Powder flow within a pharmaceutical tablet press – a DEM analysis

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ABSTRACT

Numerical simulations in pharmaceutical industry are gaining importance as an advanced tool to shed light on the underlying physics in a given unit operation such as tablet manufacturing. Thereby different simulation methods are used to describe phenomena during milling of raw material, blending of the formulation components, powder compaction to form tablets, and coating of the tablets [1].
Out of these processing stages the powder flow within the tableting machine constitutes one critical step defining product safety in terms of content and content uniformity of the active pharmaceutical ingredient (API). However, the numerical simulations reported so far either evaluated the powder flow in a simplified model die-filling system [2] without considering the complex geometrical configuration within the rotary tablet press, used unrealistic micro-mechanical particle properties and sizes [3] or considered large mono-disperse granules [4].
This work presents a systematic numerical approach for studying the powder flow within a feeder to die/cavity in a rotary tablet press with actual dimensions to evaluate the critical material and process attributes influencing the final product quality.
The computations were carried out using an open source discrete element method (DEM) code known as LIGGGHTS. The investigated system consisted of a hopper, a force feeder comprising three rotating paddle wheels, and a turret with 24 dies. The simulations were conducted according to a fractional factorial design of experiments (DoE), which was developed to distinguish the particular influence of process parameters as well as material properties on the final drug product. The former included paddle wheel and turret speed. From a formulation point of view, different particle size distributions created to mimic low and high dose formulations, cohesion and particle-wall friction were considered.
First of all, the general analysis of powder flow showed that the shape of the three different paddle wheels influenced the radial dispersion of the particles significantly. In addition, the powder feeding from the hopper into the feeder showed a gradient across the feeding hopper radius causing an intriguing particle mixing as well as particle size segregation. The origin of the filled particles in the die was influenced by the combination of paddle wheel speed and turret speed. The latter also controlled the API content, mass of the final tablet, and accordingly their relative fluctuations.
In conclusion, this study helps in visualizing powder flow in a pharmaceutical tablet press disclosing astonishing particle flow phenomena that have not been reported yet. Moreover, the detailed fractional factorial DoE identifies the most critical quality parameters. Eventually, the qualitative and quantitative support of numerical simulations in pharmaceutical development is emphasized.

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