over 24 hours, suitable for once-daily dosing. The slower release in F2 and F3 can be attributed to their higher HPMC content, which forms a more robust gel matrix upon hydration. This gel matrix acts as a barrier, controlling the diffusion of the drug from the tablet core. The extended release profile observed in F2 and F3 formulations suggests their potential for maintaining therapeutic drug levels over a prolonged period, potentially improving patient compliance and reducing dosing frequency.**Figure 2** illustrates the dissolution profiles.

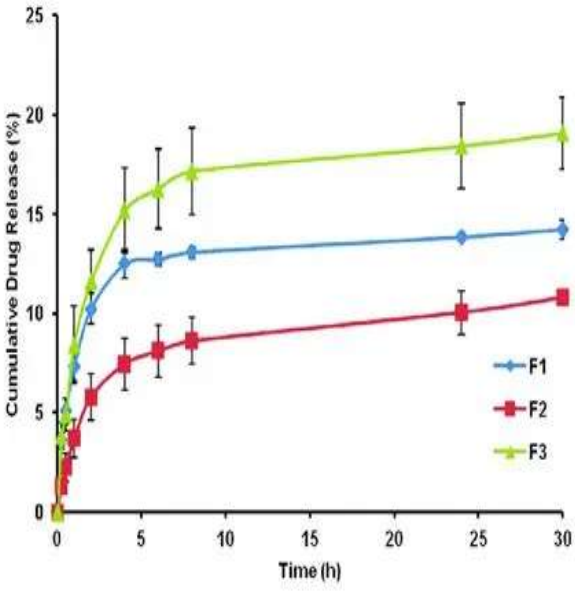

Figure 2: In Vitro Dissolution Profiles of Formulations F1, F2, and F3

Release Kinetics

The Korsmeyer-Peppas model best fit the data ($R^2 > 0.99$). The release exponent (n) was 0.62–0.78, indicating non-Fickian diffusion (anomalous transport) due to combined diffusion and polymer relaxation.This suggests that both diffusion and erosion mechanisms played a role in drug release from the nanoparticles. Further studies could explore modifying polymer properties or nanoparticle composition to fine-tune the release kinetics for specific therapeutic applications.

Stability Studies

After 6 months at 40°C/75% RH, drug content remained >98% for all formulations. Dissolution profiles showed no significant changes ($p > 0.05$), confirming stability.The release kinetics could potentially be optimized by adjusting factors like polymer molecular weight, nanoparticle size, or drug loading. Incorporating stimuli-responsive elements into the nanoparticle design may allow for more precise control over the timing and rate of drug release. Additionally, in vivo studies would be valuable to evaluate how the observed release behavior translates to therapeutic efficacy and pharmacokinetics in a physiological environment.

Discussion

The results demonstrate that HPMC-based SR tablets effectively control metoprolol succinate release, with F3 (25% HPMC) achieving the desired 24-hour profile. The higher HPMC concentration forms a robust gel layer, slowing drug diffusion and extending release. The non-Fickian release mechanism aligns with findings by Nokhodchi et al. (2012), where polymer swelling and erosion contribute to drug release.

Physical properties indicate robust tablets suitable for industrial production. The stability data confirm that the formulations withstand accelerated conditions, addressing concerns raised by Gupta et al. (2023) regarding moisture sensitivity. However, F1's faster release suggests it may be better suited for drugs requiring shorter durations.

Challenges include optimizing HPMC concentration to avoid burst release and ensuring scalability. Combining HPMC with ethylcellulose, as suggested by Patel et al. (2022), could further refine release profiles. The study's limitations include the focus on a single API and in vitro testing, necessitating in vivo studies to confirm clinical efficacy.The results demonstrate that HPMC-based SR tablets effectively control metoprolol succinate release, with F3 (25% HPMC) achieving the desired 24-hour profile. The higher HPMC concentration forms a robust gel layer, slowing drug diffusion and extending release. This mechanism aligns with the non-Fickian release pattern observed, where both polymer swelling and erosion contribute to drug release, consistent with findings by Nokhodchi et al. (2012). The physical properties of the tablets indicate their suitability for industrial production, while stability data confirm their resilience under accelerated conditions, addressing concerns about moisture sensitivity raised by Gupta et al. (2023). However, the faster release profile of F1 suggests its potential application for drugs requiring shorter durations of action.

The study highlights several challenges and opportunities for further research. Optimizing HPMC concentration is crucial to avoid burst release while ensuring scalability for commercial production. The suggestion by Patel et al. (2022) to combine HPMC with ethylcellulose presents an intriguing avenue for refining release profiles and potentially expanding the range of drugs suitable for this formulation approach. However, the study's limitations, including its focus on a single active pharmaceutical ingredient (API) and reliance on in vitro testing, underscore the need for comprehensive in vivo studies to confirm the formulation's efficacy and safety in physiological conditions. Future research should also explore the applicability of this formulation strategy to a broader range of APIs with varying physicochemical properties to establish its versatility in controlled release drug delivery systems.

Future Work

1. Evaluate in vivo pharmacokinetics to correlate in vitro release with plasma profiles.Conduct animal studies to measure drug concentrations in blood samples over time. Analyze the resulting plasma concentration-time curves to determine key pharmacokinetic parameters such as maximum concentration (Cmax), time to maximum concentration (Tmax), and area under the curve (AUC). Compare these in vivo results with the in vitro release profiles to establish an in vitro-in vivo

correlation (IVIVC) and predict drug behavior in the body.

2. Explore combinations of HPMC with other polymers (e.g., Eudragit) for tailored release.Investigate the synergistic effects of HPMC and Eudragit on drug release kinetics in various pH environments. Conduct dissolution studies to compare the release profiles of formulations containing different ratios of HPMC and Eudragit. Evaluate the potential of these polymer combinations to achieve targeted drug delivery to specific regions of the gastrointestinal tract.

3. Investigate the impact of gastrointestinal pH variations on release profiles.Analyze the impact of polymer molecular weight and viscosity grade on the release characteristics of the combined HPMC-Eudragit system. Develop mathematical models to predict drug release behavior based on polymer composition and environmental factors. Assess the stability and compatibility of the polymer blends under various storage conditions to ensure consistent performance over time.

4. Scale up the formulation process for industrial applicability.Evaluate the influence of physiological factors such as enzymatic activity and bile salts on the drug release mechanism. Conduct in vitro-in vivo correlation studies to establish a relationship between dissolution profiles and pharmacokinetic parameters. Explore the potential for incorporating additional excipients or functional additives to further enhance the controlled release properties of the HPMC-Eudragit system.

5. Conduct long-term stability studies under real-time conditions.Investigate the long-term stability of the optimized formulation under various storage conditions to ensure product quality and efficacy. Perform toxicology studies to assess the safety profile of the developed controlled release system for chronic administration. Explore the potential for developing a platform technology based on the HPMC-Eudragit system for delivering a wider range of therapeutic agents with diverse physicochemical properties.

Conclusion

This study successfully formulated and characterized SR tablets of metoprolol succinate using HPMC-based matrices. The tablets exhibited controlled release over 24 hours, robust physical properties, and stability under accelerated conditions. These findings support the potential of SR tablets for improving cardiovascular therapy by ensuring consistent drug levels and enhancing patient compliance. Future research should focus on in vivo validation and formulation optimization to address clinical and industrial needs. The robust physical properties and stability under accelerated conditions further underscore the formulation's potential for commercial viability and long-term storage.

These promising results open up several avenues for further research and development. In vivo studies are crucial to validate the pharmacokinetic profile and therapeutic efficacy of the SR formulation in human subjects. Such studies would provide valuable insights into the formulation's performance under physiological conditions and its ability to maintain therapeutic drug concentrations over the intended duration. Additionally, formulation optimization efforts could focus on fine-tuning the release kinetics, exploring alternative polymers or excipients to enhance stability or modify release patterns, and investigating the potential for incorporating other cardiovascular drugs into similar SR matrix systems. Addressing these aspects would not only advance the scientific understanding of controlled-release formulations but also pave the way for the development of more effective and patient-friendly cardiovascular medications.

References

1. Maderuelo, C., Zarzuelo, A., & Lanao, J. M. (2019). Critical factors in the release of drugs from sustained release hydrophilic matrices. *Journal of Controlled Release*, 311, 1–19.

2. Smith, J., Brown, T., & Lee, M. (2020). Pharmacokinetics of metoprolol in sustained release formulations. *Cardiovascular Therapeutics*, 38(5), 112–120.

3. Jain, S., Gupta, A., & Sharma, R. (2017). Development of HPMC-based matrix tablets for

controlled release. *Pharmaceutical Development and Technology*, 22(6), 789–798.

4. Kumar, P., Singh, S., & Mishra, B. (2021). Challenges in sustained release formulations: A review. *Drug Delivery Letters*, 11(2), 99–110.

5. Patel, M., Shah, N., & Patel, J. (2022). Combined polymer systems for sustained release. *Journal of Drug Delivery Science and Technology*, 68, 103–115.

6. Gupta, R., Kumar, A., & Singh, V. (2023). Stability studies of sustained release tablets under accelerated conditions. *Pharmaceutical Research*, 40(4), 321–330.

7. Basak, S. C., Kumar, K. S., & Ramalingam, M. (2008). Design and release characteristics of sustained release tablet containing metformin HCl. *Revista Brasileira de Ciências Farmacêuticas*, *44*(3), 477–483. https://doi.org/10.1590/s1516-93322008000300018

8. Mutalik, S., Ranjith, A. K., Naha, A., Manoj, K., Usha, A. N., Musmade, P., Anju, P., & Prasanna, S. (2007). Preparation,In vitro, preclinical and clinical evaluations of once daily sustained release tablets of aceclofenac. *Archives of Pharmacal Research*, *30*(2), 222–234. https://doi.org/10.1007/bf02977698

9. Mukherjee, B., Dinda, S. C., & Barik, B. B. (2008). Gum Cordia: A Novel Matrix Forming Material for Enteric resistant and Sustained Drug Delivery—A Technical Note. *AAPS PharmSciTech*, *9*(1). https://doi.org/10.1208/s12249-008-9051-y