Development of a Digital Twin of Extrusion Process for Pharmaceutical Applications

Roja P. Moghadam, Ahmed Metawea, Eoin P. Hinchy, Rabah Mouras
Pharmaceutical Manufacturing Technology Centre Group,
Bernal Institute, University of Limerick, Ireland

Abstract

The rapid advancement of Industry 4.0 has driven the development of Digital Twin (DT) technology; however, the lack of standardized DT architectures and complex data management requirements continue to pose significant implementation challenges. This study addresses these barriers by proposing a robust DT architecture and developing a prototype for a pharmaceutical twin-screw extruder (TSE) testbed coupled with process analytical technologies (PAT) for continuous manufacturing of caffeine-urea co-crystals. Combining these two materials in the extrusion process can enhance their physicochemical properties, such as solubility and stability, which are critical in the development of pharmaceutical products. Real-time monitoring of co-crystals formation and quality is ensured by inline PAT Raman. The project establishes a real-time process monitoring and control framework integrating a surrogate physical model with chemometrics vi with the aid of a Partial Least Squares (PLS) calibration model. This dual-sensor system strengthens fault detection through the application of Principal Component Analysis (PCA) and Statistical Process Control (SPC) techniques. Additionally, user-friendly dashboards were developed to demonstrate the DT prototype, facilitating efficient process control and monitoring for end-users. This study highlights the potential of DT technology to enhance the competitiveness and sustainability of the pharmaceutical manufacturing industry through improving efficiency, reducing time and waste and ensuring high-quality products via real-time process monitoring.

Methodology

Calibration standards were prepared by blending milled urea, caffeine, and co-crystal in varying concentrations. The co-crystal was produced by processing an equimolar mixture of caffeine and urea at room temperature using an oscillating ball mill. The formation of co-crystals was confirmed by X-ray Diffraction (XRD) analysis. According to Figure.1, Raman spectra were collected from samples spread on a belt conveyor. The wavelength range for modelling was selected based on the consistent co-crystal peak and correlation regression. Spectral treatment and PLS model structures were optimized based on the root mean square error (RMSE) of prediction. The PLS model was implemented in PharmaMV software for in-line prediction of co-crystal conversion during the extrusion process. Raman and the extruder were connected to this software through OPC (Open Platform Communications), enabling real-time data acquisition and monitoring of the co-crystal conversion. After defining fault detection scenarios and applying a PID controller, the dashboards were designed to provide comprehensive access to the DT structure.

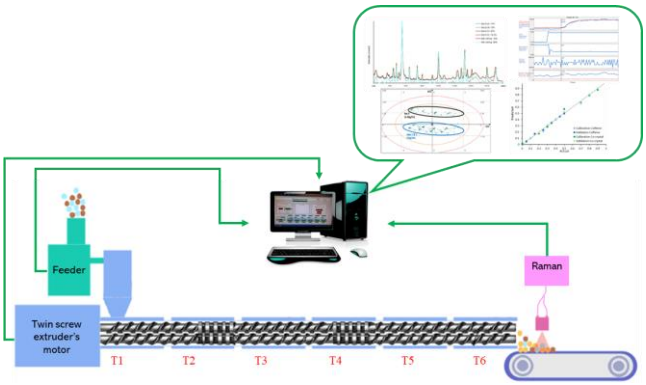

Fig. 1. Process overview