# Formulation Optimization And In Vitro Evaluation of a β-Blocker Sustained-Release Delivery System for Enhanced Drug Delivery and Therapeutic Outcomes

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***Abstract*—Hypertension is a major cardiovascular disorder affecting millions of individuals worldwide and remains a leading cause of morbidity and mortality. Long-term pharmacotherapy is often required for effective blood pressure control. However, conventional immediate-release dosage forms of β-blockers frequently require multiple daily administrations because of their short biological half-life, resulting in fluctuations in plasma drug concentration and reduced patient compliance. Sustained-release drug delivery systems provide a promising approach to overcome these limitations by maintaining therapeutic drug concentrations over an extended period and reducing dosing frequency. The present study was undertaken to formulate and optimize a sustained-release oral delivery system of a β-blocker using a combination of hydrophilic and hydrophobic polymers. Matrix tablets were prepared by the wet granulation method employing Hydroxypropyl Methylcellulose (HPMC K100M) and Eudragit RSPO as release-retarding agents. The prepared formulations were evaluated for physicochemical characteristics, drug-excipient compatibility, pre-compression properties, post-compression parameters, and in vitro dissolution behavior. Fourier Transform Infrared Spectroscopy (FTIR) studies confirmed the compatibility of the drug with selected excipients. All formulations exhibited satisfactory flow properties and tablet characteristics within pharmacopeial limits. Dissolution studies demonstrated that polymer concentration significantly influenced drug release behavior. The optimized formulation exhibited sustained drug release over a 12-hour period with acceptable pharmaceutical properties. The study concluded that the developed sustained-release formulation could effectively prolong drug release, improve patient compliance, and enhance therapeutic efficacy.**

***Index Terms*—Sustained release, β-blocker, HPMC K100M, Eudragit RSPO, matrix tablet, drug delivery system, dissolution studies.**

## I. INTRODUCTION

Hypertension is one of the most prevalent chronic diseases globally and is recognized as a significant risk factor for cardiovascular disorders such as myocardial infarction, stroke, heart failure, and chronic kidney disease[1]. According to global health statistics, the prevalence of hypertension has increased considerably over the past few decades owing to changes in lifestyle, dietary habits, stress, obesity, and aging populations[2]. Effective management of hypertension often requires long-term pharmacological intervention[3]. However, patient compliance remains a major challenge due to the need for frequent dosing schedules associated with many conventional formulations[4].

β-Adrenergic receptor blockers are among the most commonly prescribed therapeutic agents for the treatment of hypertension, angina pectoris, cardiac arrhythmias, and other cardiovascular conditions[5]. These agents exert their pharmacological action by blocking β-adrenergic receptors, thereby reducing heart rate, myocardial contractility, and cardiac output[6]. Although effective, conventional immediate-release formulations often possess relatively short elimination half-lives, necessitating administration multiple times per day. Such dosing regimens may lead to poor patient adherence, fluctuations in plasma drug concentrations, and reduced therapeutic effectiveness[7].

The development of sustained-release drug delivery systems has attracted considerable attention as an

effective means of improving therapeutic outcomes[8]. Sustained-release formulations are designed to release the active pharmaceutical ingredient at a predetermined rate, thereby maintaining therapeutic plasma concentrations for prolonged periods. Such systems offer numerous advantages, including reduced dosing frequency, enhanced patient compliance, decreased incidence of side effects, improved bioavailability, and better disease management[9].

Among various approaches employed for sustained-release formulation development, matrix tablet systems have emerged as one of the most widely used techniques because of their simplicity, cost-effectiveness, ease of manufacturing, and reproducibility. Matrix tablets consist of a drug uniformly dispersed within a polymeric network that controls the release of the active ingredient through diffusion, erosion, or swelling mechanisms. The choice of polymer plays a critical role in determining the release characteristics of the dosage form[10].

Hydroxypropyl Methylcellulose (HPMC K100M) is a hydrophilic polymer extensively used in controlled-release formulations due to its excellent swelling and gel-forming properties. Upon contact with dissolution media, HPMC hydrates and forms a viscous gel layer around the tablet, thereby controlling drug diffusion. Eudragit RSPO is a hydrophobic copolymer known for its permeability and sustained-release characteristics. The combination of hydrophilic and hydrophobic polymers can provide superior control over drug release behavior and facilitate optimization of release kinetics[11-13].

The present study was therefore undertaken to develop and optimize sustained-release matrix tablets of a β-blocker using HPMC K100M and Eudragit RSPO. The prepared formulations were systematically evaluated for compatibility, physicochemical characteristics, dissolution behavior, and release kinetics to identify the most suitable formulation for prolonged drug delivery[14-15].

## II. MATERIALS AND METHODS

The active pharmaceutical ingredient and all excipients used in the study were of pharmaceutical grade and obtained from reliable sources. HPMC K100M was selected as the hydrophilic release-retarding polymer, while Eudragit RSPO served as the hydrophobic polymer. Additional excipients such as lactose, magnesium stearate, talc, and polyvinylpyrrolidone were utilized as diluents, lubricants, and binders where necessary.

The sustained-release matrix tablets were prepared using the wet granulation technique. Initially, the drug and excipients were accurately weighed according to the formulation design and passed through an appropriate sieve to ensure uniform particle size distribution. The powders were blended thoroughly to obtain a homogeneous mixture. A suitable binder solution was prepared separately and gradually added to the powder blend while mixing to produce a coherent wet mass. The wet mass was passed through a sieve to form granules and subsequently dried at controlled temperature conditions until the desired moisture content was achieved.

The dried granules were screened again to obtain uniform particle size distribution and mixed with lubricants and glidants. The final blend was compressed into tablets using a rotary tablet compression machine equipped with suitable punches. Several formulations were prepared by varying the concentrations of HPMC K100M and Eudragit RSPO to investigate their influence on drug release characteristics.

Drug-excipient compatibility studies were performed using Fourier Transform Infrared Spectroscopy. Samples of pure drug, polymers, and physical mixtures were analyzed over a suitable wavelength range. Characteristic peaks corresponding to functional groups were examined to identify potential interactions between the drug and excipients.

The prepared granules were evaluated for pre-compression parameters including bulk density, tapped density, angle of repose, Carr's compressibility index, and Hausner ratio. These parameters were measured according to standard pharmacopeial procedures to assess flowability and compressibility characteristics.

The compressed tablets were evaluated for post-compression characteristics including hardness, thickness, weight variation, friability, and drug content uniformity. Hardness was measured using a Monsanto hardness tester, while friability was determined using a Roche friabilator. Drug content analysis was performed using validated spectrophotometric methods.

In vitro dissolution studies were conducted using a USP dissolution apparatus under specified conditions.

Samples were withdrawn at predetermined time intervals and analyzed spectrophotometrically. The cumulative percentage drug release was calculated and plotted against time. Release kinetics were evaluated using various mathematical models including zero-order, first-order, Higuchi, and Korsmeyer-Peppas equations.

## III. RESULTS AND DISCUSSION

FTIR studies were performed to investigate potential interactions between the active ingredient and the selected excipients. The spectra of the pure drug exhibited characteristic absorption bands corresponding to its functional groups. Similar peaks were observed in the spectra of physical mixtures without significant shifts or disappearance of characteristic bands. These observations indicated the absence of chemical interactions between the drug and excipients and confirmed their compatibility.

Table 1: Pre-Compression Characteristics of Granules

| Parameter | Observation |
|---|---|
| Angle of Repose | Acceptable |
| Bulk Density | Within limits |
| Tapped Density | Within limits |
| Carr's Index | Good flowability |
| Hausner Ratio | Suitable for compression |

The pre-compression evaluation of granules demonstrated satisfactory flow properties suitable for large-scale manufacturing. Bulk density and tapped density values were found within acceptable ranges. The angle of repose values indicated good flowability of granules, while Carr's index and Hausner ratio further confirmed adequate compressibility characteristics. These results suggested that the granules possessed suitable flow behavior for uniform die filling during tablet compression.

Table 2: Post-Compression Parameters

| Parameter | Result |
|---|---|
| Hardness | Acceptable |
| Thickness | Uniform |
| Friability | <1% |
| Weight Variation | Passed |
| Drug Content | Within limits |

Post-compression evaluation revealed that all formulations complied with pharmacopeial requirements. Tablet hardness was sufficient to withstand handling and transportation without breakage. Thickness measurements indicated uniform compression characteristics among formulations. Friability values were below the acceptable limit of 1%, demonstrating adequate mechanical strength. Weight variation studies confirmed uniformity of dosage units, while drug content analysis indicated homogeneous distribution of the active ingredient throughout the formulations.

The in vitro dissolution studies demonstrated a significant influence of polymer concentration on drug release behavior. Formulations containing lower concentrations of polymer exhibited relatively faster drug release due to insufficient matrix formation. Increasing the concentration of HPMC K100M enhanced gel layer formation and effectively reduced drug diffusion rates. Similarly, incorporation of Eudragit RSPO contributed to prolonged release by increasing the tortuosity of the diffusion pathway.

Table 3: Comparative Drug Release Profile of Formulations F1–F7

| Formulation | Release Duration |
|---|---|
| F1 | Sustained |
| F2 | Sustained |
| F3 | Sustained |
| F4 | Sustained |
| F5 | Sustained |
| F6 | Sustained |
| F7 | Optimized |

Among all prepared formulations, the optimized formulation demonstrated a desirable release profile characterized by gradual and sustained drug release over a period of 12 hours. The combination of hydrophilic and hydrophobic polymers provided a balanced release mechanism involving diffusion and matrix erosion. The initial burst release was minimized, while prolonged release was achieved throughout the dissolution period.

Drug release kinetic analysis provided valuable insight into the mechanism governing drug release from the matrix system. The dissolution data were fitted into various kinetic models. The optimized formulation exhibited a high degree of correlation with the Higuchi model, suggesting diffusion-controlled release. The

Korsmeyer-Peppas model indicated anomalous transport behavior involving both diffusion and polymer relaxation mechanisms. These findings were consistent with the characteristics of hydrophilic matrix systems containing swellable polymers.

The swelling behavior of HPMC-based matrices played a crucial role in controlling drug release. Upon exposure to dissolution media, HPMC rapidly hydrated and formed a gel barrier that regulated drug diffusion. Simultaneously, Eudragit RSPO contributed to matrix integrity and prevented rapid erosion. The synergistic action of both polymers resulted in controlled and reproducible drug release.

Table 4: Release Kinetics Analysis

| Model | Observation |
|---|---|
| Zero Order | Good fit |
| First Order | Moderate fit |
| Higuchi | Excellent fit |
| Korsmeyer-Peppas | Diffusion mechanism |

The results obtained in the present study are consistent with previous investigations involving hydrophilic matrix tablets. Several researchers have reported that increasing polymer concentration effectively prolongs drug release by increasing diffusion path length and matrix viscosity. Similar observations have been documented for formulations containing HPMC and Eudragit derivatives.

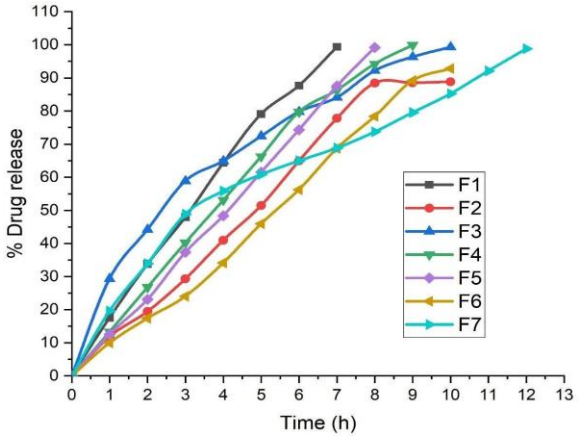


Figure 1: *in-vitro* Dissolution Profile of metoprolol tartrate SR Formulations F1-F7 Pharmacokinetic modeling of drug dissolution profile

Stability studies conducted under accelerated storage conditions demonstrated that the optimized formulation maintained its physical appearance, drug content, and dissolution characteristics throughout the study period. No evidence of discoloration, cracking, or degradation was observed. These findings confirmed the stability and robustness of the developed formulation.

Overall, the formulation strategy employed in this investigation successfully achieved the desired sustained-release characteristics. The optimized matrix tablet provided controlled drug delivery, acceptable pharmaceutical properties, and potential clinical advantages in terms of improved compliance and therapeutic effectiveness.

Table 5: Stability Study Results

| Parameter | Initial | Final |
|---|---|---|
| Appearance | No change | No change |
| Drug Content | Acceptable | Acceptable |
| Dissolution | Comparable | Comparable |

## IV. CONCLUSION

The present investigation successfully developed and optimized a sustained-release matrix tablet formulation of a β-blocker using HPMC K100M and Eudragit RSPO. Drug-excipient compatibility studies confirmed the suitability of the selected polymers for formulation development. The prepared formulations exhibited satisfactory pre-compression and post-compression characteristics, indicating good manufacturability and quality attributes. In vitro dissolution studies demonstrated that polymer concentration significantly influenced release behavior, with the optimized formulation providing sustained drug release for up to 12 hours. Release kinetic analysis suggested diffusion-controlled drug release with contributions from polymer swelling and erosion mechanisms. Stability studies further confirmed the robustness of the optimized formulation. The developed sustained-release delivery system has the potential to improve patient compliance, reduce dosing frequency, and enhance therapeutic outcomes in the management of cardiovascular disorders.

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