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Research paper

Process optimization for in-house, lab scale pellet bead production using twin-screw extruder and spheroniser

Adina Kuralgaliyeva [1], Vasvári Gábor [1], Réka Révész [1], Ádám Haimhoffer [1], Orsolya Csendes [1,*]

[1] Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary
*Correspondence: kuralgaliyeva@gmail.com, vasvari.gabor@pharm.unideb.hu, csendes.orsolya@pharm.unideb.hu

Abstract

Multiparticulate dosage forms are becoming more popular than single-unit forms because they offer benefits such as more consistent gastric emptying, a lower chance of dose dumping, and flexible drug release patterns[1]. Among the available production methods, extrusion-spheronization is preferred because it can handle high amounts of active ingredients without creating large particles, and it also allows for the easy combination of multiple drugs in one unit at any ratio[2]. The aim of this research is to determine the optimal parameters of the extruder, namely, the screw rotation speed, liquid addition rate and powder feeding rate, to determine the independent process parameters of the spheroniser, and to measure the loss-on-drying values, particle size distribution, and morphology of extrudates. The required machines to produce pellets are a twin-screw extruder, a spheroniser, a peristaltic pump, and a cooling system. Extrudates were obtained by using a mixture of microcrystalline cellulose, corn starch, lactose monohydrate, and 10% povidone solution.

Abbreviations

PSD - Particle Size Distribution
LOD - Loss on Drying
MUPS - Multiple-unit Pellet System
RPM - Rotations per Minute
SEM - Scanning Electron Microscopy

1. Introduction

A solid dosage form that has been gaining popularity recently is pellets. Pellet production is a time-consuming process that can be achieved by different techniques, for example, extrusion-spheronisation, layering, cryopelletization, freeze pelletization, spray

congealing, spray drying, and compression. This research focuses on pellet production by the extrusion-spheronisation technique, which is widely used due to its high efficiency, simplicity, and faster processing compared to other methods[3].

Pellets are multiparticulate dosage forms, with a small and uniform size, typically cylindrical or spherical shape, usually in a range of 0.5-1.5 mm[2]. These properties make pellets highly advantageous for precise dosing and uniform distribution[4]. The ideal features of pellets include an even surface and small size.

Besides therapeutic benefits, pellets have other advantages from a technological point of view[1,3,6,7,8]:

- Flexible release patterns (controlled release or immediate release)
- Increased bioavailability due to improved drug solubility and absorption
- Less irritation of the gastrointestinal tract
- Better flow properties and less friable dosage form
- Narrow particle size distribution (PSD) and uniform size
- Ease of coating and masking of unpleasant taste
- Larger surface area for drug absorption and fewer fluctuations in drug plasma levels
- Incompatible active ingredients can be pelletized separately and then encapsulated as a single formulation
- Possibility of targeted therapy formulations
- Doses can easily be adjusted for pediatric, geriatric, or special patients

Despite these benefits, some drawbacks of multiparticulate dosage forms exist[3,6]:

- Pelletization is an expensive and time-consuming process due to the need for multiple machines and steps for pellet production
- Controlling the production process is difficult, as the wetting of material happens quickly
- Compressing pellets into tablets is challenging. Therefore, they are most often encapsulated

In most cases, pellets are encapsulated in hard gelatin capsules because it is the easiest way to formulate them. However, sometimes sachets or multiple-unit pellet systems (MUPS) can be formulated as well[8,9].

Nowadays, pellets are a favorable dosage form for many different drugs such as omeprazole, esomeprazole, and lansoprazole, metoprolol, and theophylline[5]. The main reason for producing these drugs in a pellet form is to achieve a controlled release pattern,

which makes them less irritating to the gastrointestinal tract[10]. A great example of pellet usage is in the treatment of colon cancer. There was a study conducted on Wistar rats using pellets that contain 5-fluorouracil, phytic acid, microcrystalline cellulose PH 101, hydroxypropyl methylcellulose and barium sulfate[11]. Pellets were prepared by the extrusion-spheronization technique and then coated with Eudragit S100, enabling colon-specific drug delivery. Another study shows that for colon-targeted drug delivery Eudragit S100 was used to coat naproxen, and this formulation showed promising results[12].

2. Materials and methods

2.1 Materials

The procedure for pellet production began with the preparation of the required powder and liquid mixture. In this series of experiments, placebo pellets were made using microcrystalline cellulose 102, lactose monohydrate, and corn starch. A total of 600 g of dry materials was prepared per batch, with excipients added in equal proportions. As a binder, a 10% povidone (type: K30) solution was used. The liquid solution is prepared by diluting the povidone powder in distilled water. 20 g of povidone was measured and dissolved in 180 g of distilled water while stirring gently with a magnetic stirrer or manually. All the ingredients were Ph Eur grade and were purchased from Magilab Ltd. (Budapest, Hungary).

2.2 Methods

2.2.1 Pelletization

The extrusion process is carried out using several machines, including a twin-screw extruder, a powder feeder, and a liquid pump. The operating rates of each machine vary and must be regulated separately to ensure a smooth production process without any interruptions.

The powder mixture was transported into the gravimetric feeder of the powder feeder machine (Quick TS12 feeder), and then by regulating the speed, the powder was added into the hopper of the twin-screw extruder. The maximum powder addition rate of the machine is 80 RPM (rotations per minute).

The main part of the twin-screw extruder (Quick TS16 extruder) is a barrel through which extrudates are compressed. The barrel has a feeding zone, a liquid addition zone, mixing and kneading, and transporting zones. The temperature application occurs in these zones. The temperature and screw rotation speed are regulated by the extruder’s touch

screen. During the process, the temperature must be fixed. To achieve a stable temperature range, a cooling system (Julabo F25 temperature control unit with a Julabo ME circulator) was added to the process. The cooling system helps to maintain the temperature at around 20 °C. If the temperature increases during the extrusion process, the consistency of the product becomes soft, which makes spheronization more difficult. Inside the barrel, two identical screws rotate in the same direction, hence, the powders and liquid are homogenized. The 1 mm hole die was assembled at the tip of the barrel. By applying high pressure, rod-shaped extrudates were produced through this die.

The experiments were conducted using two different peristaltic pumps. The Masterflex™ L/S™ Compact Variable-Speed pump was used in the first experiments. It has analog control type only, between 1.6 to 124 ml/min flow rate values. Further experiments were conducted by using a more precise liquid pump system that consists of a Watson-Marlow 114 ST peristaltic pump with Siemens HMI (controlling the flow rate between 0.02 ml/s and 2.00 ml/s).

2.2.2 Spheronisation

After the production of extrudates by the twin-screw extruder, the spheroniser (quick spher2000) was employed. The plate located inside the machine rotates at an extremely high speed, in a range of 625-2000 RPM. This movement breaks down rod-shaped extrudates into smaller particles, and by further rotations, pellets achieve spherical or semi-spherical shapes.

2.2.3 Loss-on-drying (LOD)

LOD was characterized by a moisture analyzer (KERN DAB 100-3). The products (approximately 3 g) were placed on an aluminum plate and were dried at 130°C until completely dry. The percentage shown in the analyzer was the moisture (water) content of the product.

2.2.4 Sieve analysis

After the spheronisation process, pellets were dried for seven days. PSD of dry samples was evaluated by a sieve shaker (RETSCH AS 200 digit cA). The sieve machine consists of nine Ph Eur. sieves with different particle sizes: 125 µm, 180 µm, 250 µm, 355 µm, 500 µm, 710 µm, 1000 µm, 1400 µm. The largest sieve is located on the top, and the batch of pellets is transported onto it. Usually, the minimum weight for one batch is 25 g. Then, the sieve machine was shaken at a very high speed and small amplitude for 2 minutes.

This movement transfers materials down by gravity. Each sieve retained some of the product and must be manually weighed.

2.2.5 Particle Size Distribution (PSD) by laser diffraction

To compare the results obtained with a sieve machine, the PSD can be evaluated by laser diffraction (Mastersizer 3000+ultra). The measurements can be made using two different methods: the material can be dispersed in air or liquid (water or oil). For pellet analysis, air dispersion is recommended, as pellets may partially disintegrate into liquid, leading to inaccurate results. After that, using laser diffraction, the machine conducts the measurements of PSD[16]. Approximately 1-3 g of pellets were transferred into the hopper of the Mastersizer, and then, through the pipe, the material was transported into the main part of the machine, where further evaluations were performed. The results and graphs were generated automatically and shown on the computer.

2.2.6 Scanning electron microscopy (SEM)

Surface morphology of pellets was visualized and characterized by SEM, providing magnified pictures of the pellets. SEM consists of an electron source, anode, condenser lens, scan coils, objective lens, secondary electron detector, and a sample. Firstly, an electron source generates electrons at the top. When their thermal energy overcomes the source material's work function, electrons are emitted. Finally, a positively charged anode accelerates and attracts them[13].

3. Results and discussion

3.1 Extrusion

The first step of extrusion is to determine the design space by evaluating the powder flow rate and the liquid flow rate. These processes were evaluated manually **(Table 1)**. The graph in **Figure 1** demonstrates a linear growth, showing a direct proportionality between the powder flow rate and the feeding rate of the powder feeder.

Table 1.: Measured powder flow rates at different feeding rates

Powder					
Feeding rate, (rpm)	№1, flow rate (g/min)	№2, flow rate (g/min)	№3, flow rate (g/min)	Average flow rate (g/min)	Standard deviation (g/min)
15	10,08	9,76	9,84	**9,89**	**0,17**
25	17,36	16,88	16,64	**16,96**	**0,37**
45	29,92	30,2	30,52	**30,21**	**0,30**
60	40,32	39,88	39,37	**39,86**	**0,48**
75	49,77	49,39	51,07	**50,08**	**0,88**

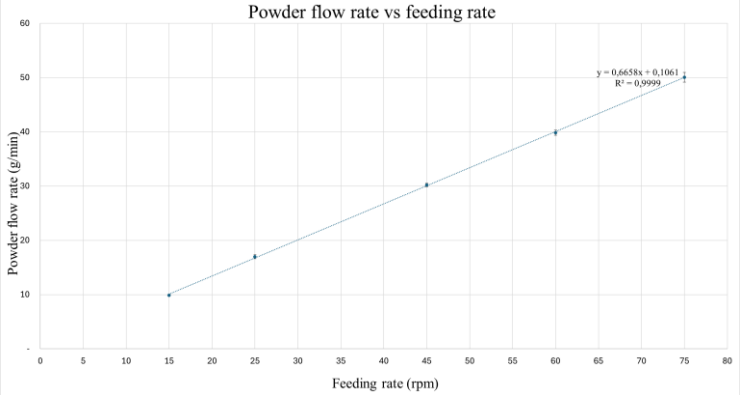

Figure 1.: Relationship between feeding rate and powder flow rate

Separate measurements were conducted for the peristaltic pump **(Table 2)**. The bar chart **(Figure 2)** illustrates the direct relationship between the liquid flow rate and the speed of the pump.

Table 2.: Measured liquid flow rates at varying speeds (Masterflex™ L/S™ Compact Variable-Speed pump)

Liquid					
Speed	№1, flow rate (g/min)	№2, flow rate (g/min)	№3, flow rate (g/min)	Average flow rate (g/min)	Standard deviation (g/min)
minimum	9,22	9,36	9,64	**9,41**	**0,21**
2nd	17,6	18,5	17,92	**18,01**	**0,46**
3rd	36,24	35,94	35,58	**35,92**	**0,33**
4th	64,66	65,44	64,64	**64,91**	**0,46**

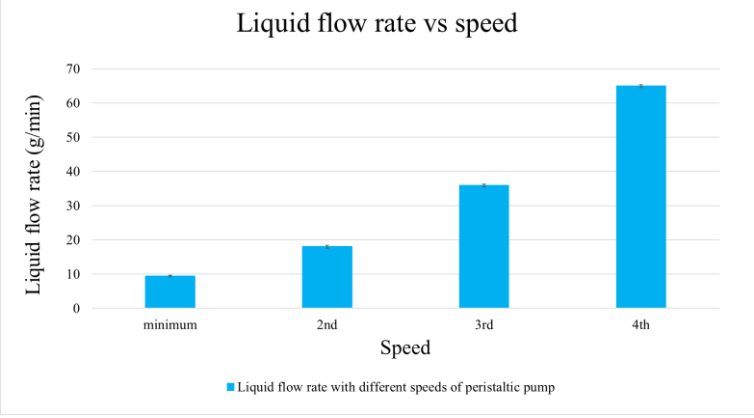

Figure 2.: Correlation between liquid flow rate and speed of the peristaltic pump

Experiment 1 yielded two unsuccessful results. The liquid addition rate and the extruder's rate were similar in both experiments, but different powder feeding rates were applied **(Table 3)**. As a result, extremely soft **(Figure 3a)** or hard **(Figure 3b)** extrudates were produced.

Table 3.: Parameters of Experiment 1

Powder feeding rate	35 RPM [23.37g/min]	40 RPM [26.71 g/min]
Liquid addition rate	2nd [18.01 g/min]	2nd [18.01 g/min]
Extruder rate	200 RPM	200 RPM

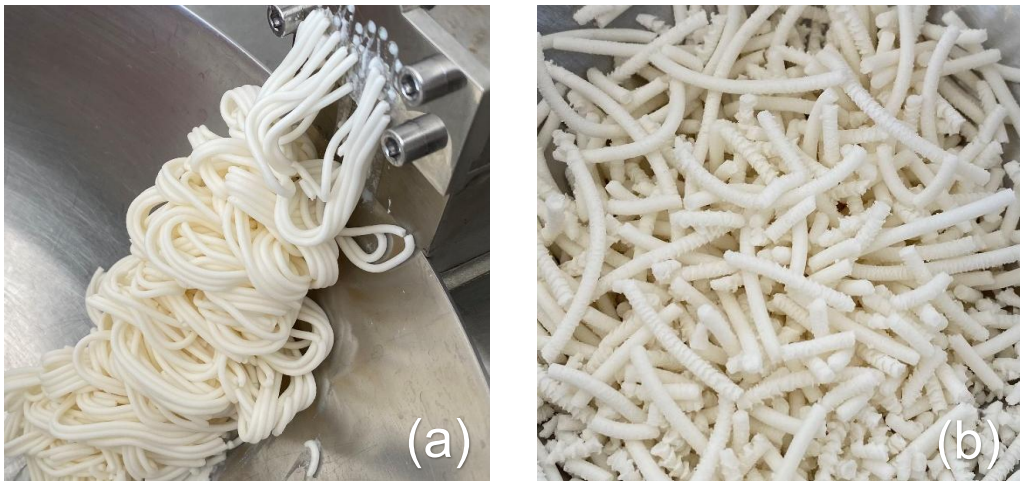

Figure 3.: The extrudates from Experiment 1: powder feeder 35 RPM (a); powder feeder 40 RPM (b)

As shown in **Table 4**, the powder feeding rate, liquid addition rate, and extruder rate were decreased significantly in Experiment 2 **(Figure 4)**. However, further evaluation revealed that the LOD value of the extrudates was 42.77%, which was considered too high for the product.

Table 4.: Parameters of Experiment 2

Powder feeding rate	26 RPM [17.36g/min]
Liquid addition rate	[11.30 g/min]
Extruder rate	150 RPM

Figure 4.: The extrudates from Experiment 2

The Masterflex™ L/S™ Compact Variable-Speed pump that was used in the first

experiments had a major disadvantage: an imprecise liquid addition rate. Four different rates were chosen manually, and it was difficult to reproduce further experiments with the same liquid addition rate because of the potentiometer's imprecision. Therefore, further experiments were conducted by using a more precise and automated liquid pump (Watson-Marlow 114 ST peristaltic pump with Siemens HMI), allowing the addition of an exact amount of liquid by entering the desired rate via a touch screen.

The use of a very precise peristaltic pump **(Table 5, Figure 5)** is a crucial point for operating the process productively, because wetting of powders happens rapidly. It is recommended to use a computerized pump from the beginning. The main advantage of this pump is that any desired speed can be chosen via the touch screen of the pump; consequently, high control over moisture content is achieved.

Table 5.: Measured liquid flow rates at varying speeds of a new peristaltic pump (Watson-Marlow 114 ST peristaltic pump with Siemens HMI)

Liquid					
Speed, ml/s	№1, flow rate (g/min)	№2, flow rate (g/min)	№3, flow rate (g/min)	Average flow rate (g/min)	Standard deviation (g/min)
0,07	3,27	3,31	3,32	**3,30**	**0,03**
0,09	4,24	4,23	4,26	**4,24**	**0,02**
0,1	4,82	4,78	4,72	**4,77**	**0,05**
0,15	7,17	7,08	7,11	**7,12**	**0,05**
0,2	9,34	9,58	9,55	**9,49**	**0,13**
0,3	14,29	14,22	14,31	**14,27**	**0,05**

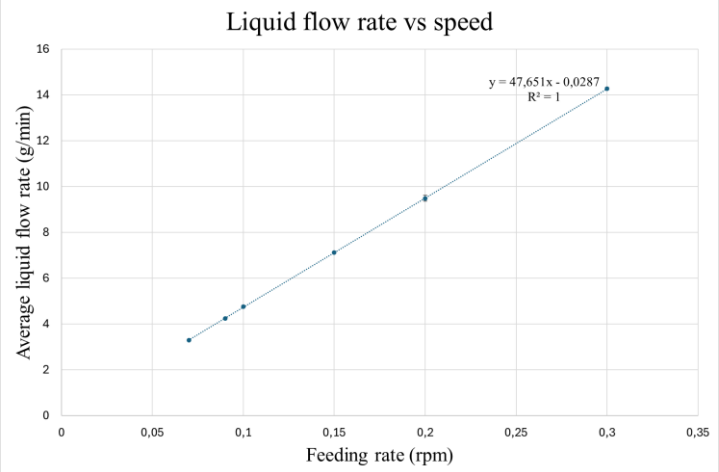

Figure 5.: Correlation between liquid flow rate and speed of the peristaltic pump

Successful results were obtained in Experiments 3 and 4. The LOD value of the extrudates from Experiment 3 was 36.66%, while the LOD of the extrudates from Experiment 4 was 33.66%.

In 10 minutes, 246.9 g of extrudates were produced in Experiment 3. The torque value was in a range of 3.9-6.5 Nm, which is a good result, and no interruptions occurred during

the extrusion process.

Table 6.: Parameters of Experiment 3

Powder feeding rate	21 RPM [14.02g/min]
Liquid addition rate	0.09 ml/s [4.24 g/min]
Extruder rate	150 RPM

Figure 6.: The extrudates from Experiment 3

In Experiment 4, the same liquid addition rate and extruder rate were applied as in Experiment 3 **(Table 6),** but the powder feeding rate was increased from 21 RPM to 22 RPM **(Table 7)**. The extrudates from Experiment 4 are more rigid **(Figure 7)** compared to results from Experiment 3 **(Figure 6)**.

Table 7.: Parameters of Experiment 4

Powder feeding rate	22 RPM [14.69 g/min]
Liquid addition rate	0.09 ml/s [4.24 g/min]
Extruder rate	150 RPM

Figure 7.: The extrudates from Experiment 4

3.2 Spheronisation

The first spheronisation process was conducted using extrudates from Experiment 2. Due to the high moisture content (42.77%), extrudates formed aggregates during spheronisation **(Figure 8)**. Different speeds of the spheroniser machine were tested, and **Figure 5** demonstrates that the smallest particles were achieved using the highest rotation rate of the spheroniser. Based on this observation, a speed of 2000 RPM was selected for future experiments.

Figure 8.: The spheronisation of extrudates from Experiment 2: speed 1057 RPM (a), speed 1500 RPM (b), speed 2000 RPM (c)

Despite a very small change in the powder feeding rate, the difference in consistency and moisture content was significant **(Figure 6, Figure 7)**. As a result, it affected the spheronisation process. When comparing the results of Experiments 3 and 4 **(Figure 9)**, it may be concluded that the products obtained from Experiment 3 are more spherical and have fewer undivided rods. On the other hand, the pellet batch from Experiment 4 contains approximately 50% undivided rods. The main reason for this is the difference in moisture contents, which was 3%.

In addition, the LOD values after the spheronisation processes decreased by 6% in both experiments **(Table 9)**. During the rotations of a plate, the extrudates cause friction with the plate and lose water content as a result.

Table 8.: LOD values of pellets from Experiments 3 and 4

Powder feeding rate	21 RPM [14.02 g/min]	22 RPM [14.69 g/min]
LOD before spheronisation	36.66%	33.66%
LOD after spheronisation	30.23%	27.83%

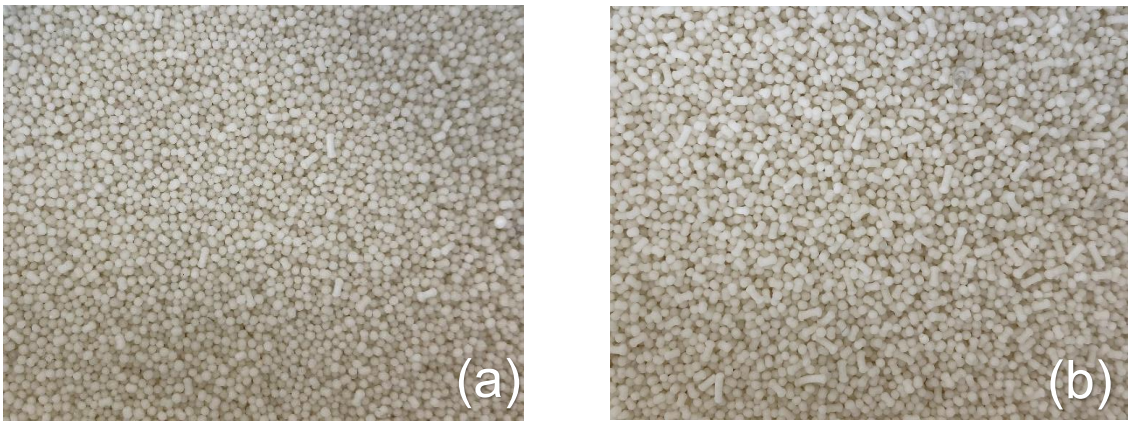

Figure 9.: The spheronisation of extrudates from Experiment 3 (a) and Experiment 4 (b)

3.3 Particle size distribution (PSD)

For PSD **(Figure 10)** testing, 47.59 g of pellets taken from Experiment 3 were evaluated. The PSD measured by the sieve machine showed that 61.57% of the whole batch had approximately 1200 µm size **(Table 9)**.

Table 9.: Measured particle size data for extrudate samples from Experiment 3

Sieve size, µm	Aproximate particle size, µm	Mass retained in each sieve, g	Percent of mass retained above each sieve, %
1400	1600	0,14	0,29
1000	1200	29,3	61,57
710	855	16,19	34
500	605	1,14	2,4
355	427,5	0,16	0,34
250	302,5	0,05	0,11
180	215	0	0
125	152,5	0	0

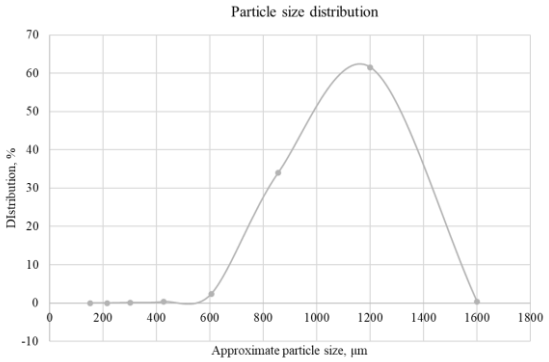

Figure 10.: PSD of extrudates from Experiment 3 using a sieve analysis

For PSD **(Figure 11)** testing, 52.8 g of pellets taken from Experiment 4 were evaluated.

The results showed that 78.05% of the batch had a size of approximately 1200 µm **(Table 10).**

Table 10.: Measured particle size data for extrudate samples from Experiment 4

Sieve size, µm	Aproximate particle size, µm	Mass retained in each sieve, g	Percent of mass retained above each sieve, %
1400	1600	0,07	0,13
1000	1200	41,21	78,05
710	855	10,21	19,34
500	605	0,53	1
355	427,5	0,2	0,38
250	302,5	0,3	0,57
180	215	0,1	0,19
125	152,5	0	0

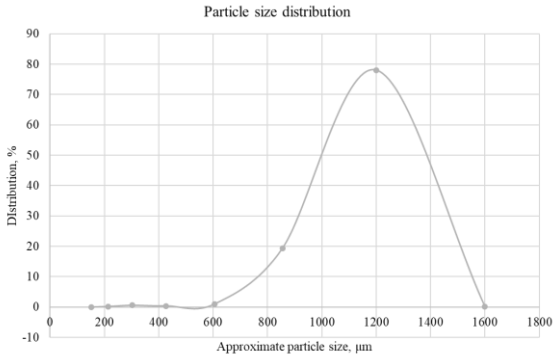

Figure 11.: PSD of extrudates from Experiment 4 using a sieve analysis

Figures 12 and 13 represent the particle size distribution graphs of the extrudates measured using the Mastersizer machine, along with D10, D50 and D90 values. D50 represents a particle size average or median diameter. For example, in Experiment 3 shown in **Table 11**, D50 indicates that 50% of the particles are larger than 1110µm, while the remaining 50% are smaller. Similarly, D10 shows that 10% of the total particles are smaller than 881 µm, while 90% are larger than 881 µm. D90 means that 90% of the batch is larger than 1500 µm, and only 10% is smaller than 1500 µm. These rules apply to Experiment 4, respectively.

The formula for PSD calculation is: D90/D10. If the value is greater than 1, the PSD is broad; if the value is smaller, the PSD is narrow [14].

PSD of pellets from Experiment 3: D90/D10= 1500 µm/ 881 µm= 1.70, which means that PSD was large in this case.

Table 11.: PSD parameters (D10, D50, D90) of extrudates from Experiment 3

D10	881 µm
D50	1110 µm
D90	1500 µm

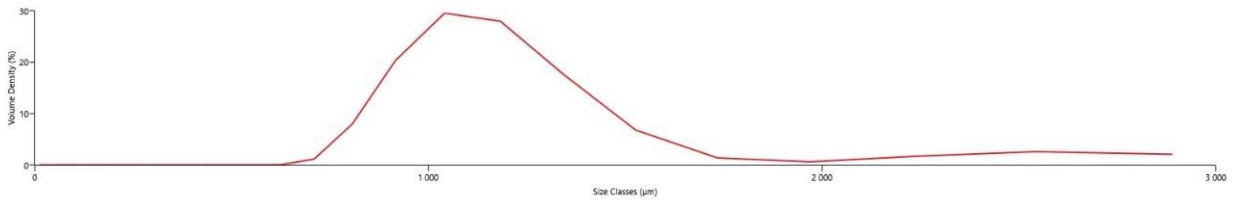

Figure 12.: PSD of extrudates from Experiment 3 using the Mastersizer machine (powder feeding rate: 21 RPM)

PSD of pellets from Experiment 4 **(Table 12)**: D90/D10= 2420 µm/ 972 µm= 2.49, which means that the PSD was broad. The results showed that the PSD for most pellets was relatively broad, which was higher than 1. Further experiments must aim to make the PSD narrower. It is essential to have a narrow PSD as it ensures better flow of particles, correct distribution, better separation, and more even retention time[14].

Table 12.: PSD parameters (D10, D50, D90) of extrudates from Experiment 4

D10	972 µm
D50	1300 µm
D90	2420 µm

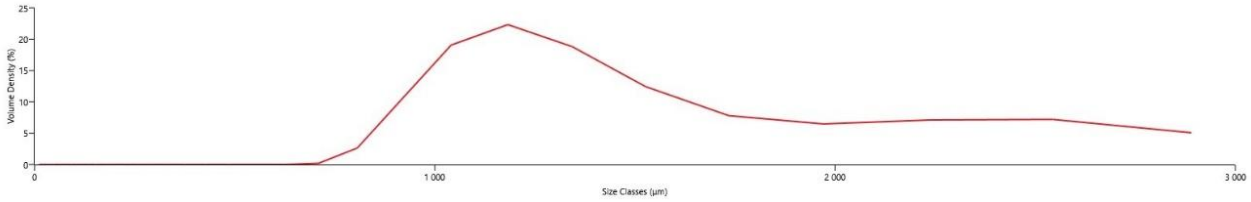

Figure 13.: PSD of extrudates from Experiment 4 using the Mastersizer machine (powder feeding rate: 22 RPM)

The PSD was evaluated using two different techniques: sieve analysis and laser diffraction. A comparison of these techniques reveals that laser diffraction offers several advantages over the conventional sieve machine. The Mastersizer 3000+ ultra machine (laser diffraction technique) is innovative, computerized and automated, thus, it provides highly accurate measurements of PSD. Additionally, mastersizer machine can detect particles in a size range between 10 nm and 3.5 mm[16]. In contrast, the sieve machine does not provide equally precise results because the mass retained on each sieve must be weighed manually using an analytical scale. Taking all this information into account, the Mastersizer machine should be prioritized for future determinations of PSD.

3.4 Scanning electron microscopy (SEM)

As a last step, the SEM was applied to visualize the surface morphology of pellets **(Figure 14)**. Images taken by SEM show that the surface of the products is not completely smooth.

This can be attributed to the use of different types of powders in pellet production. Cellulose, lactose, and corn starch have distinct properties, which affect homogenization inside the extruder. In addition, other factors such as temperature and pressure play a significant role. One of the requirements for perfect pellets is a smooth surface. However, these results can be acceptable because in some formulations, pellets require further coating. For example, the pellets can be coated with sodium benzoate and ethylcellulose to achieve a smooth surface and high sphericity[15].

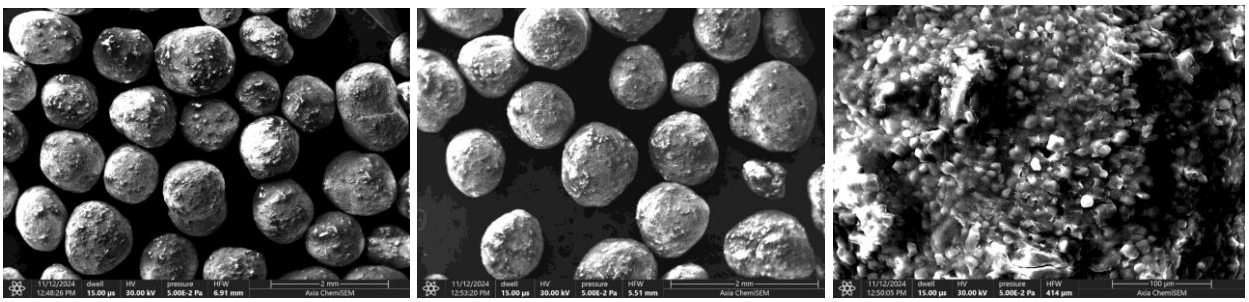

Figure 14.: SEM images of the pellets from Experiment 3

Different powders with varying properties were used in the research. Microcrystalline cellulose has great binding properties and ensures high plasticity of the product. That is why it is a very commonly used excipient for pellets prepared via the extrusion-spheronization technique[17]. Moreover, lactose is a widely used auxiliary material, which is applied in approximately 60-70% of pharmaceutical dosage forms. Lactose acts as a filler, binder, and provides flow to a formulation[18]. Corn starch plays a role in solid dosage form formulations as a binder, filler, and binder-disintegrant[19]. If an active ingredient is incorporated into the pellet formulation, adjustments to the excipient ratio may be required. For instance, pellets made by adding microcrystalline cellulose have a prolonged drug release because of reduced disintegration. This property might be useful for modified release drugs, but enteric-coated or colon-targeted delivery requires excipients with good disintegration properties[17].

Based on the results, the best products were achieved using the following parameters: powder feeding rate is 21 RPM [14.02 g/min], liquid addition rate is 0.09 ml/s [4.24 g/min], extruder's speed is 150 RPM, spheronisation speed is 2000 RPM. These results were obtained from Experiment 3 and can be used in future modifications.

4. Conclusion

Pellets are an excellent solid dosage form with numerous advantages. Apart from being used in the production of medicines for daily use, such as diclofenac, ibuprofen,

omeprazole, statins, and vitamin C, B, E, D, and K[5], they also have the potential to become a preferred choice for targeted drug delivery systems in the future [10]. For instance, budesonide can be formulated as multi-unit pellets, which are colon-targeted and can be used for the treatment of ulcerative colitis[20].

However, pellet production is a time-consuming and expensive process. This is why it is beneficial to conduct experiments on a laboratory scale, which serves as the starting point for future pellet production processes.

Several factors require strict control. During the production of extrudates, maintaining the optimal moisture content of the product is crucial. Extrudates that are too soft tend to aggregate during the spheronisation process, while those with insufficient moisture content fail to divide properly. To ensure precise liquid addition, a highly accurate pump must be used.

Temperature is another critical factor affecting the process. A cooling system must be added to maintain a stable temperature; otherwise, excessive heat production can lead to over-softening of extrudates.

Data Availability Statement:

All measurement data are available to the corresponding author in case of further requests.

References

1. A. Dukic´-Ott; M. Thommes; J.P. Remon; P. Kleinebudde; C. Vervaet. Production of pellets via extrusion–spheronisation without the incorporation of microcrystalline cellulose: A critical review. European Journal of Pharmaceutics and Biopharmaceutics. 2009, 38-46.

2. Muley, S; Nandgude, T; Poddar, S. Extrusion-spheronization a promising pelletization technique: In-depth review. Asian Journal of Pharmaceutical Sciences. 2016, 684-699.

3. Supriya, P; Rajni, B; Rana, A.C. Pelletization techniques: a literature review. International research journal of pharmacy. 2012, ISSN 2230 – 8407, 43-47.

4. Brown, P. Difference Between Granules and Pellets: A Detail Comparison to Choose the Right Formulation ZANPVC. 2023, [Online] Available at: https://www.zanpvc.com/difference-between-granules-and-pellets.html [Accessed 25 01 2025].

5. Philips, D. What pharmaceutical products or drugs can I make in pellet form? Caleva.

2020, [Online]
Available at: https://www.caleva.com/knowledge-base/what-pharmaceutical-products-or-drugs-can-i-make-in-pellet-form
[Accessed 25 01 2025].

6. Lavanya, K; Senthil, V; Rathi, V. Pelletization technology: a quick review. International Journal of Pharmaceutical sciences and research, 2011, ISSN 0975-8232, Vol. 2(6), 1337-1355.

7. Anon. Innovative dosage forms for targeted formulations. Ingredient pharm. 2025 [Online]
Available at: https://ingredientpharm.com/pharmaceutical-pellets-innovative-dosage-forms/
[Accessed 25 01 2025].

8. Panda, S. K; Parida K.R; Roy H; Talwar P; Ravanan P. A Current Technology for Modified Release Drug Delivery System: Multiple-Unit Pellet System (MUPS). International Journal of Pharmaceutical Science and Health Care, 2013, Issue 3, Vol 6, 51-63.

9. Bafna, H. R; Shirsath N.R; Jagtap V.A. A New Path for Drug Delivery by Multiple Unit Pellet System (MUPS). Indian J Pharm Drug Studies, 2023, 1-7.

10. Pöllinger, N. Multiparticulates. Modern Oral Drug Products for our Society. Pharmind, 2022. 12, 1440–1450.

11. Kaur, V; Goyal, A.K; Ghosh, G; Chandra, S.S; Rath, G. Development and characterization of pellets for targeted delivery of 5-fluorouracil and phytic acid for treatment of colon cancer in Wistar rat. Cell press, 2020, 1-12.

12. Mehta, R; Chawla, A; Sharma, Pawar, P. Formulation and in vitro evaluation of Eudragit S-100 coated naproxen matrix tablets for colon-targeted drug delivery system. Journal of Advanced Pharmaceutical Technology and Research, 2013, Vol 4(Issue 1), 31-41.13. Nanakoudis, A. Thermo fisher scientific. 2019 [Online]
Available at: https://www.thermofisher.com/blog/materials/what-is-sem-scanning-electron-microscopy-explained/
[Accessed 10 02 2025].

14. Anon. SiliCycle. 2025 [Online]
Available at: https://www.silicycle.com/faq/quality-control/what-does-the-particle-size-average-d50-and-the-particle-size-distribution-d90-d10-sections-of-a-coa-mean
[Accessed 10 2 2025].

15. Priese, F; Wiegel, D; Funaro, C; Mondelli, G; Wolf, B. Comparison of Mini-Tablets and Pellets as Multiparticulate Drug Delivery Systems for Controlled Drug Release. MDPI, 2023, 1-14.

16. Anon. Mastersizer 3000+ Ultra. Malvern Panalytical. 2025 [Online] Available at: https://www.malvernpanalytical.com/en/products/product-range/mastersizer-range/mastersizer-3000-plus-ultra
[Accessed 01 02 2025].

17. Chamsai, B; Sriamornsak, P. Novel disintegrating microcrystalline cellulose pellets with improved drug dissolution performance. Powder Technology, 2013, Vol 233, 278-285.

18. Hebbink, G. A; Dickhoff, B.H.J. Application of lactose in the pharmaceutical industry. Lactose. Evolutionary Role, Health Effects, and Applications, 2019, 175-229.

19. Kurniawansyah, I. S; Sopyan, I; Budiman, A. Corn Starch in Pharmaceuticals Isolation, Characterization, and Applications. IJPQA, 2022, Vol 13 Issue 3, 228-231.

20. Varshosaz, J; Emami, J; Tavakoli, N; Minaiyan, M; Rahmani, N; Dorkoosh, F. Development and Evaluation of a Novel Pellet-Based Tablet System for Potential Colon Delivery of Budesonide. Journal of Drug Delivery, 2012, 1-7.