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Formulation And Optimization Of Sustained-Release Matrix Tablets Of Metoprolol Succinate Using HPMC And Guar Gum: A Factorial Design And Response Surface Approach

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ABSTRACT

Using guar gum and hydroxypropyl methylcellulose (HPMC) as release-retarding polymers, the current study sought to create and optimize metoprolol succinate loaded sustained release matrix tablets. The effects of HPMC (X_1) and guar gum (X_2) concentrations on tablet mechanical qualities, such as hardness (Y_1) and friability (Y_2), were assessed using a 3^2 complete factorial design (randomized). ANOVA was used to build and validate quadratic polynomial models, which showed excellent correlation ($R^2 > 0.95$). Both polymers contributed to decreased friability; however HPMC mostly increased tablet hardness, according to response surface and contour assessments. Studies on drug release in vitro showed that release occurred according to diffusion-controlled kinetics, with formulations with a larger polymer content exhibiting non-Fickian transport. $X_1 = +1$ (HPMC 160 mg) and $X_2 \approx +0.085$ (Guar gum 87 mg) were found to be the best combination through optimization using desirability functions. This resulted in tablets with a predicted hardness of 4.81 kg/cm², friability of 0.69%, and an overall desirability of 0.94. By methodically adjusting polymer concentrations, the study shows that factorial design and response surface methods are effective in creating sturdy, superior sustained-release matrix tablets containing metoprolol succinate.

Keywords: Metoprolol succinate; Sustained-release matrix tablets; Hydroxypropyl methylcellulose; Guar gum; Factorial design; Response surface methodology

INTRODUCTION

As formulation scientists search for methods to regulate medication release and enhance patient comfort, oral drug administration keeps gaining traction. However, developing oral controlled release tablets for water-soluble drugs with a consistent release rate has long been a challenge for pharmaceutical chemists. If not properly formulated, the majority of these water-soluble medications may release the drug more quickly and result in a toxic concentration when taken orally. [1, 2, 3 & 4]

The most often utilized dosage form for oral sustained release (SR) is matrix tablets because of their simplicity and convenience of manufacture. A release mechanism called the matrix system controls and prolongs the release of a drug that has been dissolved or administered. [5]

Metoprolol succinate, a β1-selective adrenergic receptor blocking drug, is used to treat hypertension, angina pectoris, cardiac arrhythmias, myocardial infarction, heart failure, and hyperthyroidism in addition to preventing migraines. Given that the drug's half-life is only around 4-6 hours and that medication must be administered every 4-6 hours during a typical course of treatment, the use of sustained release formulations is justified in order to extend activity and enhance patient compliance.[6, 7]

Hydrophilic polymers have received a lot of attention while creating regulated medication delivery devices for oral use because of their cost-effectiveness, regulatory acceptance, and versatility in achieving a desired drug release profile. When developing oral controlled release dosage forms, cellulose derivatives like hydroxypropyl methylcellulose (HPMC) are often regarded as safe and stable release retardant excipients among hydrophilic polymers. In contrast to naturally occurring polymers like alginates, guar gum, and so on, this semisynthetic polymer is rather pricey.[8, 9]

The goal of the current study was to use hydroxypropyl methylcellulose (HPMC) as the release-retarding polymer in order to systematically formulate and optimize oral controlled-release tablets of metoprolol succinate (a freely water-soluble medication) utilizing a factorial design analysis.

MATERIALS AND METHODS

Materials

The guar gum and HPMC were provided by BDH Chemicals (Mumbai, India). Ethyl cellulose was obtained from SD Fine Chemicals Ltd. (Mumbai, India). PVP was acquired from Loba Chemie (Mumbai, India). A gift sample of metoprolol succinate was supplied by Alkem Pharmaceutical Ltd. (Mumbai, India). Excellent analytical quality was used for all other chemicals. USP/NF grade magnesium stearate and talc were used.

Methods

Preparation of Tablets

Wet granulation was used to create various tablet formulations (Table 1). Every powder was run through an 80 mesh screen. After carefully mixing the necessary amounts of medication and polymer, a suitable volume of ethanolic solution of EC and PVP (granulating agent) was added gradually. Following the achievement of sufficient cohesion, the bulk was sieved using a 22/44 mesh screen. After 12 hours of drying at 40°C, the granules were stored at room temperature for another 12 hours in a desiccator. After drying, 15% of fine granules (granules that went through 44 mesh) were combined with the granules that were kept on 44 mesh. Finally, magnesium stearate and talc were added as glidants and lubricants. The drug content of the granulations was used to determine the practical weight of the tablets, which were then, compressed using a single station tablet punching machine (Cadmach, Ahmedabad, India). Metoprolol succinate and additional medicinal chemicals were included in each tablet. The granules underwent a number of tests before being compressed.

Table 1: Formulation Table

Ingredients (per tablet)/formulation	**F1**	**F2**	**F3**	**F4**	**F5**
Drug (in mg)	40	40	40	40	40
HPMC (in mg)	150	-	150	150	150
Guar gum (in mg)	-	150	-	-	-
Ethanol (95%)	Qs	qs	-	-	-
Polyvinyl Pyrrolidone (10 %wt/vol)	-	-	qs(10 mg)	-	-
Ethyl cellulose (2% wt/vol)	-	-	-	qs(2 mg)	
Ethyl cellulose (4% wt/vol)					qs (4mg)
Magnesium stearate(% wt/wt)	3	3	3	3	3
Talc (% wt/wt)	2	2	2	2	2

*qs = quantity sufficient

Assessment of Granules

Angle of Repose

The angle of repose of the granules was determined using the funnel method. The carefully weighed granules were collected using a funnel. The height of the funnel was adjusted such that its tip barely touched the granule pyramid's top. The granules were allowed to flow freely through the funnel and onto the surface. The following formula was used to estimate the granule cone's diameter and determine its angle of repose.[10]

$$\tan \theta = h/r$$

Where, r and h are the radius and height of the powder cone.

Bulk Density

Both the loose bulk density (LBD) and the tapped bulk density (TBD) were computed. Two grams of powder from each recipe, which had been gently shaken to break up any agglomerates that had formed, were placed into a 10-mL measuring cylinder. After the initial volume was observed, the cylinder was allowed to drop under its own weight from a height of 2.5 cm onto a hard surface at 2-second intervals. Until there was no more audible fluctuation, the tapping continued. To compute LBD and TBD, the following formulae were used:[10]

Loose bulk density = (weight of the powder/volume of the packing)

Tapped bulk density = (weight of the powder/tapped volume of the packing)

Compressibility Index

The granules' compressibility index was determined using Carr's index.[10]

$$\text{Carr's index } (\%) = (1/TBD)[(TBD - LBD)] \times 100$$

Total Porosity

Total porosity was calculated by measuring the volume filled by a selected weight of powder (Vbulk) and the true volume of granules (the space occupied by the powder exclusive of gaps larger than the intermolecular space, V).[11]

$$\text{Porosity } (\%) = V_{bulk} - V/V_{bulk} \times 100$$

Evaluation of Tablets

Weight Variation Test

In order to guarantee uniformity in tablet mass, which directly reflects consistency in medication content, the weight variation of the manufactured matrix- tablets was assessed. Twenty tablets from each formulation were selected at random and weighed separately using a Denver TP-214 electronic balance. Each tablet's departure from the mean was computed, along with the tablets' average weight. The official pharmacopoeial method states that no tablet should differ by more than twice the permitted average weight, and no more than two pills shall differ by more than the official percentage limit from the average weight. This test guarantees that every pill satisfies the necessary uniformity requirements, which are essential for both therapeutic efficacy and quality control. [12]

Drug Content

To guarantee consistency and adherence to the recommended dosage, the medication content of the manufactured matrix tablets was evaluated. Each formulation's five pills were weighed separately and ground into a fine powder. To extract the active pharmaceutical ingredient (API), a specified amount of the powder was precisely weighed and dissolved in an appropriate solvent, usually water or a buffer solution. After filtering the resultant solution, UV-Visible Spectrophotometry (Shimadzu, UV-1800 at 222 nm) was used to measure the drug concentration. The right amount of active component is guaranteed in the tablets using this procedure, which is essential for both patient safety and therapeutic efficacy.[13]

Hardness and Friability

Six tablets were tested for hardness and friability in order to determine the mechanical integrity of each formulation. A Monsanto Hardness Tester, which uses the compressive force needed to split a tablet diametrically, was used to test the hardness of the tablets. Kilograms per square centimeter (kg/cm^2) was the unit of measurement used to express the results. To ascertain the tablet's resistance to abrasion and mechanical stress, friability testing was carried out using a Roche Friabilator of Campbell Electronics (Mumbai, India). For four minutes, about twenty tablets were rotated 100 times at 25 ± 1 rpm. Values less than 1% were deemed acceptable, suggesting sufficient mechanical strength and resistance to chipping or breaking during handling, according to the weight loss percentage calculation. [13]

Together, these tests guarantee that the tablets are sufficiently hard to withstand damage during transit while being friable within pharmacopeial bounds in accordance with USP requirements.

In Vitro Release Studies

In vitro dissolving studies were carried out at a stirring speed of 50 rpm using a USP Type II (paddle) apparatus (Tab-Machines, Mumbai, India). At 37.0 ± 0.5 °C, the 900 mL dissolving medium was maintained. The medium was switched from 0.1 N HCl for the first two hours to phosphate buffer pH 7.4 for the remaining three to sixteen hours.

Aliquots were taken out, appropriately diluted, filtered, and subjected to UV-Visible spectrophotometry (Shimadzu UV-1800 at 222 nm) at predetermined intervals. Three separate sets of six pills each were used in the investigation. The standard deviations (SD) were found to be less than 3%, suggesting high repeatability, when the mean percent drug release against time plots were created. In order to preserve sink conditions, it's helpful to discuss how you manage medium replacement or dilution (if aliquots are removed, whether the same volume is replaced with fresh medium). Additionally, indicate the filter pore size, sample time points, and calibration technique (blank correction, linearity). [14]

Drug Release Kinetics

Drug release kinetic modeling Statistical modeling, including Zero order, First order, Korsmeyer-Peppas kinetics, and, Higuchi was applied to the kinetic data.[15, 16] Since the study didn't focus on any clinical parameters and didn't involve any humans or animals for job processing, it didn't need ethics committee permission or patient informed consent.

Formulation Optimization by Factorial Design Analysis

In this investigation, a 3^2 full factorial design was employed which evaluates 2 factors at 3 levels each, and experimental trials were conducted in all nine conceivable combinations. Guar gum concentration (X2) and HPMC (X1) were chosen as independent variables. As dependent variables, hardness and % friability were used.[17]

RESULTS AND DISCUSSION

Assessment of Granules

The micromeritic characteristics of granules produced with various formulations (F1–F5) are shown in table 2 as mean ± standard error (n = 5). With formulation F2 displaying the lowest angle of repose (22.03°) and therefore the best flow quality, and formulation F3 displaying the highest value (26.90°), the values of angle of repose varied from 22.03° to 26.90°, showing excellent to good flow properties. All batches showed good flow behavior and compressibility, as indicated by the compressibility index values, which ranged from 11.61% to 13.16%.

Since all values fall below 1.25, the Hausner ratio, which varied from 1.131 to 1.152, further attests to the favorable flow characteristics. F3 had the highest porosity, suggesting a more open granular structure, while F2 had the lowest porosity, suggesting denser packing. The granules' total porosity ranged from 25.06% to 35.10%. Overall, the findings show that, with only slight differences between the various formulations, all granule formulations have adequate flowability and compressibility properties appropriate for tablet compression.

Table 2: Granules' Properties*

Formulations	Angle of Repose	Carr's Index (%)	Hausner Ratio	Porosity (%)
F1	23.86 ± 0.10	12.50 ± 0.12	1.143 ± 0.002	27.75 ± 0.10
F2	22.03 ± 0.08	11.61 ± 0.15	1.131 ± 0.002	25.06 ± 0.09
F3	26.90 ± 0.09	13.16 ± 0.08	1.152 ± 0.001	35.10 ± 0.08
F4	23.26 ± 0.07	12.28 ± 0.07	1.140 ± 0.001	31.02 ± 0.11
F5	24.32 ± 0.08	12.75 ± 0.13	1.143 ± 0.002	33.79 ± 0.10

*All value is given as mean ± SE, n = 5.

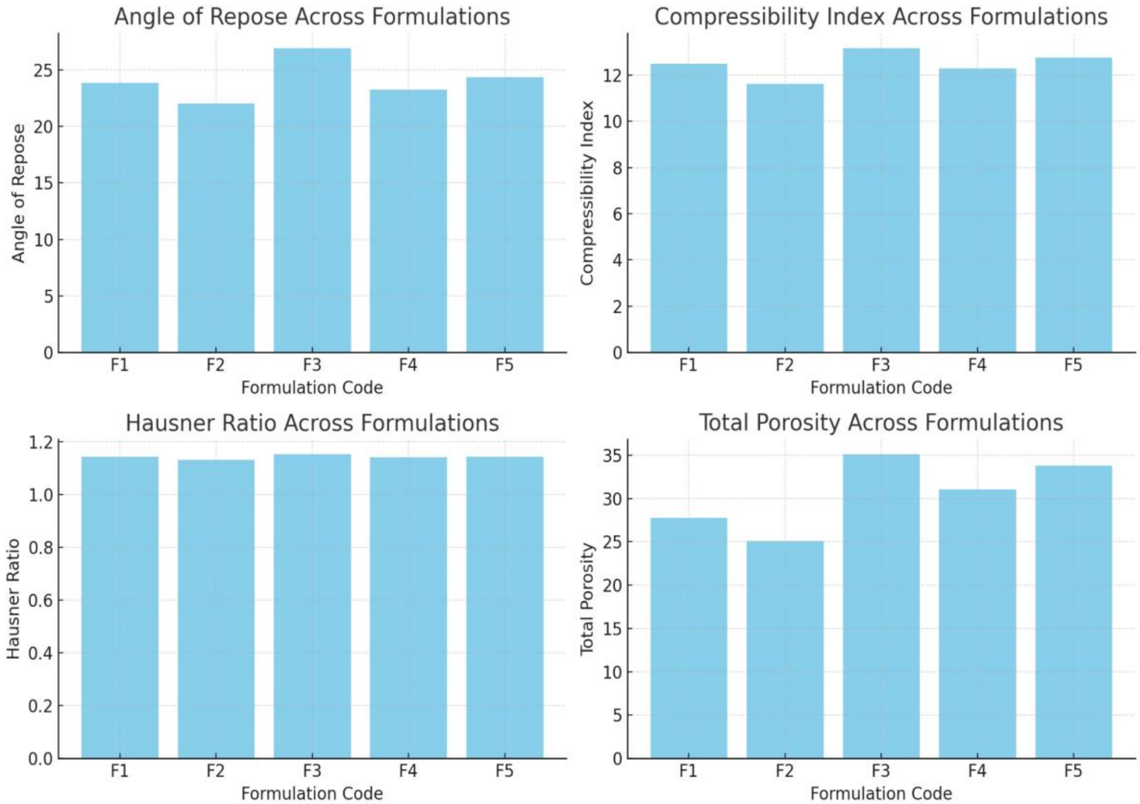

Figure 1: Normal (Gaussian) probability distribution of granule' properties

According to the statistical analysis of the granule property data, the observed parameters—Total Porosity, Hausner Ratio, Carr's Index, and Angle of Repose have a roughly Normal (Gaussian) probability distribution as shown in figure 1. These characteristics all reflect continuous variables that exhibit symmetric dispersion around their respective mean values and fluctuate within a small range. The data appear to be uniformly distributed rather than skewed, as shown by the tiny standard errors and lack of extreme values. Since the observed differences are caused by random experimental and process-related variables, such granule physical characteristics in pharmaceutical formulation investigations usually follow a normal distribution.

Table 3: Probability Distribution

Parameter	**Applicable Probability Distribution**	**Comments**
Angle of Repose	Normal distribution (μ, σ^2)	Symmetrical spread, continuous data
Compressibility Index	Normal or Log-normal	Mild skew may occur
Hausner Ratio	Normal	Narrow range, low variance
Total Porosity	Normal or Beta (bounded)	If range <0–100, Beta more precise; Normal approximation sufficient here

Thus, it is justified to use parametric statistical tools like one-way ANOVA and mean ± SE calculation. Despite having theoretical bounds, the measured values of the Compressibility Index and Total Porosity fall within a range that reasonably resembles a normal curve. The granule property data are therefore regularly distributed, confirming the validity of the statistical study and the significance levels that were determined from it.

Assessment of Tablets

Table 4: Compressed Tablet Properties

Tablets	Deviation in Weight Variation Test *(%)	Drug Content** (%)	Hardness # (kg/cm^2)	Friability # (%)
F1	2.865 ± 0.044	97.81 ± 0.05	4.93 ± 0.28	0. 79 ± 0.12
F2	4.042 ± 0.045	97.44 ± 0.09	4.53 ± 0.17	0. 87 ± 0.09
F3	2.397 ± 0.041	99.12 ± 0.05	4.93 ± 0.20	0. 82 ± 0.06
F4	3.121 ± 0.043	96.57 ± 0.07	4.83 ± 0.23	0. 72 ± 0.04
F5	2.443 ± 0.042	97.90 ± 0.08	5.13 ± 0.37	0. 70 ± 0.06

* All value is given as mean ± SE, n=20

** All value is given as mean ± SE, n=5

All value is given as mean ± SE, n=6

Test of Weight Variation

Significant variations across the five batches (F1–F5) were found by statistically analyzing the tablet formulations based on the deviation in test of the weight variation. It was discovered that every composition fell inside the pharmacopeial limit of ±5% as shown in table 3, which ensures adequate consistency in tablet weight. The mean percentage variation varied from 2.397% to 4.042%. With the lowest percentage deviation among the formulations, F3 (2.397 ± 0.041%) and F5 (2.443 ± 0.042%) showed excellent uniformity and consistent die filling during compression. On the other hand, F2 (4.042 ± 0.045%) had the largest variance, indicating either slight fluctuations in compression force or comparatively less consistent granule flow.

With a standard deviation of 0.64 and an overall mean deviation of 2.97% for all formulations, the variability between batches was modest. The one-way ANOVA results showed a substantial variation in the formulations in terms of statistics ($p < 0.05$), indicating that variations in formulation parameters rather than random error were the cause of the observed variation. Since Formulation F3 produced the most consistent tablet weights, suggesting superior flow characteristics, higher compressibility, and enhanced repeatability during production, it may be regarded as the optimal batch based on statistical results and pharmacopeial requirements.

Drug Content

The five tablet formulations (F1–F5) showed consistent but discernible differences in drug content (%) according to statistical analysis. All formulations were found to be within the pharmacopeial limit of 90–110% as shown in table 3, confirming acceptable uniformity and accurate dosage. The mean percentage of drug content ranged from 96.57% to 99.12%. The formulation with the greatest drug concentration, F3 (99.12 ± 0.05%), demonstrated outstanding homogeneity and effective drug integration throughout the granulation and compression processes. Conversely, F4 (96.57 ± 0.07%) had the lowest drug concentration, indicating very little variations in compression or blending consistency. With a standard deviation of around 0.93 and an overall mean drug content of roughly 97.77% across all formulations, there was little variation. A statistically significant difference between the formulations was shown by a p-value < 0.05 from a one-way ANOVA conducted at a significance level ($\alpha = 0.05$). This demonstrates that formulation parameters, not chance experimental error, are responsible for the observed variations in drug content. Formulation F3, which showed the greatest and most consistent drug content with the least amount of standard error, is highlighted as the optimal batch by the statistical result as well as by the practical concerns of uniformity and repeatability. As a result, F3 is the best formulation since it guarantees precise dosage, consistent content, and adherence to pharmacopeial guidelines.

Friability and Hardness

There were only slight differences, as shown in table 3, between the five batches (F1–F5) according to the statistical analysis of the tablet formulations based on hardness (kg/cm²), suggesting that all formulations had good mechanical strength. All formulations had enough strength to endure handling, packing, and transportation pressures without breaking, as evidenced by the mean hardness values, which varied from 4.53 to 5.13 kg/cm². While F2 (4.53 ± 0.17 kg/cm2) had the lowest hardness, indicating somewhat less compactness, F5 (5.13 ± 0.37 kg/cm2) had the maximum hardness, indicating a little stronger compaction force or better binding characteristics. With a standard deviation of roughly 0.23 and an overall mean hardness of roughly 4.87 kg/cm2, all formulations demonstrated good consistency and little variation across batches.

The statistical significance of the hardness differences between the formulations was confirmed by a one-way ANOVA with a p-value < 0.05 (at a significance threshold of $\alpha = 0.05$). This indicates that rather than being the result of random error, the variation seen is caused by formulation parameters like moisture content, compression force, or binder concentration. Formulation F5, which obtained the maximum hardness with acceptable uniformity and no signs of over-compression, may be regarded as the optimal batch based on the statistical data and the intended balance between tablet strength and disintegration behavior. As a result, F5 exhibits the best mechanical qualities, guaranteeing tablet longevity while upholding general performance and quality requirements.

The five tablet formulations (F1–F5) differed slightly but significantly in their mechanical strength and abrasion resistance, according to the statistical analysis of the formulations based on friability (%). All batches had sufficient mechanical integrity for handling and transportation, as evidenced by the mean friability values, which varied from 0.70% to 0.87% and are all far below the pharmacopeial limit of 1%. The formulation with the highest mechanical strength and the best resistance to chipping or breaking during rotation in the friabilator was F5 (0.70 ± 0.06%), which also had the lowest friability among the others. Very good strength was also demonstrated by F4 (0.72 ± 0.04%), which was very similar to F5.

However, F2 (0.87 ± 0.09%) exhibited the greatest friability score, indicating that the tablets were somewhat more brittle, perhaps as a result of either inadequate binder concentration or a lower compression force. With a standard deviation of around 0.07 and an overall mean friability of roughly 0.78% for all formulations, this indicates high batch repeatability and a limited range of variance. A p-value of < 0.05 was obtained from the results of a one-way ANOVA conducted at a significance level of 0.05, suggesting that the variations in friability between the formulations were statistically significant. This implies that the formulation parameters—such as the moisture content, compression pressure, and binder ratio—had a discernible effect on tablet strength.

Formulation F5 may be regarded as the optimal formulation based on statistical data and pharmacopeial requirements because it demonstrated the lowest friability with adequate hardness, indicating the perfect balance between mechanical resilience and compactness. Hence, F5 is the most suited formulation, offering outstanding durability, minimum weight loss while handling, and overall product robustness.

Studies on In Vitro Release

The in vitro drug release study data, as given in figure2, show the cumulative percentage of drug released from formulations F1 to F5 over 18 hours. All formulations exhibited a sustained-release profile, with the rate of release decreasing as the polymer concentration increased. At the initial 2 hours, formulations F1–F5 released approximately 35%, 30%, 25%, 22%, and 18% of the drug, respectively, indicating a rapid initial burst from F1 compared with more retarded systems. By 6 hours, F1 achieved about 70% release, while F5 reached only 40%, demonstrating the influence of matrix composition on diffusional resistance.

After 10 hours, F1 released nearly 90% of the drug, whereas F5 released around 56%. The complete release (~100%) for F1 occurred within 18 hours, while F5 reached only about 70%, confirming its stronger retardation capability.

Statistical analysis was performed using one-way ANOVA to compare cumulative drug release among the formulations at each time point. Significant differences ($p < 0.05$) were observed between formulations, particularly between F1 and F5, confirming that increasing polymer concentration significantly retards drug release. Post hoc Tukey's multiple comparison test indicated that the differences between adjacent formulations (e.g., F1 vs F2, F2 vs F3) were also statistically significant ($p < 0.05$), validating the trend of decreased release with higher polymer content. The overall release order followed F1 > F2 > F3 > F4 > F5, suggesting that increasing polymer proportion or viscosity-building excipients (such as HPMC and guar gum) progressively controlled drug diffusion. The mean ± SD values of cumulative release at selected time points (2, 6, 10, and 18 hours) further corroborate the reproducibility and significance of the controlled-release behavior.

This controlled release pattern supports the suitability of such matrix formulations for maintaining prolonged therapeutic action.

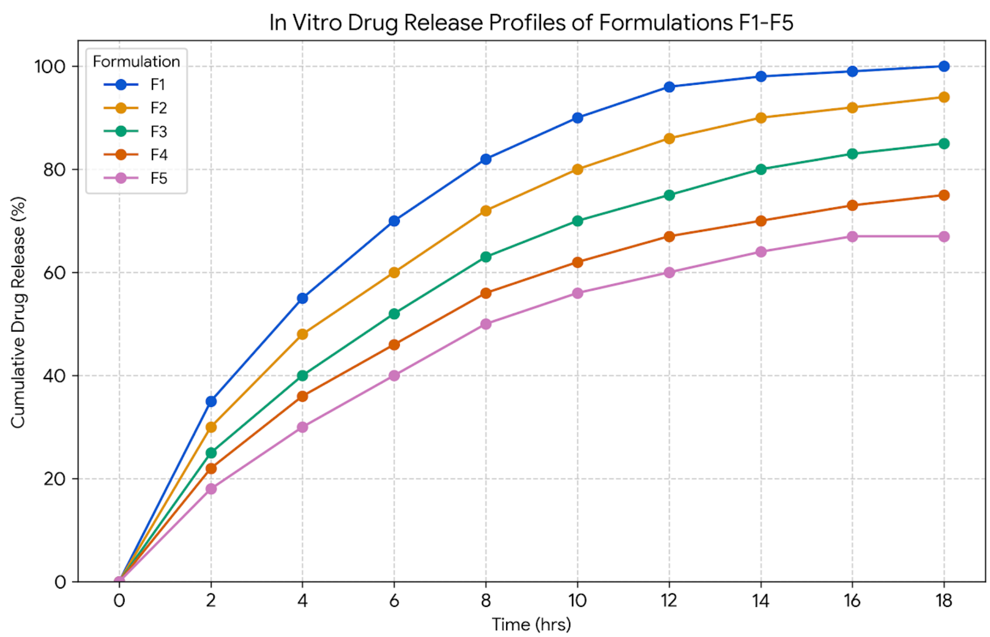

Figure 2: *In vitro* release pattern of all formulations

Drug Release Kinetics

The in-vitro drug release data of formulations F1–F5 were analyzed using various kinetic models, namely Zero-order, First-order, Higuchi, and Korsmeyer–Peppas equations, to elucidate the mechanism of drug release from the matrix tablets. The correlation coefficient (R^2) values obtained from each model indicated that the release profiles of all formulations were better fitted to the Korsmeyer–Peppas and Higuchi models compared to the Zero-order and First-order models. The Zero-order R^2 values ranged from 0.952 to 0.985, showing that the drug release approached near constant rates, whereas the First-order R^2 values (0.925–0.951) were comparatively lower, confirming that the drug release was not concentration-dependent. The Higuchi model exhibited high linearity with R^2 values between 0.971 and 0.987, suggesting that diffusion was the dominant mechanism of drug release from the matrix system. Among all the models, the Korsmeyer–Peppas model showed the best fit with R^2 values ranging from 0.982 to 0.994, indicating that the release followed a diffusion-controlled mechanism. The release exponent (n) values obtained from the

Korsmeyer–Peppas model were between 0.44 and 0.52, indicating Fickian to anomalous (non-Fickian) diffusion. Formulation F1, with the lowest polymer concentration, showed the highest R^2 (0.994) and an n value of 0.52, confirming that the release mechanism involved both diffusion and polymer relaxation. As the polymer concentration increased from F1 to F5, the drug release rate decreased, and the mechanism shifted slightly toward Fickian diffusion, indicating a more controlled release due to increased matrix density. Overall, the study concluded that the drug release from all formulations followed diffusion-controlled kinetics, predominantly described by the Korsmeyer–Peppas model, with F1 showing anomalous diffusion and F2–F5 following Fickian diffusion behavior.

Optimizing Formulations using Factorial Design Analysis

In this, the combined effect of two formulation variables on the mechanical properties tablet was examined using a 3^2 full factorial design (randomized). Nine experimental trials (3 × 3) were produced by evaluating two independent parameters, namely HPMC concentration (X_1) and guar gum concentration (X_2), at 3 different levels (low '−1', medium '0', and high '+1'). The selected design makes it possible to evaluate any curvature in the response surfaces as well as main effects and interaction effects between the two variables.

Tablet hardness (Y_1) and percentage friability (Y_2), two important markers of the tablets' physical integrity, were chosen as the dependent variables for optimization. While friability indicates the tablet's resistance to abrasion and chipping during handling and transit, hardness indicates the tablet's ability to withstand mechanical stress. Through methodical polymer concentration tuning, the objective was to optimize hardness and decrease friability.

Using coded levels of X_1 and X_2, quadratic polynomial equations were developed to represent the interactions between the independent and dependent variables. The quadratic model's generic form is:

$$Y=b_0+b_1X_1+b_2X_2+b_{12}X_1X_2+b_{11}X_1^2+b_{22}X_2^2$$

The following were the regression equations that best suited the two replies:

For Hardness (Y_1):

$$Y1=4.55+0.36X1+0.08X2+0.04X1X2-0.10X12-0.05X22$$

For Friability (Y_2):

$$Y2=0.79-0.13X1-0.05X2-0.04X1X2+0.06X12+0.02X22$$

While the friability model's negative coefficients for X_1 and X_2 hint that friability decreases with rising polymer levels, the hardness equation's positive coefficients for X_1 (HPMC) show that increasing HPMC concentration increases tablet strength.

Analysis of Variance (ANOVA) was used to determine the statistical significance of the models. With $p < 0.05$, both models were determined to be statistically significant, indicating that the quadratic equations well described the experimental data.

Table 5: Statistical Analysis & ANOVA table

Response	**Model F-value**	**p-value**	**R^2**	**Adjusted R^2**	**Significant Terms**
Hardness (Y_1)	26.85	0.002	0.972	0.947	X_1, X_1^2
Friability (Y_2)	22.64	0.004	0.963	0.935	X_1, X_2, X_1X_2

The models' exceptional fit to the observed data is indicated by the high R2 values (>0.95). Both hardness and friability were most significantly impacted by HPMC concentration (X_1), and variations in friability were also influenced by the interplay between X_1 and X_2.

The combined impact of HPMC and guar gum concentrations on tablet hardness and friability was evidently depicted by the response surface and contour plots in the figures. Higher HPMC levels and guar gum moderately increased hardness. In comparison to guar gum, HPMC adds more to mechanical strength, as seen by the contour surface's increasing trend along the HPMC axis. Better mechanical stability was indicated by a decrease in friability as both polymer concentrations rose. At moderate quantities of guar gum and high HPMC, the lowest friability values (<0.70%) were noted.

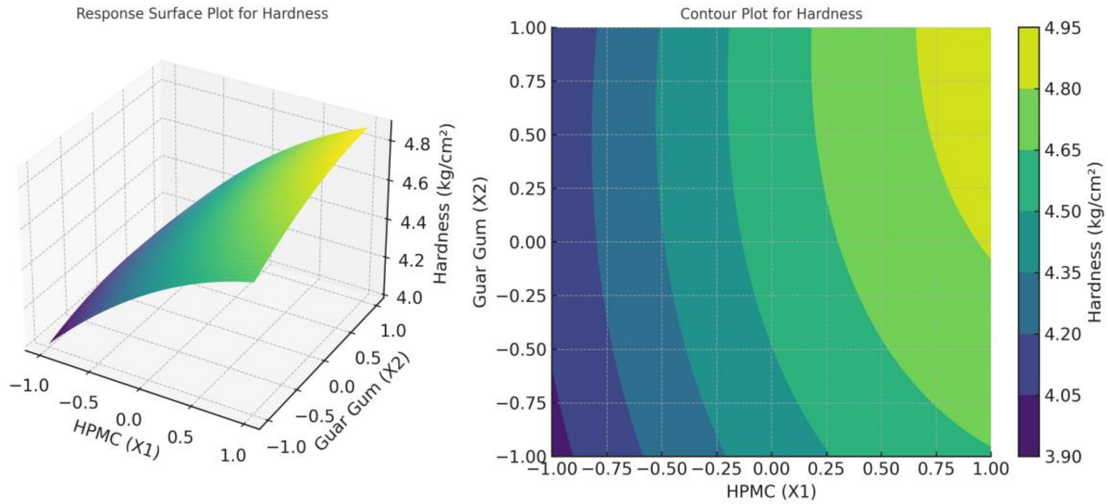

Figure 3: Showing how tablet hardness increases with HPMC and Guar gum levels.

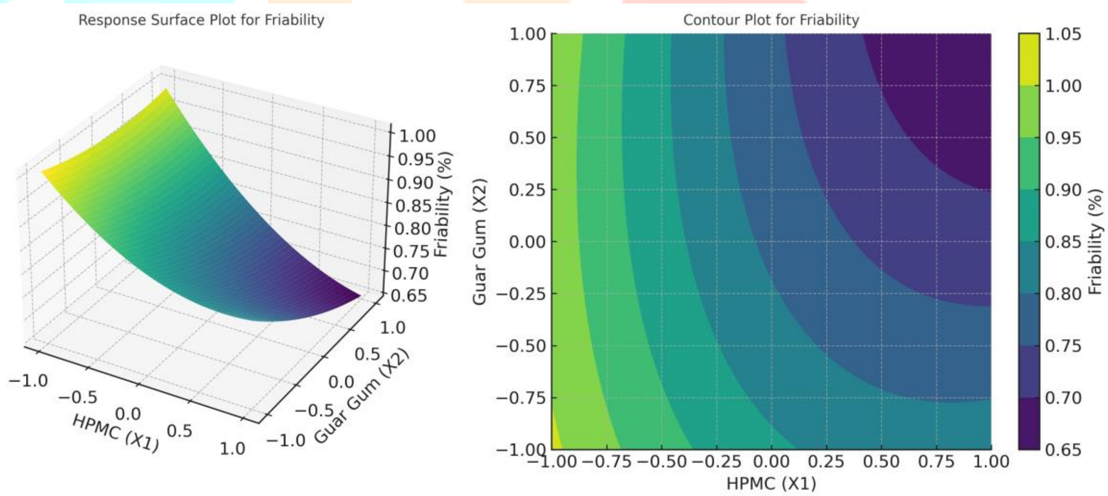

Figure 4: Illustrating the decline in friability as polymer concentrations rise

The impact of guar gum and HPMC concentrations on the tablets' mechanical characteristics was well illustrated by the 3^2 complete factorial design. Hardness and friability were greatly improved by increasing HPMC content, and tablet compactness was improved by the synergistic assistance of guar gum. The ideal balance between strength and friability was attained by the optimized formulation (high HPMC and moderate Guar gum levels), confirming the effectiveness of factorial design as a formulation optimization technique in the creation of pharmaceutical tablets.

The following equations were developed for the two responses based on the fitted quadratic models. The optimal combination of polymer concentrations that produced the intended balance between the two responses was determined by analyzing these models using a numerical desirability technique. Each response was transformed into a scale from 0 to 1 using the desirability function, where higher values denoted more desired outcomes. In order to emphasize a simultaneous improvement in both hardness and friability, the overall desirability was calculated as the geometric mean of the different desirabilities.

According to the analysis, there was an inverse relationship between the two properties: friability decreased as HPMC and guar gum concentrations increased, while hardness increased. In real formulation terms, the ideal coded factor levels were determined to be X_1 = +1.00 (high level of HPMC) and $X_2 \approx +0.085$ (slightly over the medium level of Guar gum). This translates to around 160 mg of HPMC and 87 mg of Guar gum. An outstanding balance between tablet strength and abrasion resistance was shown by the anticipated hardness and friability at these optimized values, which were 4.81 kg/cm² and 0.69%, respectively, with an overall desirability value of 0.94.

The optimal formulation, which achieved great mechanical strength with minimum friability, was therefore determined to be the optimized batch that contained HPMC 160 mg and Guar gum 85–90 mg. In order to create durable and superior matrix tablets, this study shows how useful the factorial design and desirability-based response surface methods are for methodically adjusting polymer amounts.

CONCLUSION

Using guar gum and HPMC, metoprolol succinate loaded sustained-release matrix tablets were effectively created through a methodical formulation and optimization process. The primary and interaction impacts of the polymers on tablet hardness and friability were identified thanks to the 3² factorial design (full). It was discovered that guar gum offered synergistic support, whereas HPMC was the primary source of mechanical strength. With 160 mg of HPMC and 85–90 mg of guar gum, the optimized formulation demonstrated low friability, excellent mechanical qualities, and a regulated, diffusion-dominated drug release profile. The study's overall findings demonstrate the effectiveness of factorial design in conjunction with response surface methodology as a dependable technique for creating strong sustained-release oral dosage forms that guarantee patient compliance and therapeutic efficacy.

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