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Understanding effects of process parameters and forced feeding on die filling

Hui Ping Goh, Paul Wan Sia Heng, Celine Valeria Liew*

GEA-NUS Pharmaceutical Processing Research Laboratory, Department of Pharmacy, National University of Singapore, 18 Science Drive 4, Singapore 117543, Singapore

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ABSTRACT

Die filling is a critical step during pharmaceutical tablet production and is still not well understood due to the rather complex interplay between particle attributes, die orifice diameter and fill energetics. While shoe-die filling models have been used to simulate die filling conditions, they typically lack the sophistication of the actual production-scale, feeder-based die filling conditions. The relationship between tableting process parameters and filling into die orifices of different diameters by powders of different flowabilities requires critical examination and understanding. In this study, a special die filling contraption was designed and custom-made to simulate the effects of gravity, suction and feeder paddle assistance as present in modern rotary tablet presses. Die fill performance was studied using powders with different flow properties. Suction impact was greatest on die fill, in particular, for small orifice diameters and less permeable powders. Effect of paddle velocity on die fill was greater for compressible powders and larger orifice diameters. In comparison to suction and paddle velocity, forced feeding did not significantly affect die fill performance. Relationship between process parameters and die fill performance was found to be highly dependent on the material and orifice diameter.

1. Introduction

Production of pharmaceutical tablets typically involves the three consecutive process steps of die filling, compression and tablet ejection. The die fill determines tablet weight which in turn is related to drug content and other critical quality attributes such as tablet mechanical strength, friability and disintegration. Reproducibility of die fill is hence critical as it not only affects product quality but also the overall efficiency of the tableting process (Mills and Sinka, 2013).

Research in die fill was initially driven by other industries involved in powder compaction, such as powder metallurgy and ceramics (Bocchini, 1987). The die filling process can be passive (powder delivered into a stationary die from a moving shoe) or active (powder delivered into a moving die from a stationary shoe) on the compaction system (Peeters et al., 2015; Wu, 2008). By using shoe-die models to examine the passive die fill process, interactions between powder and air during die filling could be elicited. Displacement of air from the die cavity by powder filling created a pressure gradient which opposed further powder entry into the cavity and this could be visualised by high speed video (Mills and Sinka, 2013; Wu and Cocks, 2004; Xie and Puri, 2006). Higher die fill densities achieved by the assistance of vacuum pointed to the adverse effect of the presence of air in the die hindering its filling (Wu et al., 2003). It has been found that gravity fill of powder into a die cavity is primarily governed by three types of flow regimes: nose flow, bulk flow and intermittent flow (Mills and Sinka, 2013; Sinka et al., 2004; Wu et al., 2003; Wu and Cocks, 2004). As the feed shoe moves across the die cavity, the powder adopts a nose-shaped profile due to inertia and frictional interaction between the powder and the surface on which the shoe slides. The initial cascading of particles down the slope into the die cavity is termed as nose flow. Bulk flow occurs when powder detaches smoothly from the bottom of the powder bed into the die after the feed shoe has completely covered the die cavity. In cases where powder agglomerates detach by random into the die, the flow is termed as intermittent flow.

The die fill for shoe-die model studies is usually quantified by fill ratio and feed shoe critical velocity. Fill ratio refers to the ratio between the powder mass collected in the die after one pass of the feed shoe and the powder mass in a completely filled die (Mills and Sinka, 2013). It can also be the ratio between the volume of powder collected in the die to the die volume (Wu, 2008). A higher fill ratio would mean higher fill density inside the die. The concept of critical velocity (maximum feed shoe velocity that can fill the die cavity completely with a single pass) was also used by researchers as an indicator of powder flowability and die fill performance (Mills and Sinka, 2013; Sinka et al., 2004). High fill ratio and critical velocity indicate better die fill performance.

The shoe-die model was found to underestimate powder flow performance by half when up-scaling the data to a rotary tablet press (Schneider et al., 2007). The unaccounted suction fill effect present in rotary presses was identified subsequently through a modified shoe-die model with a movable lower punch that descended just as the feed shoe

* Corresponding author.
E-mail address: phalcv@nus.edu.sg (C.V. Liew).

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translated across the die cavity (Jackson et al., 2007). Suction fill created a negative pressure gradient and eliminated the effects of air entrainment encountered during gravity fill. Under these conditions, higher packing density and lower risk of segregation during die fill were achieved (Mills and Sinka, 2013).

Regardless of the type of fill regime, die filling is primarily affected by three factors: powder properties, die characteristics and feeding mechanism (Peeters et al., 2015; Xie and Puri, 2006). Under conditions of gravity fill, large and dense particles had higher die filling rates and critical velocities than fine particles as air expelled more easily from the die cavity through coarser particles (Mills and Sinka, 2013; Wu et al., 2003). Powder systems with wider particle size distributions also showed higher filling rates and critical velocities (Wu, 2008). The effect of die geometry on the die filling process has also been studied. Net die filling rate was slower in a stepped die compared to a simple die (Wu et al., 2003). Critical velocity was also found to increase with wider die diameter or shorter die height (Sinka et al., 2004). For dies with very small widths, gravity fill of powder occurred mainly via bulk flow due to insufficient time for nose flow to occur (Schneider et al., 2007).

Die filling on rotary presses is usually an active process with powder flowing from a stationary feed frame into moving dies on the rotating turret (Wu, 2008). The feed frame can contain up to three chambers in which coplanar paddle feeders rotate continuously to circulate the tablet feed and push it into the dies through a process known as forced feeding (Peeters et al., 2015; Wu, 2008). Variations of the feed frame design in terms of number, size and shapes of paddles are available depending on the tablet press model (Gopireddy et al., 2016). High paddle speed was associated with increased die fill weights and reduced die fill variation (Mendez et al., 2010). This was attributed to the higher frequency of paddle passes to push powder into the dies as paddle speed increased. On the other hand, Peeters et al. (2015, 2016) found that the effect of paddle speed on tablet weight was dependent on the powder flow properties. Paddle speed was only positively correlated with tablet weight for poor flowing powders due to the greater forced feeding effect and did not impact tablet weight variation. In contrast, simulations of die filling process on rotary tablet press found that paddle design had only impacted tablet weight variation but not tablet weight (Ketterhagen, 2015).

While various techniques have been used to assess powder flowability in relation to die fill, it is unclear if they are able to reliably predict die filling (Freeman and Fu, 2008; Monedero Perales et al., 1996; Yaginuma et al., 2007). Shoe-die models ranked powder flowability differently from standard flow measurement techniques such as angle of repose and bulk/tapped density measurements (Mills and Sinka, 2013). Furthermore, the interplay of gravity fill (flow of powder into die by gravity), suction fill (partial vacuum created by descent of lower punch at fill cam draws powder into die) and forced feeding (rotation of paddles in feed frame assist powder flow into die) in a rotary tablet press makes the study of the actual die filling process very challenging. The shoe-die model is possibly the closest at mimicking conditions on a rotary press albeit with limitations (Schneider et al., 2007). Ideally, a “die-filling” system should be able to reproduce the effects of gravity fill, suction and forced feeding, with the flexibility of different die configurations, paddle designs and feeder velocities. It is also unclear how powders with different flowability would respond to these effects. The purpose of this study was twofold, firstly, to design an apparatus capable of performing gravity fill, suction and forced feeding of powders for different die diameters and secondly, to examine the effects of paddle design, paddle velocity and suction on die fill of three representative powders using the designed system.

2. Materials and methods

2.1. Materials

Nonpareils (NP0; Suglets®, Colorcon®, USA) of 250–355 μm size fraction were used as a model coarse and free flowing powder. Directly compressible lactose (T100; Tablettose 100 M, Meggle, Germany) was used as a fine and fair flowing powder. Magnesium stearate (M125, Productos Metalast, Spain) was employed as the lubricant.

2.2. Preparation of lubricated lactose powder

Lubricated lactose powder (T100M) was prepared by blending T100 with 1%, w/w magnesium stearate in a double cone blender (AR401, Erweka, Germany) rotated at 15 rpm for 5 min. The total blended mass was 500 g. T100M was used as a powder with flow properties intermediate between that of NP0 and T100.

2.3. Characterisation of particle size

Particle size and size distribution of NP0 and T100 were determined by a laser diffractometer (LS230, Beckman Coulter, USA) with the dry powder module and a target obscuration level of about 10%. The vacuum source for the dry powder module was preset to draw air in at 2.83 L/min. A cumulative undersize curve was generated from which particle size parameters corresponding to the 10th, 50th and 90th percentiles (D_{10}, D_{50} and D_{90}) were determined. Span, an indicator of particle size distribution, was calculated using Eq. (1).

$$\text{Span} = \frac{D_{90} - D_{10}}{D_{50}} \tag{1}$$

2.4. Flow characterisation

2.4.1. Determination of angle of repose

Approximately 100 g of sample was passed through a funnel onto a circular base plate (Copley Scientific, United Kingdom) of diameter, 2r, so that it formed a conical heap. Height of the funnel was adjusted so that the orifice was about 2–4 cm away from the expected tip of the formed powder heap. Angle of repose (AoR) was calculated from the height, h, of the cone using Eq. (2). Measurements were triplicated and averaged results reported. Low AoR values are usually indicative of good powder flow.

$$\text{AoR} = \tan^{-1}\frac{h}{r} \tag{2}$$

2.4.2. Compressibility test

Powder samples were sifted through a 1 mm aperture size sieve into an exactly 100 mL graduated cylinder. After scraping away the excess powder carefully from the top of the cylinder and dusting off adhering powder, the cylinder was transferred onto a tapping machine (JEL STAV II, J. Engelsmann AG, Germany) and tapped at 250 drops/min until a constant tapped volume. Bulk (ρ_{bulk}) and tapped (ρ_{tapped}) densities were calculated using Eqs. (3) and (4), respectively.

$$\rho_{bulk} = \frac{\text{Sample mass}}{100\ \text{mL}} \tag{3}$$

$$\rho_{tapped} = \frac{\text{Sample mass}}{\text{Tapped volume}} \tag{4}$$

Hausner ratio (HR) was calculated using Eq. (5). The measurements were triplicated with fresh powders and the results averaged. Low HR values are usually associated with good powder flow properties.

$$\text{HR} = \frac{\rho_{tapped}}{\rho_{bulk}} \tag{5}$$

2.4.3. Shear cell test

A powder rheometer (FT 4, Freeman Technology, United Kingdom) fitted with the rotational shear cell accessory was used for shear cell