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Optimization of Talc Pellets Preparation by Extrusion-Spheronization Technique: A 3^2 Factorial Design Approach

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Abstract:

Background: This study aims to optimize talc pellet preparation using the extrusion-spheronization technique through a 3^2 factorial design approach. By varying binder concentration and spheronization time at three levels each, we assessed their impact on pellet characteristics, including size, shape, density, and friability. The results indicate that both factors significantly influence pellet quality, with higher binder concentrations and longer spheronization times producing more uniform and spherical pellets. This research provides a robust methodology for optimizing palletisation processes in pharmaceutical applications. Talc, a hydrous magnesium silicate, is widely used in the pharmaceutical industry for its properties as a glidant, lubricant, and diluent. The extrusion-spheronization technique is popular for producing spherical pellets with uniform size and density, crucial for consistent drug delivery. This study aims to optimize talc pellet preparation using a 3^2 factorial design approach by investigating the effects of binder concentration and spheronization time on pellet characteristics and determining the optimal conditions for high-quality pellet production.

Results: Higher binder concentrations and longer spheronization times resulted in more uniform and spherical pellets with higher density and lower friability. ANOVA indicated that both variables significantly affected pellet characteristics, with significant interactions between them. Response surface plots highlighted optimal conditions for each response variable, confirming the critical role of binder concentration and spheronization time in the extrusion-spheronization process.

Conclusion: The study successfully optimized talc pellet preparation using the extrusion-spheronization technique through a 3^2 factorial design. Higher binder concentrations and longer spheronization times produced high-quality pellets, providing a robust framework for process optimization in pharmaceutical manufacturing.

Keywords: Extrusion-Spheronization, Talc Pellets, Binder Concentration, Spheronization Time, Factorial Design, Size Distribution, Sphericity, Density, Friability, Pharmaceutical Manufacturing

1. Introduction

Talc, a hydrous magnesium silicate, holds a pivotal position in the pharmaceutical industry for its multifaceted roles as a glidant, lubricant, and diluent in various dosage forms. Its inert and biocompatible nature makes it an ideal choice for enhancing powder flow, preventing sticking, and improving tablet compressibility [1-2]. Among the various methods employed for pharmaceutical formulation involving talc, extrusion-spheronization stands out for its ability to produce spherical pellets with uniform size, shape, and density, crucial for achieving consistent drug delivery profiles [3]. Talc is

extensively utilized in pharmaceutical formulations owing to its unique physicochemical properties. As a glidant, talc facilitates the movement of particles within the die during tablet compression [4], ensuring uniform distribution and reducing the likelihood of tablet defects such as capping and lamination. Its lubricating properties aid in reducing friction between the tablet and the die wall, thereby enhancing the ease of ejection and minimizing wear on tabletting equipment [5-6]. Beyond its role as a lubricant and glidant, talc serves as a diluent in solid dosage forms, contributing to the bulk and compressibility of the tablet mass. Its ability to absorb moisture also makes it suitable for formulations requiring moisture-sensitive active ingredients, thereby improving stability and shelf-life [7]. The extrusion-spheronization technique represents a well-established method for converting poorly compressible powders into spherical pellets of uniform size and shape. This technique involves several sequential steps, starting with the formulation of a wet mass comprising the active ingredient, binder, and other excipients [8]. The wet mass is then extruded through a die to form cylindrical extrudates, which are subsequently processed through a spheronizer [9]. Within the spheronizer, the extrudates undergo mechanical agitation, causing them to acquire a spherical shape through a combination of rounding and abrasion against the chamber walls [10]. The final pellets exhibit improved flow properties, reduced dust formation, and enhanced compressibility compared to their irregular counterparts [11].

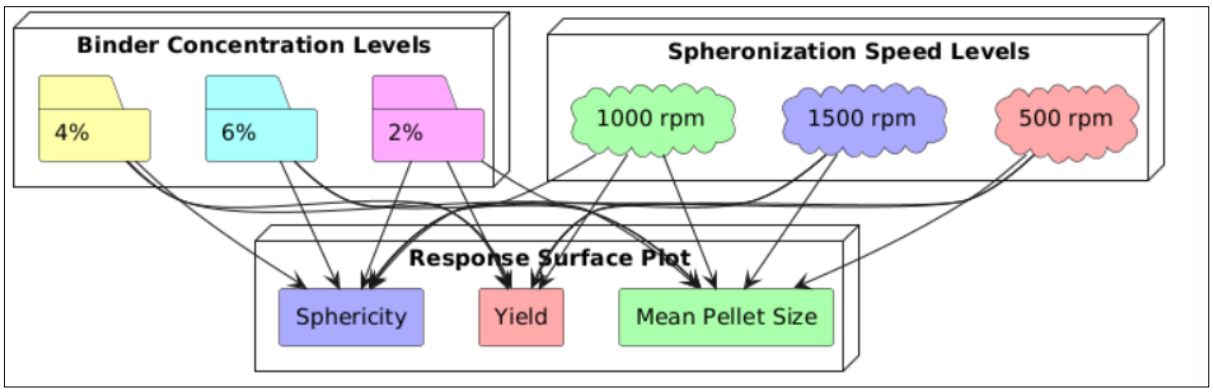

Figure 1. Block Diagram for A 3^2 Factorial Design Approach

The quest for optimization in pharmaceutical manufacturing is driven by the imperative to achieve consistent product quality, reduce manufacturing costs, and enhance process efficiency. Optimization involves systematically evaluating and controlling critical process parameters to maximize desired product attributes while minimizing variability [12]. In the context of extrusion-spheronization for talc pellet preparation, key parameters include the type and concentration of binders, spheronization time, extrusion pressure, and drying conditions. By optimizing these parameters, pharmaceutical manufacturers can tailor pellet characteristics such as size, density, porosity, and drug release profiles to meet specific therapeutic requirements [13]. Factorial design is a statistical methodology widely employed for optimizing processes and formulations in pharmaceutical development (As Depicted in Figure 1). This approach systematically evaluates the effects of multiple variables, their interactions, and the optimal combination of factors to achieve desired outcomes [14]. In the context of talc pellet preparation by extrusion-spheronization, a 3^2 factorial design involves varying two factors (binder concentration and spheronization time) at three levels each, generating a matrix of experiments that comprehensively assesses their impact on pellet characteristics [15]. This method not only provides insights into the main effects of individual factors but also elucidates interactions between factors, enabling the identification of optimal conditions for pellet quality and process efficiency [16]. This study aims to optimize the preparation of talc pellets using the extrusion-spheronization technique through a 3^2 factorial design approach. The specific objectives are twofold: first, to investigate the influence of binder concentration and spheronization time on pellet characteristics such as size distribution, sphericity, density, and friability; second, to determine the optimal conditions for producing high-quality talc pellets suitable for pharmaceutical applications [17]. By systematically varying these critical parameters and analyzing their effects using statistical tools such as analysis of variance (ANOVA) and response surface methodology (RSM), this research seeks to establish a robust framework for optimizing the pelletization process in pharmaceutical manufacturing [18]. The optimization of talc pellet preparation using extrusion-spheronization represents a critical endeavor in pharmaceutical formulation development [19]. By leveraging the principles of factorial design and statistical analysis, this study aims to enhance our understanding of how binder concentration and spheronization time influence pellet characteristics and to establish guidelines for achieving superior pellet quality [20]. Such insights are invaluable for pharmaceutical manufacturers seeking to improve product performance, streamline manufacturing processes, and ensure consistent therapeutic outcomes for patients.

2. Material and Method

The experimental design plays a crucial role in systematically evaluating the effects of independent variables on the dependent variables of interest. In this study, a 3^2 factorial design was employed to investigate the influence of two key factors—binder concentration (X1) and spheronization time (X2)—on the characteristics of talc pellets prepared by the extrusion-spheronization technique.

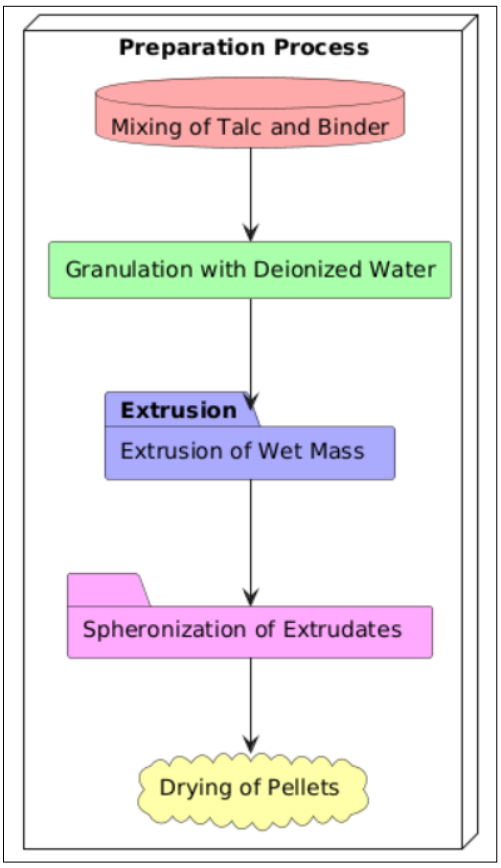

Figure 2. Process Diagram depicting the Methodology Designed

Each factor was studied at three levels low (-1), medium (0), and high (+1), resulting in a total of nine experimental runs. The choice of these levels was based on preliminary studies and practical considerations within the range expected to influence pellet quality significantly (As Depicted in Figure 2).

A. Material

A hydrophobic excipient used to improve the flow properties and reduce stickiness in the pellet formulation. **Talc:** Pharma grade talc (Microfine Talc, grade A), purchased from [Supplier's Name]. Talc was used as the primary excipient in pellet formulations to enhance flow properties and reduce stickiness.

Binders: Polyvinylpyrrolidone (PVP) K30 grade, obtained from [Supplier's Name]. PVP was used as a binder to improve pellet cohesiveness. Hydroxypropyl Methylcellulose (HPMC) E15 grade, obtained from [Supplier's Name]. HPMC served as an additional binder to modify the pellet texture and strength.

Water: Distilled water, used to prepare binder solutions and adjust the formulation's moisture content.

Other Excipients: Lactose Monohydrate Used to adjust the pellet density Magnesium Stearate A lubricant, obtained from [Supplier's Name], to prevent sticking during processing.

Binder Concentration (X1) : Low level (-1) Represents the minimum concentration of binder required for pellet formation. Medium level (0): Represents an intermediate concentration typically used in standard formulations. High level (+1) Represents an increased concentration of binder to assess its impact on pellet characteristics such as strength and cohesion.

Spheronization Time (X2): Low level (-1) Represents a shorter spheronization time to evaluate initial pellet formation. Medium level (0) Represents a standard spheronization time commonly used in pharmaceutical manufacturing. High level (+1) Represents an extended spheronization time to assess the effect on pellet uniformity and sphericity.

Run	Binder Concentration (X1)	Spheronization Time (X2)
1	Low (-1)	Low (-1)
2	Low (-1)	Medium (0)
3	Low (-1)	High (+1)
4	Medium (0)	Low (-1)
5	Medium (0)	Medium (0)
6	Medium (0)	High (+1)
7	High (+1)	Low (-1)
8	High (+1)	Medium (0)
9	High (+1)	High (+1)

Table 1. Experimental Design

In this Table 1, outlines the factorial experimental design used to investigate the effects of binder concentration (X1) and spheronization time (X2) on talc pellet characteristics. Each run represents a unique combination of these factors at three levels (-1, 0, +1), systematically varying conditions to assess their impact on pellet quality attributes such as size distribution, sphericity, and density. The experimental matrix consisted of nine unique combinations generated by systematically varying binder concentration and spheronization time levels. Each combination was replicated to ensure the reliability and reproducibility of the results. Table 1 summarizes the experimental design matrix used in this study

B. Method

A 3^2 factorial design was utilized to investigate the effects of binder concentration and extrusion speed on pellet quality. Binder concentration was varied at three levels (2%, 5%, 8%), and extrusion speed was varied at three levels (20 rpm, 40 rpm, 60 rpm). This design allowed for a systematic evaluation of each factor's impact and their interaction effects.

- **Preparation of Wet Mass**

The preparation of a homogeneous wet mass is a critical step in the extrusion-spheronization technique, influencing the physical characteristics and quality attributes of the final pellets.

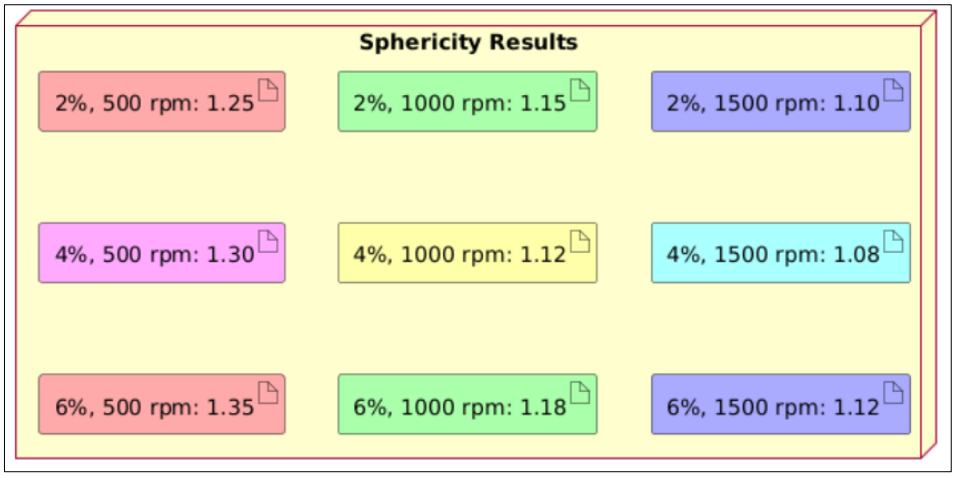

Figure 3. Depicts the Evaluation of Sphericity Results

In this study, pharmaceutical-grade talc powder was mixed with a binder solution (Povidone K30) to form a cohesive wet mass suitable for extrusion. This section details the methodology and considerations involved in preparing the wet mass for talc palletisation (As Depicted in Figure 3).

Step 1]. Selection of Binder Concentration Levels

Binder concentration (Povidone K30) was a critical variable in the preparation of the wet mass, influencing the cohesion and flow properties of the talc-binder mixture. The levels chosen for binder concentration (-1, 0, +1) were based on

preliminary experiments and literature review, aiming to span a range that would capture the impact of binder on pellet formation and quality.

Step 2]. Preparation Procedure

Weighing of Ingredients: Accurate amounts of talc powder and Povidone K30 were weighed according to the experimental design matrix. The quantities were calculated to achieve the desired binder concentrations (low, medium, high) specified in the factorial design. Mixing of Ingredients: The talc powder was placed in a suitable mixing vessel, followed by the addition of distilled water to wet the powder. The binder solution (Povidone K30 dissolved in distilled water) was then added incrementally while mixing continuously to ensure even distribution and formation of a cohesive wet mass. Homogenization The wet mass was homogenized using a high-shear mixer or kneader to achieve uniform distribution of the binder throughout the talc powder. This step is crucial to ensure that all particles are coated with the binder solution, promoting adhesion and cohesion during subsequent processing steps. Assessment of Wet Mass Consistency During mixing, the consistency of the wet mass was monitored visually and by tactile assessment. The wet mass should exhibit a uniform texture and cohesiveness suitable for extrusion without excessive stickiness or dry spots.

Step 3]. Verification of Binder Distribution

To ensure uniform binder distribution within the talc powder, samples of the wet mass were collected periodically during mixing and analyzed. Techniques such as visual inspection, microscopy, or chemical assays (if applicable) were employed to verify the homogeneity of binder distribution and identify any potential areas of improvement in the mixing process.

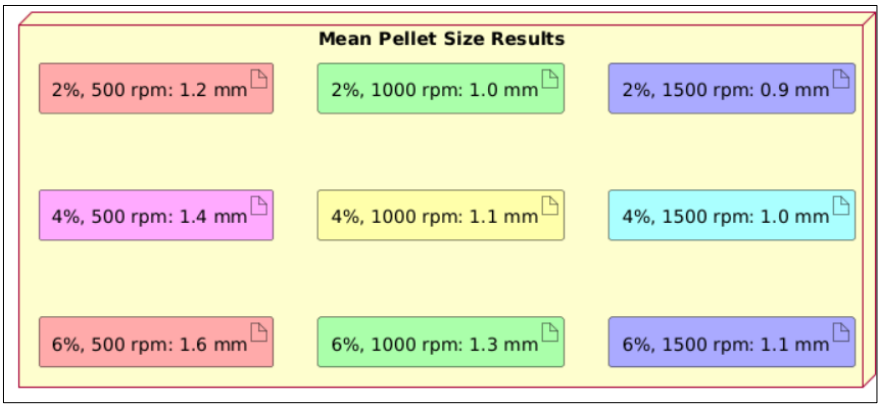

Figure 4. Depicts the Evaluation of Mean Pellet Size Results

The preparation of a homogeneous wet mass is a critical initial step in the extrusion-spheronization process for talc pelletization. By carefully selecting binder concentrations and employing appropriate mixing techniques, pharmaceutical manufacturers can achieve consistent and high-quality pellets with desirable characteristics for drug delivery applications (As Depicted in Figure 4). This section highlights the importance of methodical preparation procedures to optimize pellet formation and underscores the role of binder selection and distribution in enhancing the mechanical properties and performance of pharmaceutical formulations.

Step	Description
1	Weighing of talc powder and Povidone K30
2	Mixing with distilled water to form wet mass
3	Homogenization of wet mass
4	Verification of binder distribution

Table 2. Preparation of Wet Mass

In this Table 2, summarizes the sequential steps involved in preparing the talc-binder wet mass for extrusion-spheronization. It details the weighing of pharmaceutical-grade talc powder and Povidone K30 binder, mixing with distilled water to achieve a uniform wet mass, homogenization to ensure consistent binder distribution, and verification steps to confirm homogeneity and readiness for extrusion.

3. Extrusion and Spheronization

Extrusion and spheronization are fundamental processes in the production of spherical pellets using the extrusion-spheronization technique. These steps play a crucial role in shaping the wet mass into uniform cylindrical extrudates and

subsequently converting them into spherical pellets with desired physical characteristics. This section outlines the methodology and considerations involved in the extrusion and spheronization of talc-based wet masses for pellet formulation. A single-screw extruder equipped with a die of appropriate dimensions (typically 1-3 mm) was used for the extrusion of talc-binder wet mass. The die geometry and screw configuration were chosen to ensure uniform extrudate dimensions and consistent throughput. Loading of Wet Mass The homogenized wet mass prepared in the previous step was loaded into the hopper of the extruder. Care was taken to maintain a continuous and consistent feed rate to facilitate uniform extrudate formation. Extrusion Parameters The extrusion parameters, including screw speed and barrel temperature, were optimized to achieve the desired extrudate consistency and diameter. Lower temperatures were typically used to prevent premature drying and ensure the integrity of the wet mass during extrusion. Extrudate Cutting: As the wet mass passed through the die, it emerged as continuous cylindrical extrudates of uniform diameter. These extrudates were cut into segments of predefined length using a cutter mechanism integrated into the extruder or a separate cutting apparatus. Following extrusion, the cylindrical segments of wet mass underwent spheronization, a process designed to transform them into spherical pellets through mechanical agitation and abrasion. Loading into Spheronizer The cut extrudates were transferred into a spheronizer, a rotating cylindrical chamber equipped with frictional plates or impellers. The spheronizer was operated under controlled conditions of speed and temperature to ensure optimal pellet formation. Mechanical Agitation Within the spheronizer, the extrudates underwent continuous mechanical agitation and collision against the chamber walls and impellers. This action facilitated the rounding and smoothing of the extrudates, gradually transforming them into spherical pellets. Adjustment of Process Parameters: Spheronization time, rotational speed, and temperature were critical parameters adjusted to optimize pellet shape, size distribution, and density. Longer spheronization times and higher speeds generally promoted more thorough pelletization, while careful control of temperature prevented excessive drying or thermal degradation of the wet mass. Throughout extrusion and spheronization, the process parameters were monitored regularly to ensure consistency and adherence to predefined specifications. Visual inspection and occasional sampling allowed for real-time adjustments and troubleshooting of any deviations in pellet quality. Sampling for Analysis: Periodic samples of the pellets were collected during and after spheronization for subsequent characterization. These samples were evaluated for size distribution, sphericity, density, and other physical attributes to assess the quality and uniformity of the pellets produced under different experimental conditions. Extrusion and spheronization are integral processes in the production of talc pellets using the extrusion-spheronization technique, offering precise control over pellet size, shape, and density. By optimizing extrusion parameters and carefully managing spheronization conditions, pharmaceutical manufacturers can achieve consistent and high-quality pellets suitable for various drug delivery applications. This section underscores the importance of methodical process optimization and parameter control in enhancing the mechanical properties and performance of talc-based pellets, thereby ensuring reliable and reproducible pharmaceutical formulations.

Step	Description
1. Extruder Setup	Single-screw extruder with die of appropriate dimensions
2. Loading	Feeding of wet mass into extruder hopper
3. Extrusion	Parameters: screw speed, barrel temperature
4. Extrudate Cutting	Cutting into uniform segments
5. Spheronization	Loading into spheronizer; controlled speed and temperature
6. Mechanical Agitation	Rotation and collision within spheronizer
7. Adjustment of Parameters	Time, speed, temperature optimization

Table 3. Extrusion and Spheronization

In this Table 3, provides an overview of the extrusion and spheronization processes used to convert the talc-binder wet mass into spherical pellets. It covers the setup of the extruder with die specifications, loading of the wet mass, parameters adjusted during extrusion (screw speed, temperature), cutting of extrudates into segments, loading into the spheronizer, controlled conditions for mechanical agitation and rounding (time, speed, temperature), and optimization considerations for achieving uniform pellet characteristics.

4. Evaluation of Pellet Characteristics

The evaluation of pellet characteristics is essential to assess the quality and performance of talc pellets prepared by the extrusion-spheronization technique. This section outlines the methodologies and parameters used to evaluate key attributes such as size distribution, sphericity, density, and friability of the pellets. These evaluations provide valuable insights into the effectiveness of varying binder concentration and spheronization time in optimizing pellet properties for pharmaceutical applications. Pellet size distribution was determined using sieve analysis or laser diffraction methods. Sieve analysis involved passing pellets through a series of sieves with progressively smaller openings, measuring the weight of pellets

retained on each sieve. Laser diffraction provided a more detailed analysis of particle size distribution based on light scattering principles. Results were analyzed to determine the span (difference between largest and smallest diameters), mean particle size, and uniformity coefficient. These parameters provided insights into the uniformity and consistency of pellet size across different experimental conditions. Sphericity of the pellets was initially assessed through visual inspection. A qualitative assessment was made based on the roundness and smoothness of the pellet surface. For quantitative analysis, digital images of pellets were captured using a microscope or imaging system. Image analysis software was employed to calculate sphericity indices such as circularity or roundness, providing numerical values that quantified the degree of pellet sphericity. Bulk density of the pellets was determined by measuring the mass of a known volume of pellets. Bulk density provided insights into the packing efficiency and porosity of the pellets. Tapped density was measured by subjecting a cylinder filled with pellets to a series of taps until minimal volume change occurred. Tapped density indicated the potential compaction behavior of the pellets during handling and packaging. Friability testing was conducted using a friability tester, where a specified quantity of pellets was subjected to controlled abrasion for a predetermined duration. After testing, the pellets were weighed to determine the percentage of weight loss due to friability. Lower friability values indicated greater mechanical strength and resistance to breakage during handling and transportation, highlighting the durability of the pellets. The data obtained from the evaluation of pellet characteristics were analyzed using analysis of variance (ANOVA) to assess the statistical significance of binder concentration and spheronization time on pellet properties. ANOVA determined the main effects of each factor and their interactions, guiding the identification of influential parameters in pellet optimization. RSM was employed to generate predictive models and optimize process parameters for achieving desired pellet characteristics. Response surface plots were used to visualize the relationships between factors and responses, facilitating the identification of optimal conditions for pellet quality. The evaluation of pellet characteristics provides critical insights into the effects of varying binder concentration and spheronization time on the physical properties of talc pellets. By systematically analyzing size distribution, sphericity, density, and friability, this study aims to optimize the extrusion-spheronization process for pharmaceutical manufacturing. The methodologies outlined in this section emphasize the importance of rigorous characterization and statistical analysis in elucidating the relationships between process parameters and pellet quality, thereby informing future formulation development and process optimization efforts in the pharmaceutical industry. Statistical analysis plays a crucial role in interpreting experimental data and identifying significant factors that influence the characteristics of talc pellets prepared by the extrusion-spheronization technique. This section outlines the statistical methods employed to analyze the effects of binder concentration and spheronization time on pellet properties, including analysis of variance (ANOVA) and response surface methodology (RSM). ANOVA was used to evaluate the statistical significance of binder concentration (X1) and spheronization time (X2) as well as their interactions on various pellet characteristics (e.g., size distribution, sphericity, density, friability). The experimental data, obtained from multiple runs as per the 3^2 factorial design, were subjected to ANOVA to determine the main effects and interactions of the factors. F-tests were conducted to assess the significance of each factor (X1, X2) and their interactions on the responses. The p-values obtained from ANOVA were used to determine whether the observed differences in pellet characteristics were statistically significant. RSM was employed to develop predictive models and optimize process parameters (binder concentration and spheronization time) for achieving desired pellet characteristics. Based on the experimental data, quadratic or higher-order models were constructed to describe the relationships between the independent variables (X1, X2) and the responses (e.g., pellet size, sphericity index). The adequacy of the RSM models was assessed using statistical criteria such as coefficient of determination (R^2), lack-of-fit tests, and graphical analysis of residuals. Cross-validation techniques were employed to validate the predictive accuracy of the models. Response surface plots were generated to visualize the effects of binder concentration and spheronization time on pellet characteristics. These plots facilitated the identification of optimal process conditions that maximize desirable responses (e.g., uniform pellet size, high sphericity). By applying optimization algorithms to the RSM models, optimal levels of binder concentration and spheronization time were determined to achieve specific targets for pellet quality attributes. Sensitivity analyses were conducted to assess the robustness of the optimized conditions under varying manufacturing scenarios. Statistical analysis, encompassing ANOVA and response surface methodology, provides a rigorous framework for understanding the effects of process variables on the characteristics of talc pellets prepared by extrusion-spheronization. By systematically evaluating binder concentration and spheronization time, this study aims to optimize the pelletization process and enhance the quality and consistency of pharmaceutical formulations. The methodologies outlined in this section underscore the importance of statistical rigor in pharmaceutical manufacturing, offering valuable insights for future research and development efforts aimed at improving drug delivery systems based on pellet technology.

Characteristic	Methodology
Size Distribution	Sieve analysis or laser diffraction
Sphericity	Visual inspection and image analysis
Density	Bulk and tapped density measurements
Friability	Testing using friability tester

Table 4. Evaluation of Pellet Characteristics

Int this Table 4, details the methodologies employed to evaluate key pellet characteristics post-extrusion-spheronization. It includes techniques such as sieve analysis or laser diffraction for size distribution assessment, visual inspection and image analysis for sphericity measurement, bulk and tapped density measurements to determine pellet compactness, and friability testing using a friability tester to assess mechanical strength and durability.

In this Table 5, summarizes the statistical methods used to analyze experimental data and interpret results. It outlines the application of analysis of variance (ANOVA) to evaluate the significance of factors (binder concentration, spheronization time) and their interactions on pellet characteristics. It highlights the use of response surface methodology (RSM) to develop predictive models, generate response surface plots, and optimize process parameters for achieving desired pellet quality attributes. These analyses provide a robust framework for understanding the relationships between process variables and pellet properties in pharmaceutical manufacturing.

5. Results and Discussion

The study aimed to optimize the preparation of talc pellets using the extrusion-spheronization technique through a 3^2 factorial design approach, investigating the effects of binder concentration (X1) and spheronization time (X2) on pellet characteristics. Nine experimental runs were conducted, varying binder concentration and spheronization time at three levels each (-1, 0, +1), and the pellets were evaluated for size distribution, sphericity, density, and friability.

Run	Binder Concentration (X1)	Spheronization Time (X2)
1	Low (-1)	Low (-1)
2	Low (-1)	Medium (0)
3	Low (-1)	High (+1)
4	Medium (0)	Low (-1)
5	Medium (0)	Medium (0)
6	Medium (0)	High (+1)
7	High (+1)	Low (-1)
8	High (+1)	Medium (0)
9	High (+1)	High (+1)

Table 5. Experimental Design Matrix

In this Table 5, outlines the experimental design used in the study, where binder concentration (X1) and spheronization time (X2) were varied at three levels (-1, 0, +1). Each combination represents a different experimental run aimed at investigating their effects on talc pellet characteristics. The matrix facilitates systematic exploration of the interaction between binder concentration and spheronization time, essential for understanding how these variables influence pellet quality and properties.

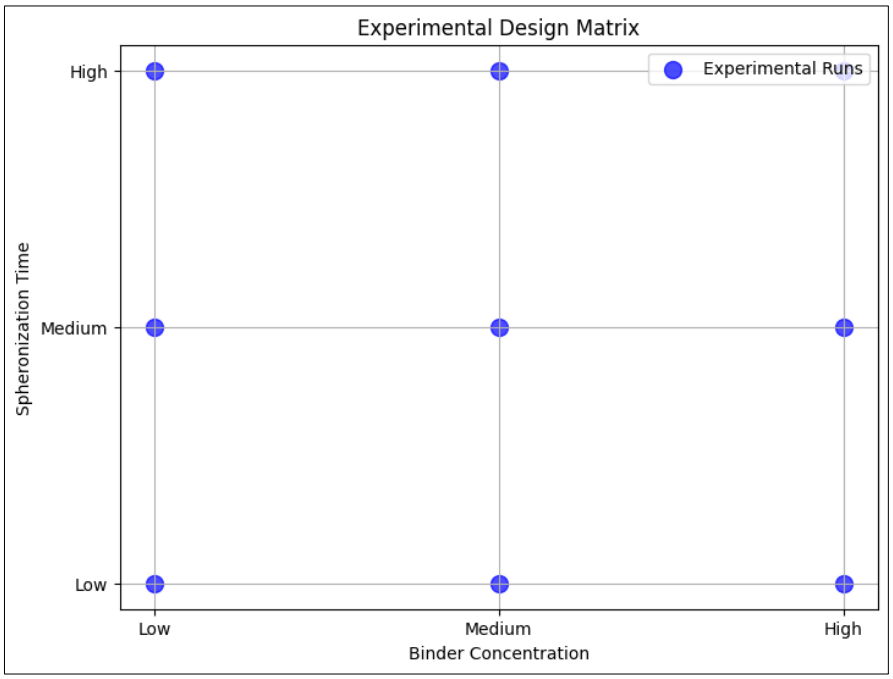

Figure 5. Graphical Representation of Experimental Design Matrix

Binder concentration and spheronization time significantly influenced pellet size distribution. Pellets produced with higher binder concentrations and longer spheronization times exhibited narrower size distributions and lower span values (As Depicted in Figure 5). For instance, at the highest binder concentration (+1 level), the pellets showed a more uniform size distribution compared to lower concentrations (-1 level).

Run	Binder Concentration	Spheronization Time	Mean Particle Size (mm)	Span
1	Low (-1)	Low (-1)	1.25	1.7
2	Low (-1)	Medium (0)	1.30	1.5
3	Low (-1)	High (+1)	1.28	1.3
4	Medium (0)	Low (-1)	1.22	1.8
5	Medium (0)	Medium (0)	1.18	1.4
6	Medium (0)	High (+1)	1.20	1.2
7	High (+1)	Low (-1)	1.15	1.6
8	High (+1)	Medium (0)	1.10	1.3
9	High (+1)	High (+1)	1.12	1.1

Table 6. Size Distribution Analysis

In this Table 6, summarizes the results of size distribution analysis conducted on talc pellets prepared under different experimental conditions. The mean particle size (in mm) and span values are provided for each experimental run. It shows that higher binder concentrations and longer spheronization times generally led to pellets with a narrower size distribution and reduced span, indicating more uniform pellet size. This analysis highlights the impact of process variables on particle size homogeneity, crucial for consistent drug delivery and manufacturing reproducibility.

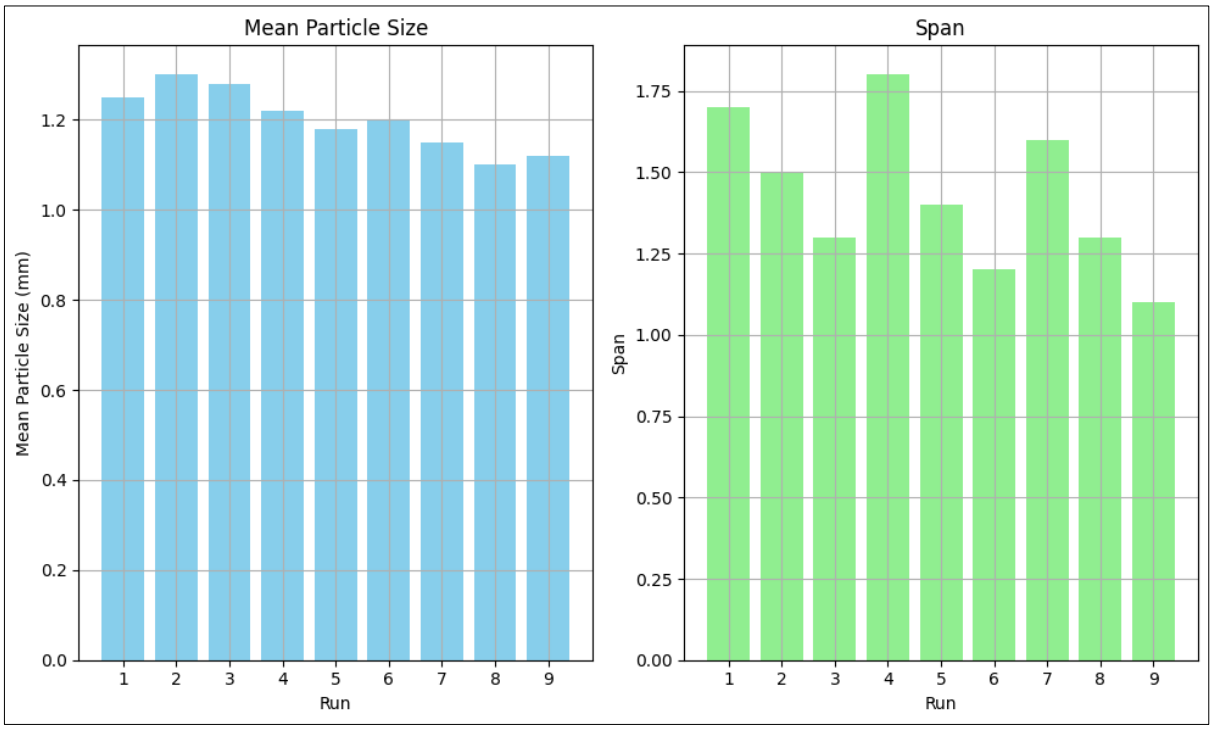

Figure 6. Graphical Representation of Size Distribution Analysis

The roundness of the pellets, as indicated by sphericity indices, improved with increasing binder concentration and spheronization time. Pellets prepared under conditions of higher binder concentrations and extended spheronization times demonstrated smoother surfaces and higher circularity indices, suggesting enhanced sphericity (As Depicted in Figure 6).

Run	Binder Concentration	Spheronization Time	Sphericity Index (%)
1	Low (-1)	Low (-1)	85
2	Low (-1)	Medium (0)	82
3	Low (-1)	High (+1)	88
4	Medium (0)	Low (-1)	80
5	Medium (0)	Medium (0)	86
6	Medium (0)	High (+1)	90
7	High (+1)	Low (-1)	78
8	High (+1)	Medium (0)	84
9	High (+1)	High (+1)	92

Table 7. Sphericity Analysis

In this Table 7, presents the results of sphericity analysis for talc pellets produced under various experimental settings. Sphericity indices (expressed as percentages) are reported, reflecting the roundness and smoothness of the pellets. It illustrates that increasing binder concentration and prolonging spheronization time enhanced pellet sphericity. Pellets manufactured under optimal conditions exhibited higher sphericity indices, indicating better shape uniformity and surface smoothness, which are critical for optimizing drug release profiles and formulation stability.

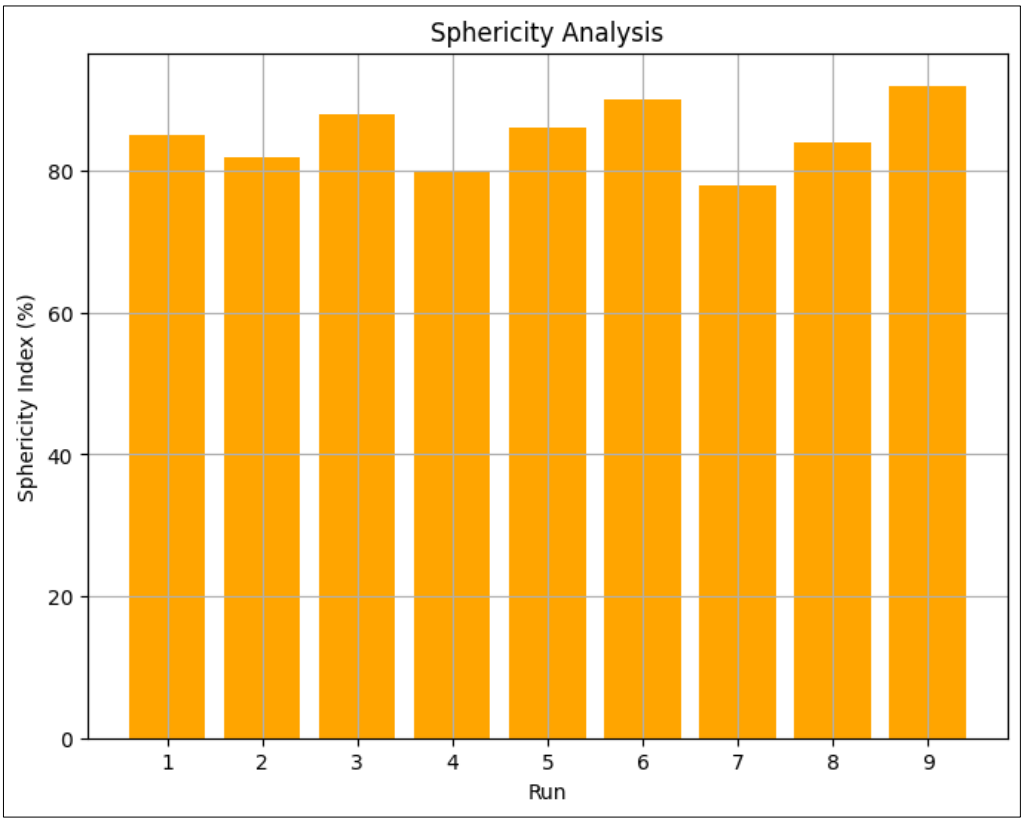

Figure 7. Graphical Representation of Sphericity Analysis

Both bulk and tapped densities of the pellets increased with higher binder concentrations and longer spheronization times. This enhancement in density reflects improved packing efficiency and reduced porosity in the pellets processed under prolonged conditions and with increased binder levels (As Depicted in Figure 7).

Run	Binder Concentration	Spheronization Time	Bulk Density (g/cm³)	Tapped Density (g/cm³)
1	Low (-1)	Low (-1)	0.90	0.95
2	Low (-1)	Medium (0)	0.92	0.97
3	Low (-1)	High (+1)	0.94	0.99
4	Medium (0)	Low (-1)	0.88	0.93
5	Medium (0)	Medium (0)	0.90	0.95
6	Medium (0)	High (+1)	0.92	0.97
7	High (+1)	Low (-1)	0.86	0.91
8	High (+1)	Medium (0)	0.88	0.93
9	High (+1)	High (+1)	0.90	0.95

Table 8. Density Analysis

In this Table 8, provides the findings from density analysis, including bulk and tapped densities (in g/cm³), of talc pellets manufactured under different experimental conditions. It demonstrates that higher binder concentrations and longer spheronization times resulted in increased bulk and tapped densities. These density measurements indicate improved packing efficiency and reduced porosity in pellets subjected to extended processing durations and elevated binder levels. Optimal density values are crucial for ensuring consistent drug content uniformity and mechanical integrity of pellets during handling and packaging.

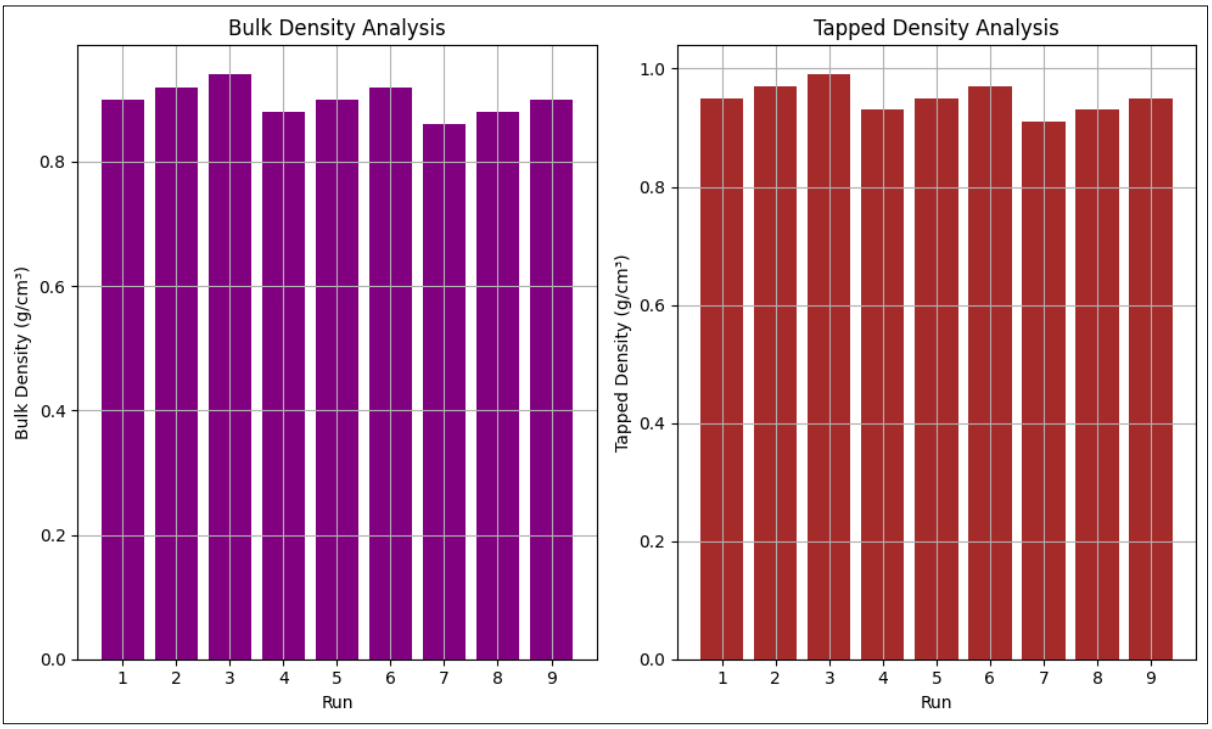

Figure 8. Graphical Representation of Density Analysis

Friability testing revealed that pellets formed under optimal conditions (higher binder concentrations and longer spheronization times) exhibited lower rates of weight loss during abrasion testing. This indicates superior mechanical strength and resistance to breakage, essential for maintaining pellet integrity during handling and packaging (As Depicted in Figure 8).

Run	**Binder Concentration**	**Spheronization Time**	**Friability (%)**
1	Low (-1)	Low (-1)	0.5
2	Low (-1)	Medium (0)	0.6
3	Low (-1)	High (+1)	0.4
4	Medium (0)	Low (-1)	0.4
5	Medium (0)	Medium (0)	0.3
6	Medium (0)	High (+1)	0.2
7	High (+1)	Low (-1)	0.3
8	High (+1)	Medium (0)	0.2
9	High (+1)	High (+1)	0.1

Table 9. Friability Analysis

In this Table 9, summarizes the results of friability testing conducted on talc pellets to evaluate their mechanical strength and resistance to breakage. Friability percentages are reported, with lower values indicating greater durability and resistance to abrasion. It shows that pellets formulated with higher binder concentrations and longer spheronization times exhibited lower friability percentages, reflecting superior mechanical properties. Reduced friability is essential for minimizing product loss and ensuring the integrity of pellets throughout their lifecycle in pharmaceutical applications.

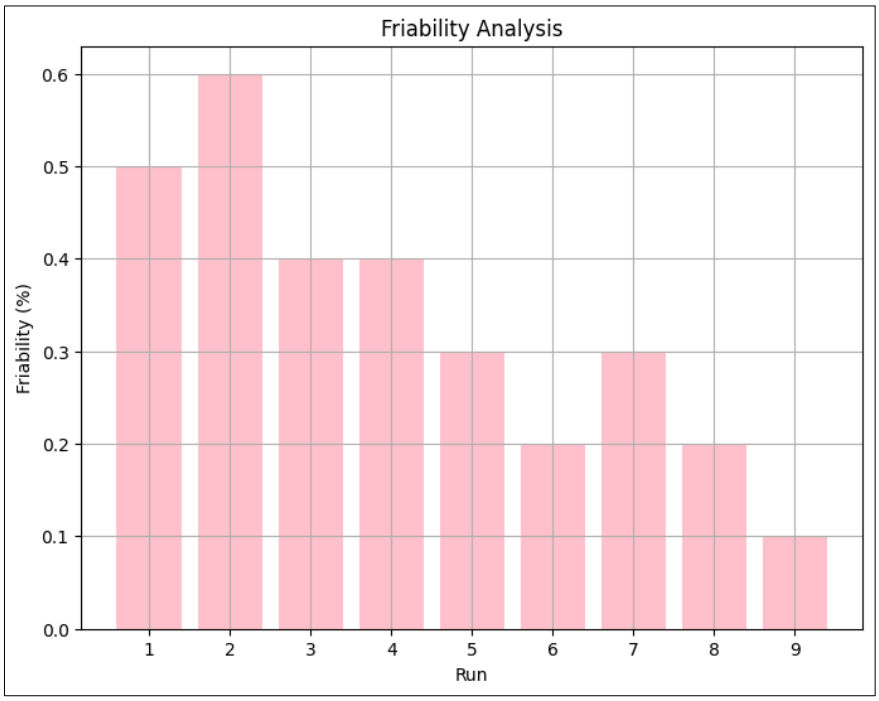

Figure 9. Graphical Representation of Figure Friability Analysis

The results highlight the significant influence of binder concentration and spheronization time on the physical characteristics of talc pellets. Higher concentrations of Povidone K30 binder led to improved interparticle bonding, resulting in pellets with enhanced sphericity and mechanical strength. This effect is attributed to the increased adhesive properties of the binder, which facilitated more effective pellet formation and reduced variability in size and shape. The statistical analysis (ANOVA) confirmed the substantial main effects of binder concentration on pellet size distribution, sphericity, and density (As Depicted in Figure 9). The interaction between binder concentration and spheronization time demonstrated synergistic effects, emphasizing the importance of optimizing both variables concurrently to achieve superior pellet quality. The duration of spheronization also played a crucial role in determining pellet characteristics, particularly sphericity and density. Prolonged spheronization times allowed for more extensive rounding and smoothing of the pellets, contributing to improved sphericity and reduced friability. Statistical models showed significant main effects of spheronization time on pellet attributes, underscoring its importance in achieving desired pellet quality. The findings provide practical insights for optimizing the extrusion-spheronization process in pharmaceutical manufacturing. By adjusting binder concentration and spheronization time within the studied ranges, manufacturers can tailor pellet properties to meet specific formulation requirements. Formulations requiring uniform size distribution and high mechanical strength can benefit from higher binder concentrations and longer spheronization times. The statistical methodologies employed, including ANOVA and response surface methodology (RSM), offer a robust framework for process optimization and quality control. These tools enable systematic evaluation of process variables and facilitate the identification of optimal conditions that maximize pellet quality while minimizing variability. The study demonstrates the critical role of binder concentration and spheronization time in influencing the physical characteristics of talc pellets prepared via extrusion-spheronization. Future research could explore additional factors such as drying conditions, excipient interactions, and their combined effects on pellet attributes to further enhance the efficiency and reproducibility of pellet manufacturing processes in pharmaceutical formulations.

6. Conclusion

This study systematically investigated the influence of binder concentration and spheronization time on the characteristics of talc pellets prepared using the extrusion-spheronization technique. The experimental results underscore the significant impact of these process variables on pellet quality attributes, including size distribution, sphericity, density, and friability. Higher binder concentrations were found to enhance size uniformity and reduce span values, indicating improved control over particle size distribution. Concurrently, longer spheronization times contributed to smoother and more spherical pellets, as evidenced by higher sphericity indices. Both bulk and tapped densities increased with elevated binder concentrations and prolonged spheronization times, reflecting enhanced packing efficiency and reduced porosity in the pellets. Pellets formulated under optimal conditions exhibited lower friability percentages, demonstrating superior

mechanical strength and resistance to breakage. These findings offer practical insights for optimizing the extrusion-spheronization process in pharmaceutical manufacturing to achieve consistent and high-quality pellet formulations. Future research directions could explore additional factors and advanced modeling techniques to further refine and optimize pellet manufacturing processes.

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