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**BUDAPEST UNIVERSITY OF TECHNOLOGY AND ECONOMICS  
FACULTY OF CHEMICAL TECHNOLOGY AND BIOTECHNOLOGY  
GEORGE OLAH DOCTORAL SCHOOL**

# **Development of granulation-based continuous technologies and their combination with process analytical technologies**

Summary of Ph.D. Thesis

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# 1 Introduction

In recent years, a fundamental paradigm shift has begun in the pharmaceutical industry, driven by the need for more agile, efficient, and robust manufacturing while simultaneously enhancing product quality. The key innovations include the integration of continuous manufacturing (CM)<sup>1</sup> technologies, the Quality by Design framework<sup>2</sup>, the advanced quality assurance tools based on modern process analytical technologies (PAT)<sup>3</sup>, digitalization, the Pharma 4.0<sup>4</sup> concept, and the application of artificial intelligence<sup>5</sup>. While these innovations offer significant advantages over traditional practices, their widespread industrial application remains limited, highlighting the need for further research. Notably, a particularly promising opportunity lies in the simultaneous implementation of these modern approaches, as their synergistic effects can help maximize their overall benefits.

Twin-screw granulation (TSG)<sup>6</sup>, a continuous granulation technique, presents an excellent opportunity to integrate these advanced practices and demonstrate their advantages. As granulation<sup>7</sup> is a critical formulation method required for most solid drug formulations to enhance powder properties and enable tableting, TSG holds significant potential in pharmaceutical production. While granulation is still most commonly carried out using traditional batch processes, the benefits of TSG accelerate its implementation and highlight its transformative potential. Additionally, applying TSG provides an excellent opportunity to develop connected CM lines and to implement advanced monitoring and quality assurance systems. This holistic approach can help realize the full potential of these modern practices, leading to improved efficiency and quality.

Therefore, this work focuses on the development and investigation of a TSG-based formulation line, highlighting its suitability for both wet and melt granulation, its ability to improve powder properties, and its applicability to challenging materials. The study also aimed to advance CM through integrated production lines and enhance quality assurance and process understanding using PAT tools and ANN based soft sensors.

A review of the current state-of-the-art in CM, PAT, QbD, and AI applications underscores their growing importance and the need for integrated solutions. Despite significant progress, further work is needed to fully implement connected CM lines with advanced monitoring. TSG offers a promising platform to realize these benefits and drive innovation in pharmaceutical manufacturing.

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<sup>1</sup> Jukka Rantanen Peter Kleinebudde, Johannes Khinast, *Continuous Manufacturing of Pharmaceuticals* (John Wiley & Sons, 2017).

<sup>2</sup> W. Grymonpré and others, 'Downstream Processing from Melt Granulation towards Tablets: In-Depth Analysis of a Continuous Twin-Screw Melt Granulation Process Using Polymeric Binders', *European Journal of Pharmaceutics and Biopharmaceutics*, 124, December 2017 (2018), 43–54 <<https://doi.org/10.1016/j.ejpb.2017.12.005>>.

<sup>3</sup> James Munson, C. Freeman Stanfield, and Bir Gujral, 'A Review of Process Analytical Technology (PAT) in the U.S. Pharmaceutical Industry', *Current Pharmaceutical Analysis*, 2.4 (2006), 405–14 <<https://doi.org/10.2174/157341206778699582>>.

<sup>4</sup> Baoyang Ding, 'Pharma Industry 4.0: Literature Review and Research Opportunities in Sustainable Pharmaceutical Supply Chains', *Process Safety and Environmental Protection*, 119 (2018), 115–30 <<https://doi.org/10.1016/j.psep.2018.06.031>>.

<sup>5</sup> U.S. Food and Drug Administration (FDA), 'Good Machine Learning Practice for Medical Device Development: Guiding Principles', October, 2021, 1 <<https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles>>.

<sup>6</sup> Tim Chan Seem and others, 'Twin Screw Granulation - A Literature Review', *Powder Technology*, 276 (2015), 89–102 <<https://doi.org/10.1016/j.powtec.2015.01.075>>.

<sup>7</sup> Srinivasan Shanmugam, 'Granulation Techniques and Technologies: Recent Progresses', *BioImpacts*, 5.1 (2015), 55–63 <<https://doi.org/10.15171/bi.2015.04>>.

Consequently, the following objectives were set for this work:

- Twin-screw melt granulation of drug-loaded electrospun fibres to enhance their flowability and facilitate their successful tableting without adding an excessive amount of excipients while preserving their enhanced dissolution properties.
- Development of a TSG-based, integrated, continuous powder-to-tablet line suitable for both wet and melt granulation, its optimization and scale-up.
- Investigation of the integrated TSG of glucose monohydrate to improve its flowability and tableting, prevent capping, and produce tablets with adequate mechanical properties.
- Monitoring the moisture content and the crystal form, two important characteristics influencing critical quality attributes, of the glucose granules in-line and real-time with near-infrared (NIR) and Raman spectroscopy, respectively.
- Development of a data-driven soft sensor based on an explainable artificial neural network (ANN) to indirectly monitor the moisture content of the granules, produced on the integrated TSWG-based line, solely based on the real-time gathered parameters, without any direct measurement.

## 2 Methods

### 2.1 High-speed electrospinning (HSES)

The large-scale production of drug-loaded electrospun fibers was carried out using a HSES device developed by our research group.

### 2.2 Continuous line based on TSG

A fully continuous, integrated manufacturing line based on TSG was developed, suitable for both wet and melt granulation (Figure 1). The system consisted of a feeder – either a DDW-MD0-MT type gravimetric feeder, a K-SFS-24 type gravimetric feeder, or a LABORETTE 24 type vibratory feeder was used – a TS16 type twin-screw granulator, a continuous dryer, a continuous mill, a vibratory feeder, and a continuous, Dott Bonapace CPR6 type tablet press. In wet granulation experiments, the granulating liquid was added to the system using a Watson-Marlow 120 U peristaltic pump, whereas in melt granulation, the continuous dryer was operated with cold air to cool the granules.

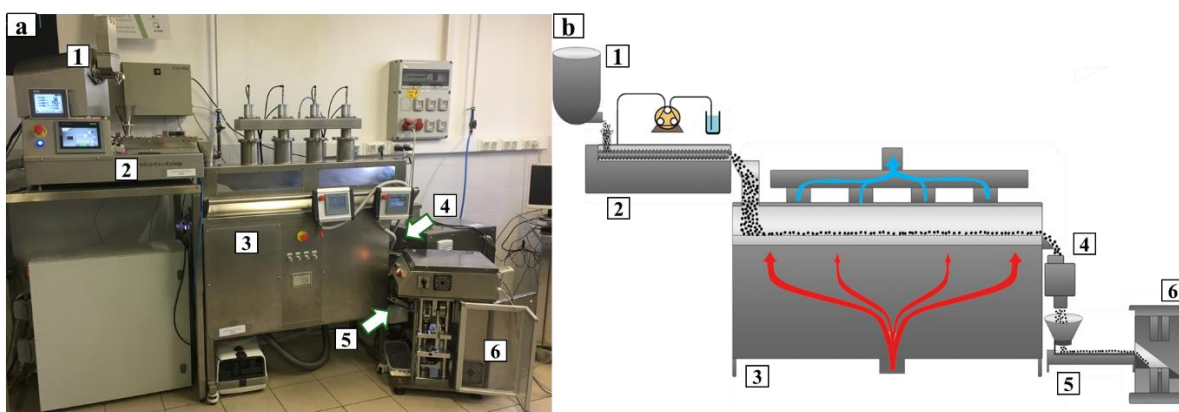


Figure 1: The (a) photo and (b) schematic drawing of the continuous system comprising of a (1) gravimetric feeder, (1) twin-screw granulator, (3) continuous dryer, (4) continuous mill, (5) vibratory feeder, (6), tableting machine.

## 2.3 Experiment setups

### 2.3.1 Melt granulation of drug-loaded electrospun fibres

Amorphous solid dispersions containing itraconazole (ITR) were prepared using HSES, with either poly(1-vinylpyrrolidone-*co*-vinyl acetate) or hydroxypropyl methylcellulose (HPMC) as the carrier polymer. In both formulations, the fibers contained 40% ITR and 60% polymer. To improve the powder flow properties, melt granulation was performed using polyethylene glycol (PEG) as a binder, while the influence of granulation temperature and screw configuration on the process performance was systematically investigated.

### 2.3.2 Melt granulation of caffeine

The twin-screw granulator was also employed for the melt granulation of caffeine using PEG as a binder. In this case, the complete powder-to-tablet continuous line was operated together. The effects of the molecular weight of the applied PEG and process parameters were examined. Additionally, scale-up experiments were conducted, increasing the production rate from 0.5 kg/h to 8 kg/h. The scale-up was achieved without equipment change, solely by increasing the throughput.

### 2.3.3 Wet granulation of glucose

The system was also utilized for the wet granulation of glucose using distilled water as the granulation liquid. The effect of screw configuration, granulation temperature, and drying temperature were tested to evaluate their effect on granule quality. Throughout the process, the in-line, real-time monitoring of the granule moisture content was conducted using NIR spectroscopy (Figure 2). The moisture content was determined from the collected spectra using a calibration model based on partial least squares (PLS) regression, developed in MATLAB.

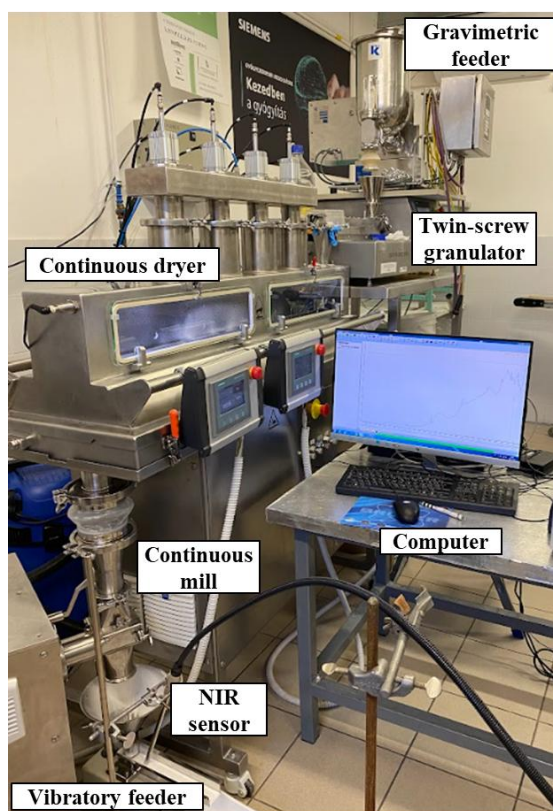


Figure 2: The in-line monitoring of the granulation process.

Next, experiments were performed where a Raman probe was used instead of the NIR sensor, enabling real-time monitoring of the crystalline form (anhydrate content) of glucose in the granules. The anhydrous content was determined by a PLS model (also developed in MATLAB), while the granulation temperature was systematically increased.

#### 2.3.4 Indirect monitoring of the moisture content using an ANN

The wet granulation of a placebo formulation was also accomplished, with the moisture content first monitored in-line, with a NIR spectra-based PLS model. Simultaneously, the process parameters (e.g., feeding rate, liquid-to-solid ratio, drying temperature, drying airflow) were continuously recorded using SIMATIC SIPAT software. Two ANN models were developed in MATLAB to indirectly predict moisture content based solely on recorded process parameters (Figure 3).

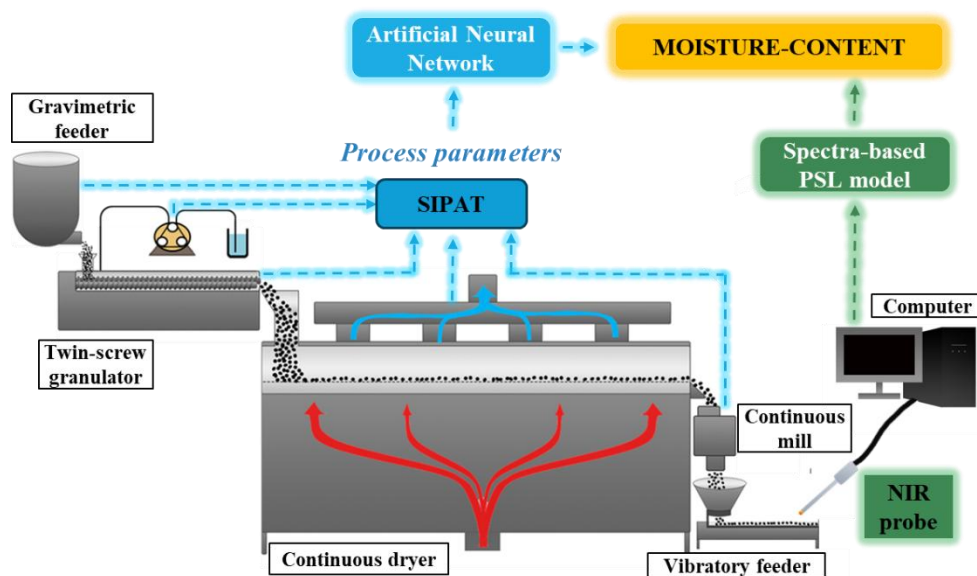


Figure 3: Monitoring moisture content using the NIR-based PLS model (green) and ANN-based data-driven model (blue).

## 2.4 Analytical methods

### 2.4.1 Scanning Electron Microscopy and Polarized Light Optical Microscopy

The morphology of the fibers, powders, and granules was examined using a JEOL JSM 6380LA scanning electron microscope and a Carl Zeiss Jena polarized light optical microscope equipped with an OLYMPUS C4040 Z camera.

### 2.4.2 Differential Scanning Calorimetry (DSC)

Samples were analyzed using a DSC3+ instrument. Modulated differential scanning calorimetry measurements were also performed using the same machine in a stochastic temperature modulation.

### 2.4.3 Thermogravimetric Analysis (TGA)

Samples were analyzed using a Q5000 TGA instrument.

### 2.4.4 Powder X-ray Diffraction (XRPD)

Diffraction patterns of the samples were obtained using a PANalytical X'pert Pro MDP instrument.

### 2.4.5 Laser diffraction

Particle size distribution was measured using a Malvern Mastersizer 2000 instrument.

#### 2.4.6 Powder Characterization

Powder characteristics were evaluated via bulk and tapped density measurements using an ERWEKA SVM12 device. Carr index, Hausner ratio, and corresponding flowability categories were determined. Additionally, flowability tests, porosity measurements (using an Anton Paar Ultrapyc 5000 II gas pycnometer), and loss-on-drying (LOD) measurements were also performed.

#### 2.4.7 Mechanical Characterization of Tablets

Tablet mechanical properties were evaluated by determining hardness, breaking force, and friability.

#### 2.4.8 In Vitro Dissolution Testing

Tablet dissolution was assessed using a Pharma Test Apparatebau instrument or a Hanson SR8-Plus dissolution tester connected to an Agilent 8453 UV–Vis spectrophotometer.

#### 2.4.9 Thermal Imaging

The temperature of the granules was monitored using a FLIR T660 thermal camera.

#### 2.4.10 NIR Spectroscopy (PAT tool)

A Bruker MPA multi-purpose FT-NIR spectrometer was used for the in-line, real-time monitoring of granule moisture content.

#### 2.4.11 Raman Spectroscopy (PAT tool)

A Kaiser RamanRxn2® hybrid in situ spectrometer equipped with a PhAT probe was used for the in-line, real-time monitoring of the crystal form of the granules.

#### 2.4.12 ANNs

During some granulation experiments, process parameters were continuously recorded using SIMATIC SIPAT software. Two ANNs – a multilayer perceptron (MLP) model and a nonlinear autoregressive model with external inputs (NARX) – were developed in MATLAB using the Statistics and Machine Learning Toolbox to indirectly predict moisture content based solely on recorded process parameters. To make the model explainable, SHAP (SHapley Additive exPlanations) analysis was performed, providing insights into the model and revealing, how each process parameter influenced the predictions at any given moment.

### 3 Results

#### 3.1 Melt granulation of drug-loaded electrospun fibers

The poor dissolution properties of ITR – a broad-spectrum antifungal active pharmaceutical ingredient (API), belonging to the II. class of the Biopharmaceutics Classification System – were enhanced via HSES (from 16% to 100%). However, the resulting fibrous material exhibited poor powder flowability. Therefore, this limitation was effectively addressed through twin-screw melt granulation, improving processibility and enabling tablet production without large amounts of excipients.

The study further revealed that harsher granulation conditions (e.g., elevated temperature and increased shear force) could compromise the fibrous structure, promoting recrystallization even below the glass transition temperature of the amorphous solid dispersion, thereby decreasing dissolution. It was also confirmed that the polymer selection influenced the stability of the amorphous solid dispersion during granulation. The ITR-HPMC demonstrated superior

stability, likely due to hydrogen bonding between the drug and polymer, making them more suitable for processing.

By applying appropriate processing parameters, granules with good flow properties were produced from the ITR-HMPC fibers, while retaining the enhanced dissolution properties of the original fibers. Additionally, tablet size was reduced by 34%, not only reducing excipient need but also improving patient compliance. This study demonstrated that the combination of two continuous technologies, HSES and TSG can simultaneously address multiple formulation challenges while being seamlessly integrateable into a continuous manufacturing line.

### **3.2 Melt granulation of caffeine and process scale-up**

The fully continuous, TSG-based powder-to-tablet line was suitable for both wet and melt granulation, and was applied to improve the physical properties of several powder blends, including both API-containing and placebo mixtures.

During the melt granulation of a caffeine-containing powder blend with poor initial flow and tablet properties, the average particle size increased, powder flowability improved, and the tablet properties enhanced. While the initial material was unsuitable for direct compression – the directly compressed tablets had poor mechanical properties – granulation significantly improved tablet tensile strength (increased the breaking force from ~40 N to over 80 N) and reduced friability to below 0.3% while retaining immediate release characteristics.

By increasing the production rate, the original throughput (0.5 kg/h) was increased to 8 kg/h on the same system while maintaining adequate product properties. This scale-up was achieved seamlessly, without equipment change – an important aspect in the pharmaceutical industry, where scaling up batch production is a common challenge, usually requiring new optimization due to the change in geometry. The system's scalability and ability to achieve industrially relevant production rates highlights its potential for commercial application.

### **3.3 Wet granulation of glucose and in-line monitoring of the process**

The system was also successfully applied for the wet granulation, confirming its flexibility. The flowability and compressibility of  $\alpha$ -D-glucose-monohydrate were successfully enhanced. It was revealed that using a screw configuration with reverse conveying elements influenced the process positively, as the resulting high pressure and increased residence time promoted the fragmentation of the initially long crystallines, thereby preventing the formation of weak spots during tableting. Thus, tablets with satisfactory mechanical strength not prone to capping were produced (Figure 4). The described system showed promising potential for industrial application as it can be readily integrated into existing crystallization production lines directly after the centrifugation step. The system's ability to process wet materials makes it particularly suitable for this purpose, potentially simplifying the overall manufacturing process.

The in-line, real-time monitoring of the system was also accomplished using a NIR spectra-based PLS model. The granule moisture content, a critical property, was accurately predicted, and the influence of the drying temperature was revealed. Therefore, the adequate drying temperature, where the drying was complete, was identified at 85°C, where the moisture content was close to the theoretical crystalline water of glucose monohydrate (9.08%). This method enabled the precise monitoring of the drying conditions, thereby ensuring consistent granule and tablet properties.

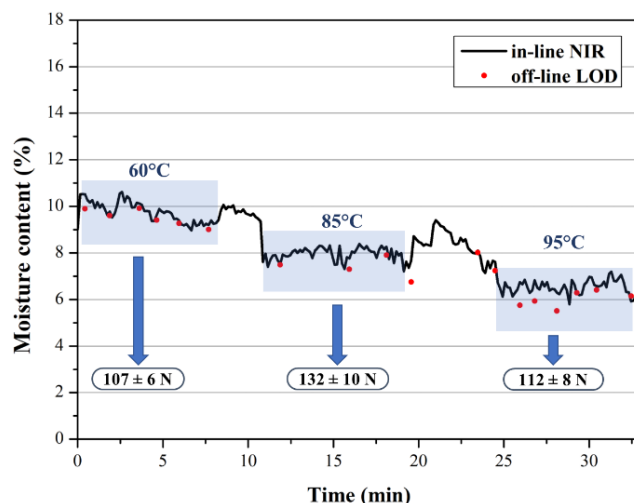


Figure 4: The in-line monitoring of granule moisture content during the stepwise increase of the drying temperature, with the breaking force of the tablets pressed from granules indicated by blue arrows.

Due to evidence that high drying temperatures may induce partial conversion of  $\alpha$ -D-glucose monohydrate to its anhydrous form, the crystal form of glucose in the granules was investigated next. The Raman spectra-based PLS model enabled the in-line, real-time monitoring of the anhydrate content, while the drying temperature was increased stepwise (Figure 5). Results indicated that the transformation was minimal at lower temperatures (e.g. 60 °C), whereas over 50% conversion occurred at 120 °C. Given the strong impact of crystal form on critical quality attributes, Raman spectroscopy proved suitable for continuous monitoring, ensuring consistent product quality. The results of the in-line monitoring were validated using multiple off-line analytical techniques, TGA, DSC, and XRPD, all of which showed good agreement. This multi-analytical approach highlighted the reliability of the Raman-based model and the value of orthogonal validation strategies to enhance detection confidence.

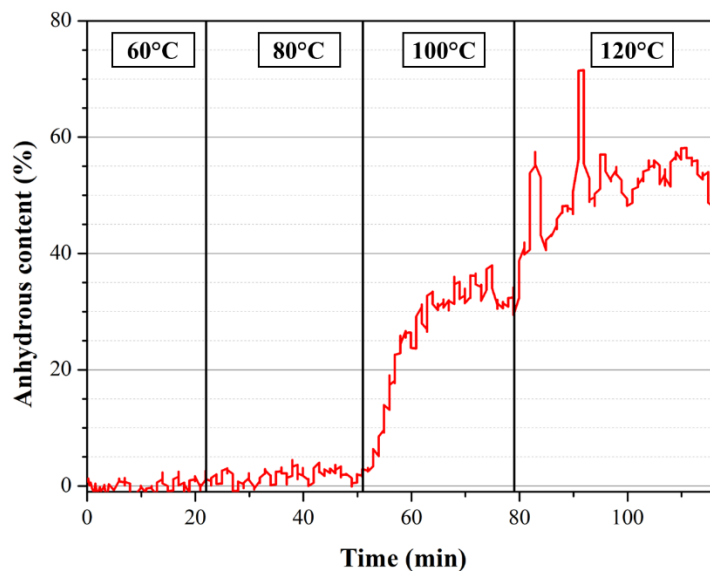


Figure 5: The in-line monitoring of the anhydrous content during the stepwise increase of the drying temperature.

### 3.4 The wet granulation of a placebo system and indirect monitoring using ANNs

The system was also successfully applied for the granulation of the placebo blend. First, the moisture content was monitored in-line using a NIR spectra-based PLS model, followed by an indirect approach utilizing ANNs.

In the first two experiments, the moisture content was estimated by the MLP model based on only recorded process parameters (Figure 6). The results were in good agreement with both the NIR-based predictions and the off-line reference measurements (LOD), confirming the reliability of this approach.

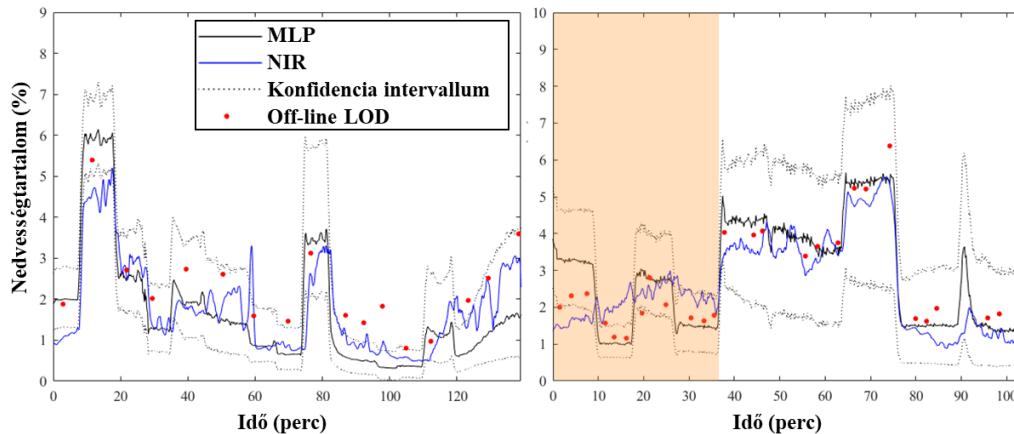


Figure 6. In-line monitoring of granule moisture content using an MLP model compared with NIR and off-line LOD measurements. During the orange-shaded period, the NIR predictions were outside the model's domain and were, therefore, considered unreliable.

Although a deviation between NIR and MLP predictions was observed at the beginning of the second experiment, further investigation revealed that the NIR spectra during this period fell outside the model's domain, indicating issues with the spectra collection – likely due to the inadequate coverage of the chute of the vibratory feeder tray by the granules. Consequently, the NIR spectra-based results were not reliable in this period, while the MLP model predictions remained valid, as supported by their agreement with off-line LOD measurements.

Since a major limitation of ANN models is their "black boxes" nature, hindering trust in the predictions, the next goal was to make the MLP explainable. The SHAP analysis provided insights into the model, revealing, how each process parameter influenced the predictions at any given moment (Figure 7). This method enabled a high level of process understanding, offering a significant advantage over conventional analytical techniques.

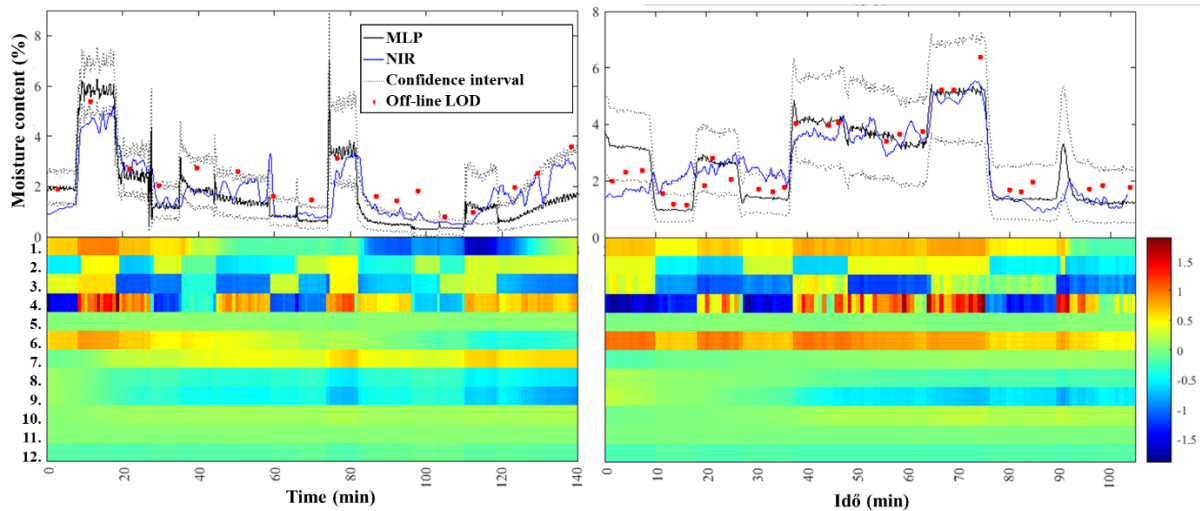


Figure 7: Top panel: Granule moisture content as measured by various methods. Bottom panel: SHAP analysis results. The y-axis lists the relevant process parameters:(1) dryer temperature (zones 1–3), (2) drying air flow (zones 1–4), (3) mass flow rate, (4) liquid-to-solid ratio, (5) granulator screw speed, (6) dryer temperature (zone 4), (7–10) granulator barrel temperature (zones 1–4), (11) mill type, (12) mill screen size. The color scale indicates each parameter’s influence on the MLP-predicted moisture content at each time point.

In the next experiment, the moisture content was estimated using the NARX model. The predictions also aligned well with the results of both the NIR-based and off-line LOD reference measurements (Figure 8).

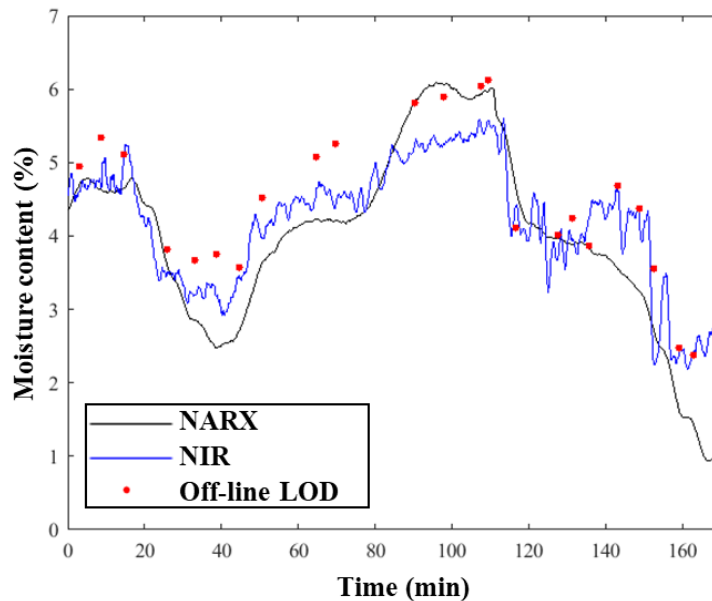


Figure 8. In-line granule moisture content monitoring using the NARX model compared with NIR and off-line LOD measurements.

In summary, this study demonstrates that explainable ANN-based soft sensors offer a promising, cost-effective alternative to traditional monitoring techniques. The methodology presented here can serve as an orthogonal tool to complement off-line reference methods or spectroscopic techniques, thereby enhancing the robustness, reliability, and process understanding.

## 4 Thesis findings

1. The twin-screw melt granulation of drug-loaded electrospun fibers was successfully achieved for the first time, significantly improving the flow properties while maintaining adequate dissolution. With this approach, tablets containing amorphous solid dispersions were produced without the addition of excess excipients, resulting in a 34% reduction in tablet size compared to the direct compression route.[III]
2. The significant influence of the electrospinning polymer on the stability of the amorphous solid dispersion during granulation was confirmed. It was demonstrated that the use of hydroxypropyl methylcellulose improved the stability of the itraconazole-containing amorphous solid dispersion during granulation, preventing phase separation or the crystallization of the active pharmaceutical ingredient, which would otherwise impair dissolution performance.[III]
3. A fully continuous, scalable, twin-screw granulation-based integrated powder-to-tablet line was developed, consisting of feeding, twin-screw granulation, continuous drying, milling, and tableting, which is applicable to both melt and wet granulation, and was proved suitable for enhancing the flowability and tableability of various materials and improve the mechanical tablet properties, such as breaking force and friability. Furthermore, it was confirmed that an increase in the production rate of more than one order of magnitude can be achieved using the same equipment, only by increasing production speed. The productivity was significantly increased (from 0.5 to 8 kg/h) without equipment change and without any substantial change in product quality. [I, II]
4. The flowability and tableability of glucose monohydrate were significantly enhanced using the twin-screw granulation line, proposing a system that is easily integrable into the current industrial production process of crystalline glucose. The system proved suitable for producing pure glucose tablets (only containing a lubricant) with adequate breaking force, while tablet capping was effectively prevented.[I, VI]
5. It was proved that the remaining moisture content in glucose granules negatively affects the mechanical properties of tablets produced from them. The effect of the drying temperature on the moisture content, a critical granule property, was systematically investigated, and the in-line and real-time monitoring was achieved using near-infrared spectroscopy and multivariate data analysis. By applying this method, sufficient drying was ensured, consequently the tablets with adequate breaking force could be produced that were not prone to capping.[I]
6. It was confirmed that glucose-monohydrate can transform into anhydrous form during the continuous granulation process, affecting the tablet properties. The impact of different drying temperatures on the anhydrous content was revealed, and drying conditions that minimized or prevented this transformation were identified. The in-line crystal form quantification of glucose in granules following an integrated granulation process was achieved for the first time, using Raman spectroscopy and multivariate data analysis, thereby ensuring consistent product quality.[I, V]
7. Artificial neural network-based data-driven soft sensors were developed for the first time to predict the moisture content of granules after a continuous twin-screw granulation-based pharmaceutical process, only from the applied process parameters. Two models, a fully connected, feedforward network and a recurrent, time-series network, were proved to be suitable for accurately determining the granule moisture content indirectly with a root mean square error below 1%. The accuracy of the predictions was confirmed by their alignment with the results obtained from simultaneous in-line monitoring with near-infrared spectroscopy and off-line reference measurements. The proposed methods provide cost-efficient, orthogonal alternatives to traditional monitoring techniques (e.g. near-infrared spectroscopy). By carrying out

SHAP (SHapley Additive exPlanations) analysis on the feedforward network, an explainable artificial neural network model was developed for the first time to indirectly predict the moisture content after twin-screw granulation. This approach enhances process understanding, providing a significant advantage over traditional monitoring techniques.[IV]

## 5 Application of the results

Given the critical role of granulation as an essential pharmaceutical formulation step, its continuous alternative, TSG holds significant potential in the pharmaceutical industry. This work demonstrated the advantages of the technology, highlighting its efficiency, flexibility, and robustness, thereby supporting its industrial implementation. Furthermore, TSG provided an excellent platform to showcase the benefits of continuous manufacturing, advanced PAT tools and explainable ANNs in pharmaceutical production. Although these advanced approaches have gradually gained ground over the past decades, their widespread industrial implementation and the complete realization of their benefits still require further research. The findings of this study contribute to this effort by demonstrating the advantages and potential of these approaches, which can have a particularly strong impact when applied in combination.

Additionally, during the course of this PhD work, several industrial projects have been carried out on the developed continuous manufacturing line, applying it to establish alternative manufacturing routes for various commercially available drug products and successfully scaling up the process to a throughput of 40 kg/h.

## 6 Publications

### Publications on which thesis findings are based:

- I. **P. Záhonyi**, E. Szabó, A. Domokos, A. Péter-Haraszti, M. Gyürkés, E. Moharos, Zs. K. Nagy, Continuous integrated production of glucose granules with enhanced flowability and compressibility, *International Journal of Pharmaceutics*, 626 (2022) 122197  
IF: 5.8; Q1; 60%
- II. **P. Záhonyi**, F. Dániel, E. Szabó, L. Madarász, Á. Fazekas, A. Péter-Haraszti, Zs. K. Nagy, Integrated continuous melt granulation-based powder-to-tablet line: process investigation and scale-up on the same equipment, *European Journal of Pharmaceutics and Biopharmaceutics* 189 (2023) 165-173  
IF: IC: 4.4 Q1; 80%
- III. **P. Záhonyi**, Á. G. Müncz, A. Péter-Haraszti, Zs. K. Nagy, I. Csontos, Gy. Marosi, E. Szabó, Continuous twin-screw melt granulation of drug-loaded electrospun fibers, *European Journal of Pharmaceutics and Biopharmaceutics* 206, (2025) 114580  
IF: 4.4 Q1; 70%
- IV. **P. Záhonyi**, F. Dániel, E. Szabó, Zs. K. Nagy, B. Nagy, Explainable artificial neural network as a soft sensor to predict the moisture content in a continuous granulation line, *European Journal of Pharmaceutical Sciences – accepted with revision*  
IF: 4.3; Q1; 51%
- V. **P. Záhonyi**, F. Dániel, E. Moharos, Zs. K. Nagy, E. Szabó, In-line Raman-based quantification of the anhydrous content in a fully integrated continuous powder-to-granule line, *AAPS PharmSciTech – accepted with revision*  
IF: 3.4 Q1; 51%
- VI. **P. Záhonyi**, A. Domokos, Zs. K. Nagy, E. Szabó, TTEC-014/2021 Eljárás dextróz-monohidrát folyamatos granulálására a gördülékenység és tablettázhatóság javítása céljából, (2021)

### Further related publications:

- VII.** E. Szabó, **P. Záhonyi**, D. Brecka, D. L. Galata, L. A. Mészáros, L. Madarász, K. Csorba, P. Vass, E. Hirsch, J. Szafraniec-Szczyński, I. Csontos, A. Farkas, G. Van den Mooter, Zs. K. Nagy, Gy. Marosi, Comparison of amorphous solid dispersions of spironolactone prepared by spray drying and electrospinning: The influence of the preparation method on the dissolution properties, *Molecular Pharmaceutics*, 18 (2020) 317-327  
IF: 4.939
- VIII.** E. Szabó, **P. Záhonyi**, M. Gyürkés, B. Nagy, D. L. Galata, L. Madarász, E. Hirsch, A. Farkas, S. K. Andersen, T. Vigh, G. Verreck, I. Csontos, Gy. Marosi, Zs. K. Nagy, Continuous downstream processing of milled electrospun fibers to tablets monitored by near-infrared and Raman spectroscopy, *European Journal of Pharmaceutical Sciences*, 164 (2021) 105907  
IF: 4.3
- IX.** E. Szabó, **P. Záhonyi**, D. L. Galata, L. Madarász, P. Vass, A. Farkas, J. Dhondt, S. K. Andersen, T. Vigh, G. Verreck, I. Csontos, Gy. Marosi, Zs. K. Nagy, Powder filling of electrospun material in vials: A proof-of-concept study, *International Journal of Pharmaceutics*, 613 (2022) 121413  
IF: 5.8
- X.** M. Gyürkés, L. Madarász, **P. Záhonyi**, Á. Köte, B. Nagy, H. Pataki, Zs. K. Nagy, A. Domokos, A. Farkas, Soft sensor for content prediction in an integrated continuous pharmaceutical formulation line based on the Residence Time Distribution of unit operations, *International Journal of Pharmaceutics*, 624 (2022) 121950  
IF: 5.8
- XI.** E. Szabó, A. Péter-Haraszti, **P. Záhonyi**, D. Vadas, I. Csontos, Zs. K. Nagy, G. Van den Mooter, Gy. Marosi, Evaluation of Different Thermoanalytical Methods for the Analysis of the Stability of Naproxen-Loaded Amorphous Solid Dispersions, *Pharmaceutics*, 14(11) (2022) 2508  
IF: 4.421
- XII.** P. Vass, A. Domokos, E. Pantea, B. Szilágyi, M. Molnár, **P. Záhonyi**, B. Nagy, Zs. K. Nagy, Processing of thermosensitive biological API from suspension using an integrated continuous granulation – Drying – Milling line into powder ready for tableting *Drying Technology*, 41(4) (2023) 492-502  
IF: 2.7
- XIII.** O. Péterfi, L. Madarász, M. Ficzer, K. Lestyán-Goda, **P. Záhonyi**, G. Erdei, E. Sipos, Zs. K. Nagy, D. L. Galata, In-line particle size measurement during granule fluidization using convolutional neural network-aided process imaging, *European Journal of Pharmaceutical Sciences*, 189 (2023), 106563  
IF: 4.3
- XIV.** A. Péter-Haraszti, **P. Záhonyi**, A. Farkas, I. Csontos, Zs. K. Nagy, E. Szabó, G. Van den Mooter, Gy. Marosi, Thermal investigation of relaxations of interacting and non-interacting amorphous solid dispersions, *Journal of Thermal Analysis and Calorimetry*, 149(15) (2024) 8067-8083  
IF: 3.0
- XV.** D. L. Galata, A. Domokos, B. Démuth, **P. Záhonyi**, G. Fülöp, Zs. K. Nagy, B. Nagy, In-line indirect concentration measurement of ultralow dose API during twin-screw wet granulation based on NIR and Raman spectroscopy, *International Journal of Pharmaceutics*, 664 (2024) 124650

IF: 5.3

- XVI.** A. Péter-Haraszti, L. Gy. Bakucz, L. A. Mészáros, **P. Záhonyi**, E. Szabó, Drug Content Determination of Amorphous Solid Dispersion Containing Tablets Using a Non-Destructive and Rapid UV Imaging Method, *International Journal of Pharmaceutics* (2025) 125726  
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#### Oral Presentations:

- XVII.** **P. Záhonyi**, Elektrosztatikus szálképzéssel előállított hatóanyag-tartalmú minták folyamatos homogenizálása, *TDK Konferencia*, Budapest (2019.11.12.) és *OTDK Konferencia*, online (2021.05.17-19.) és *OTDK Plusz Konferencia*, Budapest (2021.09.03.)
- XVIII.** **P. Záhonyi**, In-line alkalmazható spektroszkópiai módszereket befolyásoló tényezők vizsgálata szálas minták folyamatos feldolgozásánál *TDK Konferencia*, Budapest (2020.11.12) és *OTDK Konferencia*, online (2021.05.17-19.)
- XIX.** **P. Záhonyi**, Folyamatos granuláláson alapuló technológia fejlesztése *TDK Konferencia*, Budapest (2021.11.16) és *OTDK Konferencia*, Szeged (2023.04.12-15.)
- XX.** **P. Záhonyi**, E. Szabó, I. Csontos, Gy. Marosi, Zs. K. Nagy, Elektrosztatikus szálképzéssel előállított hatóanyag-tartalmú minták folyamatos feldolgozása és in-line analitikai vizsgálata, *XIV. Szent-Györgyi Albert Konferencia*, Budapest (2020.04.16-17.)
- XXI.** **P. Záhonyi**, E. Szabó, A. Domokos, A. Farkas, É. Kiserdei, Zs. K. Nagy, Gy. Marosi, Folyamatos technológiák a gyógyszer és az élelmiszeriparban, *Kristályosítási és Gyógyszerformulálási Szakosztály 12. Kerekasztal Konferenciája*, Balatonszemes (2021.10.14-15.)
- XXII.** **P. Záhonyi**, E. Szabó, Zs. K. Nagy, Continuous integrated production of glucose granules with enhanced flowability and tabletability, *IV. Oláh György Konferencia*, Budapest (2022. 09. 26.)
- XXIII.** **P. Záhonyi**, E. Szabó, D. Fekete, Zs. K. Nagy, Folyamatos olvadék alapú granuláló és integrált tablettázó sor fejlesztése, *Gyógyszertechnológiai és Ipari Gyógyszerészeti Konferencia*, Siófok (2022. 10. 26-28.)
- XXIV.** **P. Záhonyi**, D. Fekete, E. Szabó, B. Nagy, Zs. K. Nagy, Integrated continuous twin-screw granulation – process investigation, scale-up and monitoring with artificial neural network-based soft sensor, *14th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology*, Vienna (2024.03.18-21.)
- XXV.** **P. Záhonyi**, D. Fekete, E. Szabó, B. Nagy, Zs. K. Nagy, Monitoring the moisture content of granules after a twin-screw wet granulation process with spectra-based methods and artificial neural network-based soft sensor, *European Federation for Pharmaceutical Sciences Annual Meeting*, Debrecen (2024.05.23-25.)
- XXVI.** **P. Záhonyi**, E. Szabó, Zs. K. Nagy, Investigation of the dehydration of dextrose monohydrate during twin-screw wet granulation and in-line, real-time monitoring of the anhydrous content in granules, *VI. George Olah Conference*, Budapest (2024.09.23.)

#### Poster Presentations:

- XXVII.** **P. Záhonyi**, E. Szabó, Á. Müncz, Zs. K. Nagy, Continuous granulation of drug-loaded electrospun amorphous solid dispersion, *V. George Olah Conference*, Budapest (2023.09.12.)