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Effects of Dry Granulation Operating Parameters on Forming Quality

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Abstract: To address the issues of the existing dry granulation process, which mostly relies on manual adjustments based on empirical experience and lacks the analysis of theoretical data, a simplified model of tablet pressing based on a modified Drucker–Prager Cap (DPC) material constitutive model was proposed to simulate and analyze the forming process of tablets, and study the impacts of the feeding speed, roller speed, friction coefficient and roller clearance on the density distribution of the pressed tablets via ABAQUS. The results show that the roller speed significantly impacts the density of tablets, and a lower roller speed and a higher friction coefficient are beneficial to the formation of tablets. As the roller clearance decreases, the average density at the clearance increases, and the unevenness of the lateral density distribution of the tablets increases, showing a distribution trend of larger density at the center and smaller density on both sides.

Keywords: dry granulation; operating parameters; forming quality; DPC

Citation: Xie, X.; Gao, H.; Xie, Z.; Wu, M. Effects of Dry Granulation Operating Parameters on Forming Quality. *Appl. Sci.* **2023**, *13*, 10619. https://doi.org/10.3390/app131910619

Academic Editors: Marcin Graba and Stanisław Adamczak

Received: 11 August 2023
Revised: 20 September 2023
Accepted: 21 September 2023
Published: 23 September 2023

1. Introduction

Granulation methods commonly used by pharmaceutical companies are mainly dry granulation and wet granulation. Dry granulation is a physical processing method that turns raw materials into granules. Compared to wet granulation, dry granulation eliminates the need for subsequent production processes such as drying and milling, thereby reducing the need for excipients and resulting in a relative increase in drug loading [1]. Dry granulation technology is more mature in developed countries and widely used in the food and pharmaceutical industries, but its theoretical knowledge is relatively weak [2]. In industrial applications, there are still problems, such as uniform feeding and powder leakage. The process itself and process parameters are mostly controlled by operators based on experience, which cannot guarantee the uniformity of drug particles and can result in low production efficiency and energy consumption. Numerical simulation can shorten the research and development cost and cycle and has become one of the methods studied and analyzed by many scholars. Some scholars have conducted simulation research on dry granulation in the fields of pharmaceuticals, feed, and chemicals, mainly on the compression process of tablets.

Ariel et al. [3] compared powder rolling experiments using a two-dimensional finite element model and a one-dimensional finite element model proposed by Johanson [4] and found that the predicted trends of the meshing angles were the same for both methods. Mazor et al. [5] analyzed the distribution of compressive stress on tablets during the rolling process for the two rolling systems and verified the results through experiments. Ariel et al. [6] used a pneumatic piston feeding device to simulate the distribution of density in the width direction of the tablet under horizontal feeding and obtained phenomena in agreement with the experimental results. John et al. [7] developed two- and three-dimensional rolling models with adaptive meshes, analyzed the stress changes at the gap between rollers under different feed stresses and roller surface frictions and followed the experimental trend, which was beneficial to process optimization. Michrafy et al. [8] analyzed the distribution of the exit tablets under constant pressure and at a constant speed and found that the density of the tablets changed less in the width direction under a constant feed pressure than at a constant speed. Mazor et al. [9] used a combined finite element and discrete element simulation model to link the feeding process and rolling processes and obtained the law of uneven distribution of powder. Sinka et al. [10] analyzed the local density distribution of the curved powder after compaction via finite element analysis and optimized the geometric shape of the tablets to achieve the best results.

The simulation of the rolling process via the finite element method, compared to the advantages of the discrete element method on the amount of powder and the interaction between the particles, do not need to be taken into account, avoiding a large number of calculations, but to analyze the form of the motion of the sheet molding from a macroscopic point of view.

Rodriguez et al. combined DEM and MBD with a novel particle displacement model (PRM) and found that rotating the side plates with studs produced a more uniform force in the bed and that the edge effect was independent of roll length [11]. Weerasekara and others think that the application scale and complexity of DEM in simulated crushing technology have increased and put forward the prospect of incorporating DEM output into a standard crushing model for equipment and process design and optimization in the future [12]. Cleary et al. used DEM to study HPGR to explore the pressure distribution and how the pressure distribution and the roughness of particles change along the roller [13].

In summary, research on the rolling and pressing process for granular solids is still in its infancy, and there are few simulations of rolling tablets using drug powder as the research object. In this paper, the Drucker–Prager Cap (DPC) model is introduced into the granulation process of drug powders, and the influence of adjustable process parameters based on the existing equipment of enterprises on the molding quality of dry granulation prelude tablets is investigated through the establishment of a rolling model of granular solids, which can save the cost and time of experiments and guide theoretical research and practice.

2. Model Description

Conservation of mass and momentum, as well as energy, is maintained during the process of sheet pressing. For the motion methods describing the sheet molding process, there are mainly Lagrangian and Eulerian methods. For the Lagrangian method, the mesh nodes move with the material, and it is easy to impose free boundary conditions that reflect the molding process changes. For the Eulerian motion description, the mesh remains fixed, and the material moves in the mesh, so it cannot reflect the changes in an elastic–plastic material. Therefore, the Lagrangian method was chosen in this study to describe the spatial motion changes. The ABAQUS software has certain advantages in the field of numerical simulation in handling compressible hyperelastic materials and geological materials. In this study, the Abaqus dynamic-explicit module is selected for simulation research on the pressing process via ABAQUS 2019.

2.1. Drucker–Prager Cap Model

Many continuum media-based material models have used different assumptions, including the Mohr–Coulomb model, the Drucker–Prager model, the Cam–Clay model, and the Drucker–Prager Cap model. The DPC model is regarded as an ideal model to describe the compression process in uniaxial compression experiments [14], which can describe the shear failure properties of the particles and can be characterized via experiments with real powders. It has been widely used in the geotechnical field. The drug powder used in dry granulation is a viscous plastic material similar to the geotechnical properties, so the modified Drucker–Prager Cap model was chosen for this study.

The DPC model mainly consists of three parts: shear failure surface, smooth transition surface, and cap surface. It solves the yield caused by material compression and can also control the expansion of the material under shear. The functions of each surface satisfy the following relationships [15].

$$F_s = q - p\tan\varphi - d = 0 \tag{1}$$

$$F_t = \left\{ (p - p_a)^2 + \left[q - \left(1 - \frac{\lambda}{\cos\varphi}\right)(d + p_a \tan\varphi)\right]^2 \right\}^{1/2} - \lambda(d + p_a \tan\varphi) = 0 \tag{2}$$

$$F_c = \sqrt{(p - p_a)^2 + \left(\frac{Rq}{1 + \lambda - \lambda/\cos\varphi}\right)} - R(d + p_a \tan\varphi) \tag{3}$$

where φ is the internal friction angle of the powder, d is the cohesive force, R is the cap parameter, and α is the parameter of the easing curve of the transition zone.

$$p = \frac{1}{3}(\sigma_1 + \sigma_2 + \sigma_3) \tag{4}$$

$$q = \sqrt{\frac{3}{2}\left[(\sigma_1 - \sigma_\mathrm{m})^2 + (\sigma_2 - \sigma_\mathrm{m})^2 + (\sigma_3 - \sigma_\mathrm{m})^2\right]} \tag{5}$$

$$P_b = P_a(1 + R\tan\varphi) + D \tag{6}$$

where p is the hydrostatic pressure, q is the von Mises stress, and D is the relative density. Where P_a is the hydrostatic pressure corresponding to the intersection of the transition surface and one end of the cap surface and P_b is the hydrostatic pressure corresponding to the other end of the cap surface.

2.2. Physical Model

Figure 1 shows the LGS5 granulator with a class A sealed rolling device. The main components for tablet forming are the rollers, the sealing plates (fixed cheek plates on both sides of the rollers and upper and lower seals in the thickness direction of the rollers), and the horizontal feeding channel.

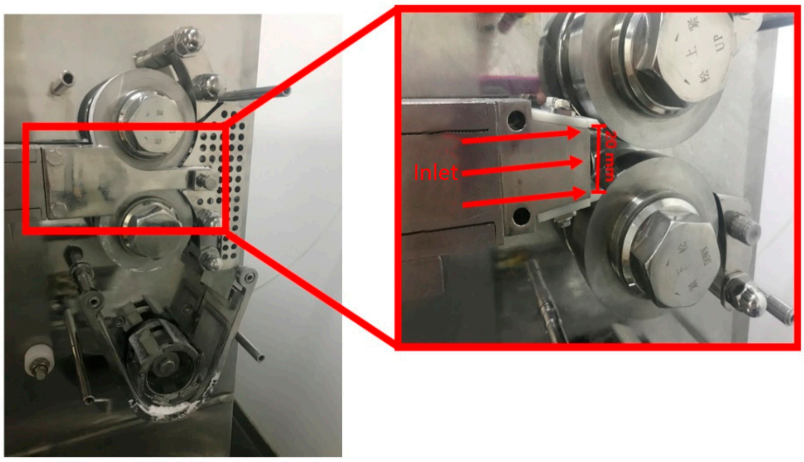


Figure 1. Tablet institutions.

The rolling components of the above LGS prototype were selected, and the structures that have little impact on the results were omitted. The powder is simulated as a deformable body and defined as a continuous medium without considering the impacts of temperature and air. The stiffness of the sealing structure and the roller is much greater than that of the powder, so they were defined as discrete rigid bodies without considering their deformation and wear during the rolling process. The simplified model is shown in Figure 2 below, with the radius of the roller being 50 mm, its thickness being 25 mm, and the thickness of the sealing structure being 1 mm.

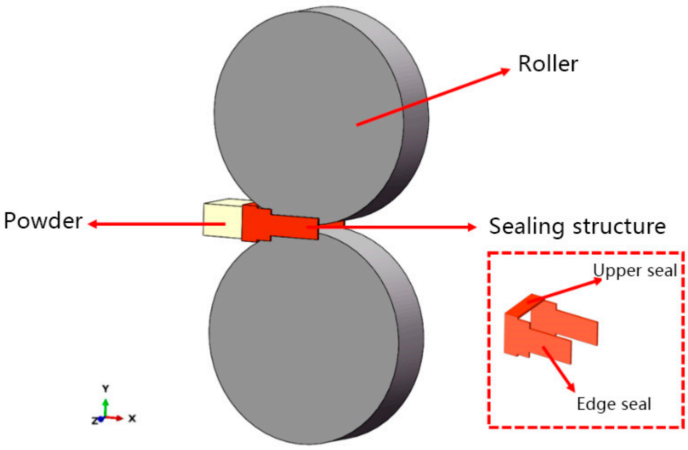


Figure 2. Simplified model of sheet pressing mechanism.

2.3. Material Parameters

The material used for the simulation is microcrystalline cellulose, commonly used in experiments, and the constitutive model for plastic material (the DPC model) was chosen. The property parameters of the material are shown in Tables 1 and 2 below [3].

Table 1. Plastic parameters of cap of microcrystalline cellulose.

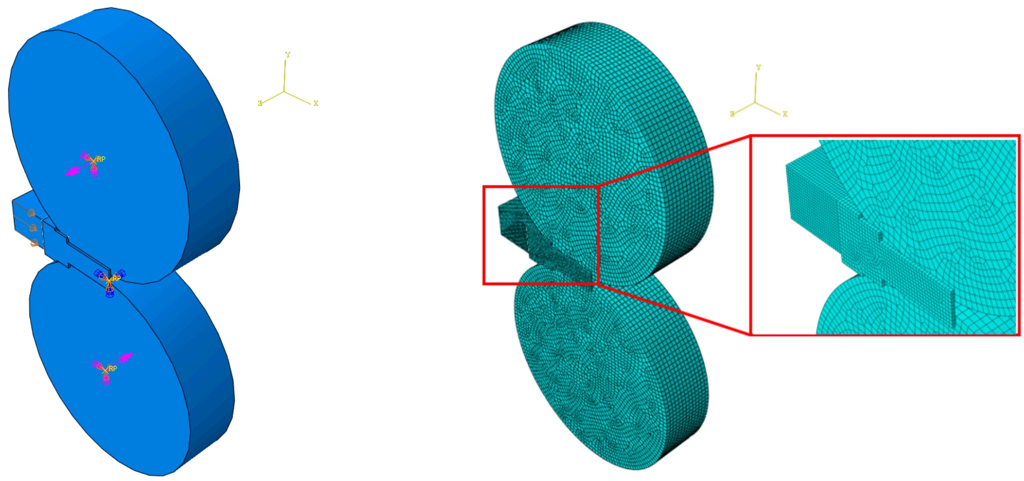
Parameters	Value
Elastic modulus (MPa)	481
Poisson's ratio	0.062
Cohesive force (N)	0.127
Internal friction angle (°)	54
Cap eccentricity	0.166
Transition surface radius (mm)	0.05
Flow stress ratio	0.779
Relative density	0.35

Table 2. Hardening law of materials.

Hydrostatic Stress/MPa	Plastic Volumetric Strain
0.05	0
0.43	0.124
1.35	0.374
1.94	0.478
2.95	0.572
6.03	0.742
10.04	0.884
15.93	1.010
28.87	1.120

2.4. Boundary Conditions

The sealing structure is set to full constraint (*ENCASTRE), and an equivalent axial horizontal speed is applied to the powder block. An axial rotational speed is applied to the center of the roller, and the degrees of freedom for other displacement and rotation directions to rotate around the axis. When the powder block is transported horizontally, the contact between the powder block and the roller and between the powder block and the sealing plate mainly manifests as surface-to-surface contact (*SURFACE_TO_SURFACE). The surfaces of the roller and sealing plates are the master surfaces, and the powder surface is the slave surface, with tangential and normal contact behavior. The constraint form is the kinematic contact method (*KINEMATIC_CONTACT_METHOD), which helps prevent penetration after the powder is compressed and deformed, making it easier to obtain a converged solution. The coefficient of friction between the roller surface and the powder and between the side sealing plate and the powder is 0.4 on average. The boundary conditions of the model are shown in Figure 3a.



(**a**) (**b**)

Figure 3. The powder rolling model by ABAQUS: (**a**) Boundary condition. (**b**) Mesh division.

2.5. Mesh Generation and Mesh Independence Verification

The mesh element type for the roller and sealing mechanism, as shown in Figure 3b, is a 4-node rigid element with a size of 1. The powder is divided into hexahedrons, and the element type is an 8-node linear reduced integration element. The rollers and sealing mechanism are discrete rigid bodies, and the accuracy of the mesh has a negligible impact on them. Therefore, the mesh size of the powder needs to be refined.

Before conducting a numerical simulation study, it is necessary to determine the size and number of the mesh. The size and number of the mesh have an important relationship with the solution speed and the accuracy of the results; that is, the mesh independence needs to be verified. Table 3 shows the maximum density of the tablet after rolling at the same time step (horizontal speed of 25 mm/s and roller speed of 1.5 rad/s) as the indicator for mesh independence verification.

Table 3. Grid independence result.

Unit Size	Number of Units	Number of Nodes	Maximum Density (g/cm^3)
2.00	2600	3234	0.580
1.60	5200	6188	0.619
1.30	8835	10,240	0.585
1.00	20,000	22,386	0.636
0.80	38,750	42,432	0.671
0.70	59,508	64,380	0.678
0.60	92,862	99,416	0.698

The mesh-independent verification results show that the density of the mesh size varies within 5% for mesh sizes between 0.6 and 0.8. In order to ensure the accuracy of the results and the solution speed, a mesh size of 0.8 was chosen.

3. Results and Discussion

3.1. Impact of the Feeding Speed on Tablet Formation

To analyze the impact of the feeding speed on tablet formation, the process parameters were set as follows (in Table 4): the roller speed was 2 rad/s; the roller clearance was 4 mm; the friction coefficient between the roller surface and sealing structure was 0.4; and the horizontal feeding speed was 24 mm/s, 30 mm/s, and 36 mm/s, respectively. The corresponding screw speeds were calculated to be 115 r/min, 144 r/min, and 172 r/min, respectively.

Table 4. Different combinations of process conditions for the study of feeding speed.

Screw Speed	Axial Velocity	Roller Speed	Rotational Speed Ratio
115 r/min	24 mm/s	2 rad/s	6:1
144 r/min	30 mm/s	2 rad/s	7.5:1
172 r/min	36 mm/s	2 rad/s	9:1

The density clouds and slice diagrams of the tablet at the gap between rollers with the same time step after being solved using the dynamic-explicit solver are shown below in Figure 4.

The quality parameters of the tablet formed after rolling are evaluated via the density distribution, and the rollers and sealing structures are hidden during the analysis. A monitoring surface was established in the width direction of the tablet at the gap between rollers, and the density on the path was extracted and used to solve for the average density. By comparing the simulation results of the model at different feeding speeds, it can be found that the tablet has the maximum density at the gap between the rollers, mainly concentrated in the middle, and decreases approximately in a circular manner towards both sides. This is mainly because the powder expands towards both sides under the pressure, and there is also the influence of the edge effect. The edge effect means that the pressure at the edge of the roller will decrease even if there is an edge seal [11,13]. This edge effect is reduced due to the increase of pressure generated in the feed powder speed. The powder is more concentrated in the middle, and the actual screw feed shows uneven material in the space. The filling rate of the powder in the middle is higher, leading to a greater contact pressure. The analysis of the slice diagram of the tablet shows that with the increase of the feeding speed, the area of the maximum density of the tablet in the center increases towards both sides, and the average density increases from 0.49 g/cm^3 to 0.58 g/cm^3, which makes the tablet thicker and is conducive to increasing the efficiency of the tablet formation. As shown in Figure 4c, there is an expansion at the tail of the powder, mainly because when the feeding speed is too high and the roller speed is constant, the amount of feeding is increased, and the powder accumulates near the sealing plates. There are some burrs or distorted grids on both sides of the tablet, which is due to the rolling effect of the small gap, causing some of the meshes to extend to both sides and interact with the sealing plate, thereby causing curling towards the gap between the sealing plate and the roller. This is consistent with the actual leakage of the powder, but the finite element method cannot show the volume reduction caused by the leakage of the powder.

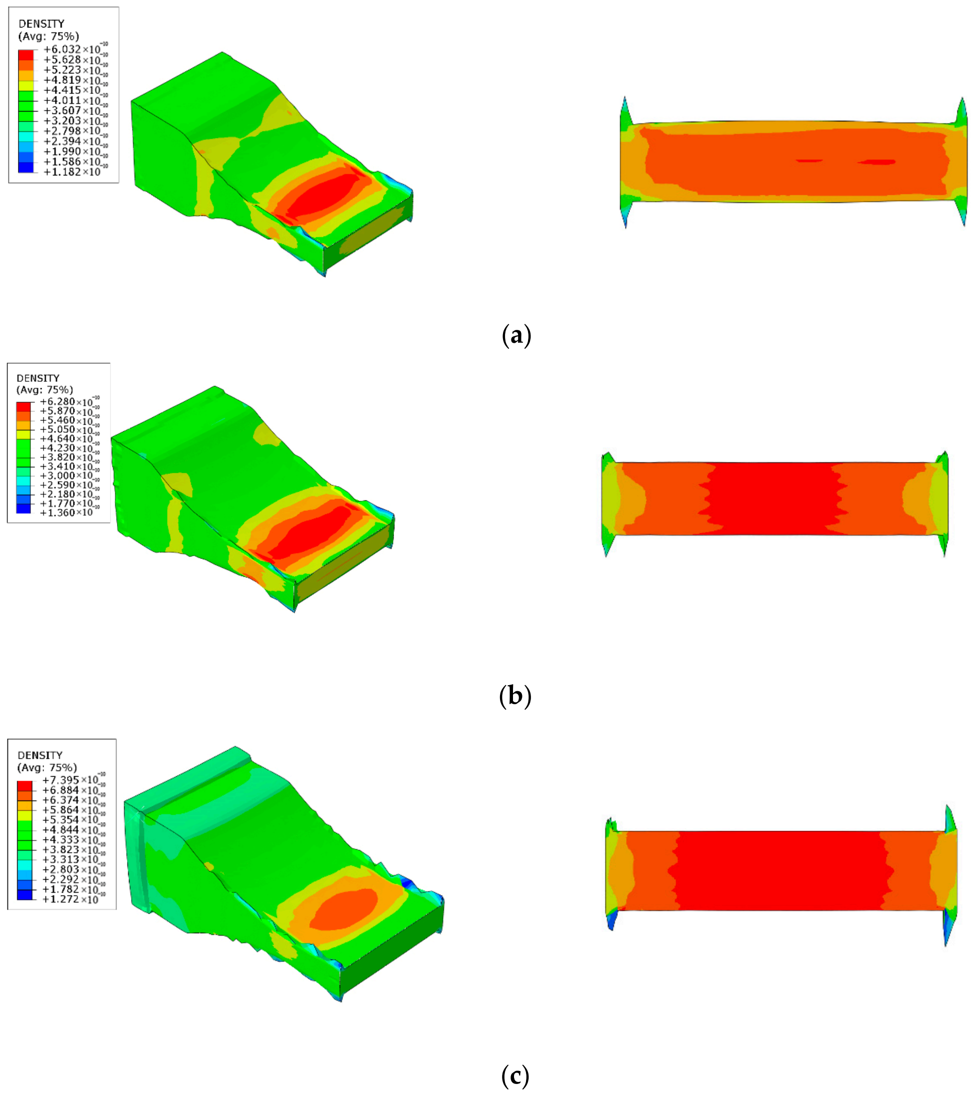


Figure 4. The density distribution of the sheet under different feeding speeds: (**a**) Sheet forming with a feeding speed of 24 mm/s, with a maximum density of 0.603 g/cm^3 and an average density of 0.49 g/cm^3. (**b**) Sheet forming with a feeding speed of 30 mm/s, with a maximum density of 0.628 g/cm^3 and an average density of 0.51 g/cm^3. (**c**) Sheet forming with a feeding speed of 36 mm/s, with a maximum density of 0.739 g/cm^3 and an average density of 0.58 g/cm^3.

3.2. Impact of the Roller Speed on Tablet Formation

The quality parameters of the tablet formed after rolling are evaluated via the density distribution, and the rollers and sealing structures are hidden during the analysis. A monitoring surface was established in the width direction of the tablet at the gap between the rollers, and the density on the path was extracted and used to solve for the average density. By comparing the simulation results of the model at different feeding speeds, it can be found that the tablet has the maximum density at the gap between the rollers, mainly concentrated in the middle, and decreases approximately in a circular manner towards both sides. This is mainly because the powder expands towards both sides under the pressure. The powder is more concentrated in the middle, and the actual screw feed shows uneven material in the space. The filling rate of the powder in the middle is higher, leading to a greater contact pressure. The analysis of the slice diagram of the tablet shows that with the increase of the feeding speed, the area of the maximum density of the tablet in the center increases towards both sides, and the average density increases from 0.49 g/cm^3 to 0.58 g/cm^3, which makes the tablet thicker and is conducive to increasing the efficiency of the tablet formation. As shown in Figure 4c, there is an expansion at the tail of the powder, mainly because when the feeding speed is too high and the roller speed is constant, the amount of feeding is increased, and the powder accumulates near the sealing plates. There are some burrs or distorted grids on both sides of the tablet, which is due to the rolling effect of the small gap, causing some of the meshes to extend to both sides and interact with the sealing plate, thereby causing curling towards the gap between the sealing plate and the roller. This is consistent with the actual leakage of the powder, but the finite element method cannot show the volume reduction caused by the leakage of the powder.

To analyze the impact of the roller speed on tablet formation, the friction coefficient between the roller surface and the sealing structure was set to 0.4, the horizontal feeding speed was set to 25 mm/s, and the roller clearance was set to 4 mm. As shown in Table 5, the roller speeds of 1.5 rad/s, 2.5 rad/s, and 3.5 rad/s were taken as three variable parameters. The density cloud and the slice diagram of the tablet after solving are shown in Figure 5.

Table 5. Different combinations of process conditions for the study of roller speed.

Screw Speed	Axial Velocity	Roller Speed	Rotational Speed Ratio
120 r/min	25 mm/s	1.5 rad/s	14:1
120 r/min	25 mm/s	2.5 rad/s	5:1
120 r/min	25 mm/s	3.5 rad/s	3.5:1

By comparing the simulation models at different roller speeds, it can be seen from Figure 5 that the area of the highest tablet density is concentrated at the gap, which is consistent with the simulation results in the previous section. When the speed of the feeding powder remains constant, increasing the roller speed accelerates the roll pressure on the tablets. The maximum tablet density decreased from 0. 64 g/cm^3 to 0.52 g/cm^3 because the increased linear speed of the roller surface drove a large amount of powder, while the time the formed tablets stayed at the gap between rollers was reduced. The pressure time applied by the rollers at the gap decreased, and the average density of the powder decreased. As the roller speed increased, the maximum density of the powder density shifted from the edge to the center of the powder, and the density around the center was relatively low, which indicates that the tablet forming quality was poor, and the surface of the tablet was soft.

As the roller speed increased, the linear speed of the roller surface increased, which directly affected the distribution of the surface speed of the tablet. In order to analyze the speed distribution characteristics in the rolling area, the speed distribution diagram of Figure 5a was selected, as shown in Figure 6. At the tail of the tablet, the powder speed was low (blue-green area), mainly due to the friction of the baffle, which hindered the movement of the tablet in the feeding direction. At the gap, the speed of the tablet in the width direction was lower than the speed in the center, which indicates that the powder flow was low and, therefore, the density was low. The sealing structure on the upper and lower sides mainly affected the powder speed on the roller surface by hindering the powder before compression. From the beginning of the powder engagement to the gap extrusion, the speed field presented a certain distribution. As the linear speed of the roller surface was high, the powder was rolled, and the speed gradually increased, approaching the speed of the roller surface.

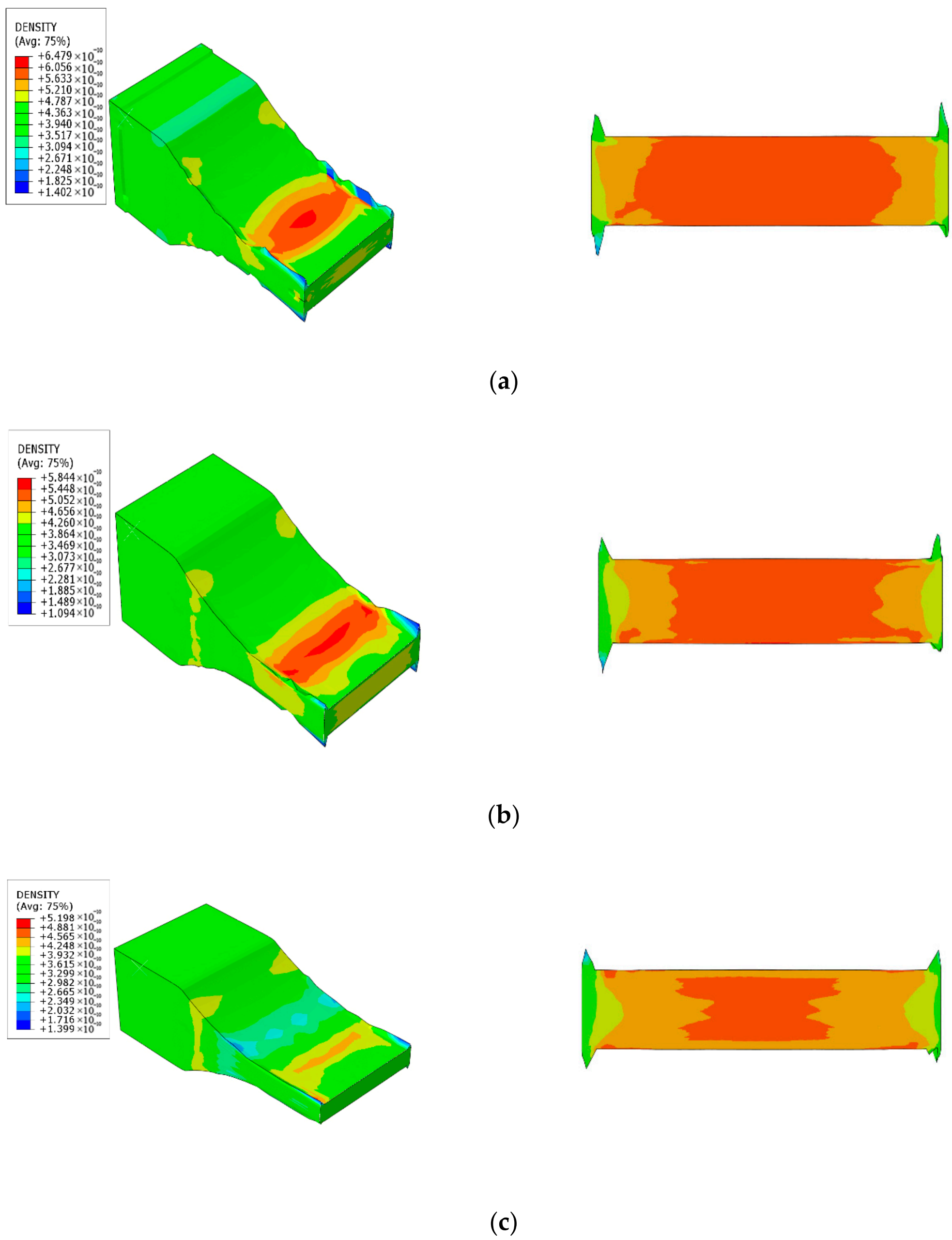


Figure 5. Density and stress distribution at different roller speeds: (**a**) sheet forming with a roll speed of 1.5 rad/s, with a maximum density of 0.64 g/cm^3 and an average density of 0.56 g/cm^3; (**b**) sheet forming with a roll speed of 2.5 rad/s, with a maximum density of 0.58 g/cm^3 and an average density of 0.47 g/cm^3; (**c**) sheet forming with a roll speed of 3.5 rad/s, with a maximum density of 0.51 g/cm^3 and an average density of 0.40 g/cm^3.

3.3. Impact of the Friction Coefficient on Tablet Formation

In the process of pressing, different rolling surfaces are generally selected according to the viscosity of the material, and increasing the friction coefficient appropriately is conducive to the pressing of tablets. To analyze the impact of different friction coefficients on tablet formation, the horizontal feeding speed was set to 30 mm/s, and the clearance was set to 4 mm. The friction coefficient of the roller surface was set as a variable parameter at three levels of 0.2, 0.4, and 0.6. The density distribution of tablets after solving is shown in Figure 7 below.

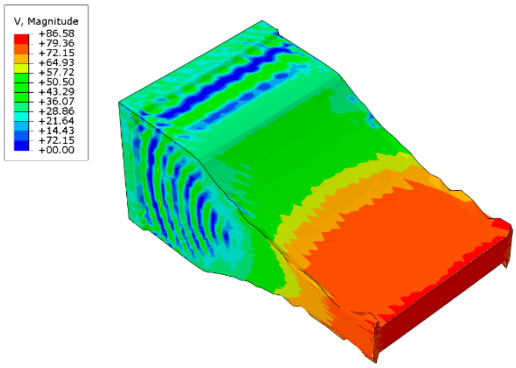
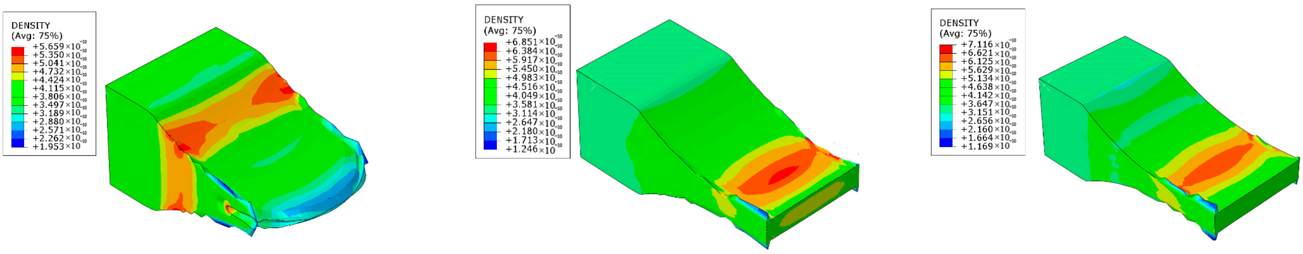


Figure 6. The velocity distribution of the wafer (mm/s).



(**a**) (**b**) (**c**)

Figure 7. Density distribution under different friction coefficients of rolling surface: (**a**) sheet forming with a friction coefficient of 0.2; (**b**) sheet forming with a friction coefficient of 0.4; (**c**) sheet forming with a friction coefficient of 0.6.

By comparing the tablet formations at different friction coefficients, we found that when the friction coefficient was 0.2, the tablet formation failed, and the tablet could not be formed at the gap. The powder was mainly concentrated in the engagement area, and the maximum density reached 0.56 g/cm^3. As the friction coefficient increased, the powder was driven by the friction force on the roller surface to pass through the gap, which was conducive to the formation of the powder, and the maximum density of the tablet increased from 0.56 g/cm^3 to 0.71 g/cm^3. The mesh extensions on both sides of the baffle were aggravated. From a practical point of view, when the friction coefficient of the roller surface is low, the powder is not easily compressed by the roller, and a large amount of powder stays at the gap between rollers, causing blockage of the powder. Therefore, the choice of the roller surface is important. Usually, a surface with a pattern is chosen to improve the rolling efficiency.

3.4. Impact of the Roller Clearance on Tablet Formation

The roller clearance was adjusted to 3 mm, 5 mm, 6 mm, and 7 mm, with a feed rate of 30 mm/s, roller speed of 2 rad/s, and friction coefficient of 0.4. The results are shown in Figure 8.

The model calculation results were compared under different clearances, and the forming of tablets under different clearances was analyzed. When the clearance was small (3–4 mm), the tablets were strongly squeezed by the rollers and the sealing structure, showing a sharp increase in density at the gap, with a large high-density red area, and the actually obtained tablets have a lower porosity.

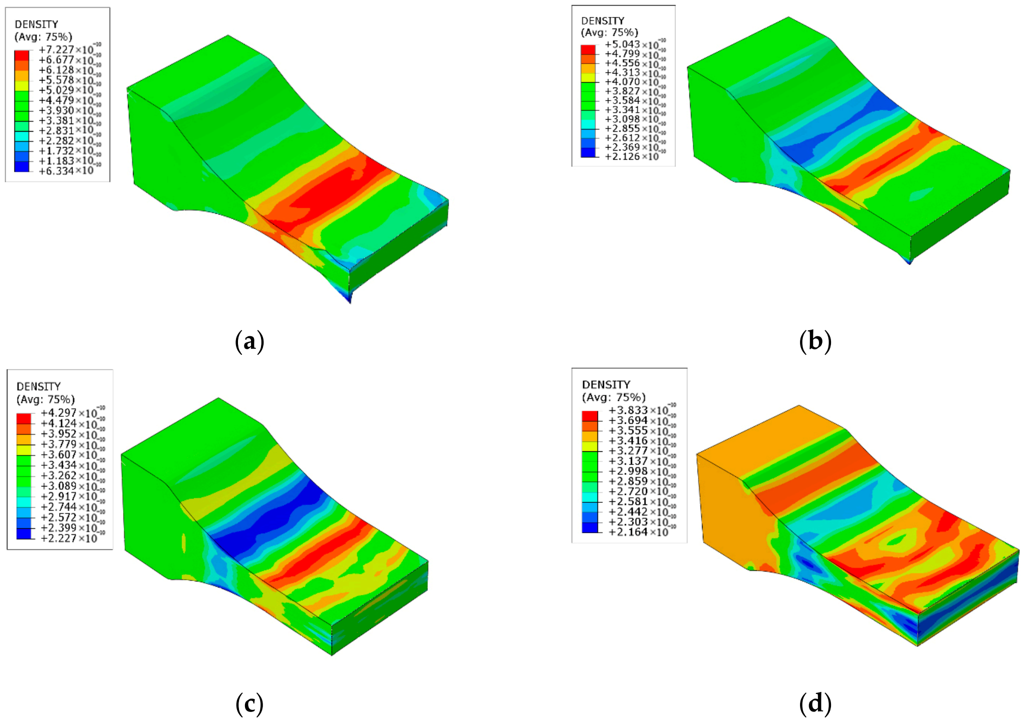


Figure 8. Density distribution under different roller clearance: (**a**) sheet forming with roller clearance of 3 mm; (**b**) sheet forming with roller clearance of 5 mm; (**c**) sheet forming with roller clearance of 6 mm; (**d**) sheet forming with roller clearance of 7 mm.

The tablet part at the gap between rollers was taken for analysis, and the density distribution in the width direction of the tablet was extracted to study the uniformity of the tablet (change in density). As shown in Figure 9, with the increase of the clearance, the density reduction from the center of the tablet to the sides decreases. The tablet is subjected to the squeezing effect of the sealing structure and the rollers, which decreases with the increase of the clearance. However, the sealing structure has a tangential blocking effect on the edge powder, resulting in the uneven distribution of tablet density, which decreases with the increase of the clearance. When the clearance increases from 6 mm to 7 mm, the tablet density in the width direction basically no longer changes, and the density distribution is more uniform, approaching the initial density of 0.35 g/cm^3. The forming quality is poor, indicating a failure of tablet formation, mainly producing fine powder and soft tablets. In the case of a small roller clearance, the average density of tablets is higher, resulting in a higher hardness of tablets, but the change in density in the width direction is greater, and the uniformity is relatively low. The variation in the width direction is larger, and the uniformity is relatively poor.

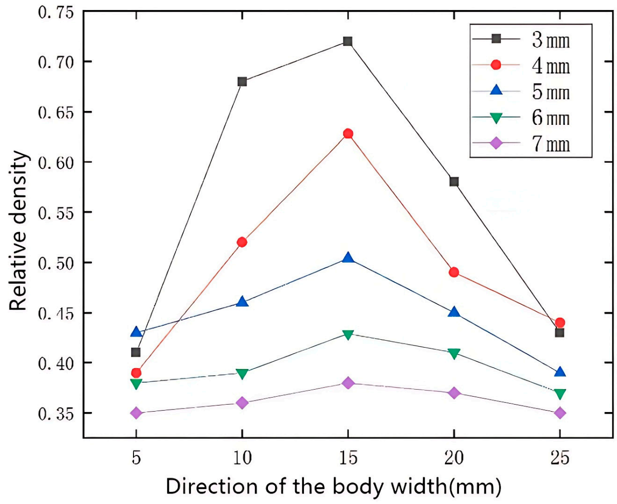


Figure 9. Density distribution in the direction of the width of the body with different roller clearances.

4. Conclusions

This paper used numerical simulation to analyze the force on the granular solids during rolling and the motion of powder during screw transfer and studied the impacts of process parameters and structural parameters on tablet formation. By comparing simulations of different process combinations, the following conclusions were drawn:

(1) When the roller speed is constant, the tablet density increases with the increase of the feeding speed, and the tablet density decreases from the center to the periphery at the gap. When the feeding speed is low, the maximum density area of the tablet is mainly concentrated in the middle, and the forming quality is poor. When the feeding speed of the powder remains unchanged, as the roller speed increases, the time that the tablet stays in the rolling zone decreases, and the average density of the tablet decreases. Therefore, the speed ratio is a key factor affecting the density of the tablet;

(2) Increasing the friction coefficient of the roller surface is conducive to the formation of the powder. However, excessive friction will increase the stickiness of the roller surface; the friction coefficient should not be too high. The presence of the sealing plates is beneficial to prevent the leakage of powder. The upper and lower sealing plates have little impact on the speed of powder. In contrast, the side sealing plates have a negative impact on tablet formation, hindering the peripheral powder with tangential resistance, resulting in a lower speed compared to the center, and affecting the uniformity of the formed tablets, showing a trend of distribution with a large center and small sides. As the roller clearance decreases, the degree of unevenness deepens, but the average density of the tablet increases.

Author Contributions: Conceptualization, Z.X. and M.W.; software, H.G.; validation, M.W.; data curation, H.G.; writing—original draft preparation, X.X.; writing—review and editing, M.W.; supervision, M.W. All authors have read and agreed to the published version of the manuscript.

Funding: This work was sponsored by the Key Technology Research and Development Program of Zhejiang (2019C02019), and the China Postdoctoral Science Foundation (2022M721604).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: This study did not report any data.

Conflicts of Interest: The authors declare no conflict of interest.

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