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# Simulation of powder flow in a lab-scale tablet press feed frame: Effects of design and operating parameters on measures of tablet quality

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ABSTRACT

The feed frame of a pharmaceutical tablet press is an important process component critical in defining both the total tablet mass and the amount of the active pharmaceutical ingredient (API) within the tablets. In addition to these quantities, the mechanical agitation of the feeder can cause attrition or over-lubrication of the powder blend or granulation flowing through the device. In order to better understand these effects, the discrete element method is used to model powder flow in a single paddle wheel feed frame of a laboratory-scale tablet press with varying particle, process, and equipment parameters. Results show that widely varying particle flow patterns and residence time distributions are achieved for varying paddle wheel shape, rotation direction, and rotation speed. Faster paddle wheel speeds generally lead to more uniform tablet masses whereas slower paddle wheel speeds perform less work on the particles (a surrogate for attrition) and move the particles a smaller distance (a surrogate for the extent of lubrication) in the feed frame before they enter a die and are compressed into a tablet. Finally, the effects of paddle wheel design and powder cohesion are also described.



## 1. Introduction

In the pharmaceutical industry, tablets are one of the most common dosage forms for delivery of therapeutic substances to patients. Due to this popularity, tablet presses and their component parts – such as the powder feed frames studied here – are ubiquitous throughout the industry. The feed frame or powder feeder plays an important role in the tablet manufacturing process as this is the last piece of equipment the powder flows through before it is compressed into a tablet, at which point the tablet mass and content (potency) become fixed.

Generally, there are specifications on the mean and range (or variability) of both the tablet mass and the mass of the active pharmaceutical ingredient (API) within the tablets. Thus, it is important to maintain consistent powder fill weights into the tablet dies and avoid any segregation of the powder blend in the process. In addition, the mechanical action of the feed frame may impact the powder blend in other ways including particle attrition or over-lubrication which could reduce tablet strength and slow dissolution. For these reasons, this work is devoted towards gaining a better understanding of powder flow in the tablet press feed frame for varying process conditions.

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### 1.1. Background

Despite the ubiquitous nature of feed frames and their potential effects on quality attributes of the final tablets, many aspects of powder flow in the feed frame are not yet well understood. In contrast, a large amount of work has been devoted to powder flow in other parts of tablet presses such as powder flow from the feed hopper (see, for example, [1–5]) or flow in transfer chutes [1,6,7], investigating flow rate, segregation, and equipment design considerations. Additionally, several groups have examined the die filling process [8–15] which governs the tablet mass and the overall flow rate through the feed frame. Finally, the compaction process where the powder is formed into the tablet has also been well studied (see, for example, [16–21]). Despite the significant work that has been completed to understand many aspects related to the tableting process, the feed frame has not been studied to such an extensive degree.

Until recently, there has been little attention given to the bulk powder flow within the feed frame. Mendez et al. [22] studied flow of blends consisting of varying levels of acetaminophen, lactose, and magnesium stearate in a Manesty Beta Press tablet press feed frame consisting of two paddle wheels and fitted with a clear lid to enable some visualization of the flow. In all cases, the mean die fill weight increased and the fill weight relative standard deviation (RSD) generally decreased with increased feed frame paddle wheel speed. They also observed the powder residence time decreased with increases in die size, die table rotation speed, and, to a small extent, feed frame paddle wheel speed. Finally, improvement in the flow properties of the powder and a decrease in fill weight RSD were observed for increasing numbers of paddle wheel blade passes.

Mendez et al. [23] further investigated the lubrication of powders in the feed frame and the subsequent effects on tablet hardness and dissolution. They observed a linear increase in powder hydrophobicity – used to quantify the extent of powder lubrication – with feed frame paddle wheel speed. Later, Mendez et al. [24] examined particle attrition and flow properties in the feed frames of a Manesty Beta Press and a Fette 3090 tablet press, which consists of three paddle wheels. In all cases, the particles showed attrition after passing through the feed frame with a relatively small dependence on the paddle wheel speed in the smaller Manesty Beta Press feed frame but a more significant effect in the larger Fette 3090. The importance of the paddle wheel speed was also demonstrated by Mateo-Ortiz et al. [25]; their DEM simulations revealed increased size-based particle segregation due to percolation at smaller rotation rates.

### 1.2. Particle attrition

Particle attrition has been studied in less complex geometrically systems, such as shear cells, to better understand the mechanisms by which attrition occurs. For instance, Potapov and Campbell [26] reported results from discrete element method (DEM) simulations of a two-dimensional shear cell containing composite, non-spherical particles. They demonstrated that the breakage of these particles could be related to the total amount of work done on the particles. However, experimental work has shown that particle attrition more closely followed similar, yet more complex relationships that typically cannot be generalized across differing systems [27,28]. More recently, Hare et al. [29], used a hybrid numerical and experimental approach to predict attrition of paracetamol in an agitated filter dryer. The discrete element method was used to model particle dynamics in the dryer and determine the distributions of stress and strain. Experiments in a shear cell were then carried out to relate particle attrition to varying stress and strain conditions. Finally, predictions of attrition were made based on the stress and strain present in the dryer. In the present work, although particle attrition is not modeled explicitly, the total work done on the particles is computed following Potapov and Campbell's [26] approach to qualitatively assess the potential extent of attrition. The total work done is useful to gauge how certain process parameters and equipment design alternatives may impact particle attrition for a given formulation. However the exact breakage rate is material specific and will depend on, for instance, the particle size distribution and the ultimate or yield strength of the particles or granules.

### 1.3. Powder lubrication

Lubrication of powder in the feed frame is another phenomenon that may affect the powder blend or granulation. Tablet formulations are typically lubricated by blending the powder with some lubricant such as magnesium stearate [30]. This lubrication process aids manufacturability by reducing die-wall friction, increasing the powder bulk density, and reducing powder adhesion to the metal components of the process equipment; however, if the formulation is susceptible to reaching a so called over-lubricated state, adverse effects on the final tablet characteristics such as reduced tensile strength as well as slower disintegration and dissolution times can be observed (see, for example, [30,31] and references therein).

Observations of these lubrication effects have been reported in the literature for many years [32,33] and have typically been attributed to so called over-mixing, or exposure of the powder to excessive shear strain. Only recently have these effects begun to be more systematically quantified using both formulation and process parameters. For example, Kushner and Moore [31] quantified tensile strength of compacts of various formulations after lubrication in bin blenders for varying process conditions. Based on this data, they developed a semi-empirical model where the tensile strength is predicted as a function of two formulation dependent parameters and the extent of lubrication generated in a bin blender, $K_{bb}$, given by

$$K_{bb} = V^{1/3} F_{headspace} r \quad (1)$$

where $V$ is the bin volume, $F_{headspace}$ is the fractional headspace in the bin, and $r$ is the number of bin revolutions. This model was subsequently extended by Blackwood et al. [34] to predict the extent of lubrication generated in a tablet press feed frame, $K_{ff}$, given by

$$K_{ff} = v_{tip} \tau \quad (2)$$

where $v_{tip}$ is the tip speed of the paddle wheel, and $\tau$ is the mean particle residence time in the feed frame which is assumed to be given by the ratio of the mass of powder in the feed frame to the mass throughput. In practice, the total extent of lubrication induced by the manufacturing process is given by the sum of $K_{bb}$ and $K_{ff}$, assuming there are no other unit operations causing additional lubrication. This sum can then be used to calculate the effect on quality attributes such as the tensile strength, as described by Kushner and Moore [31].

An extension of the approach proposed by Blackwood et al. [34] is used in the present work to enable characterization of the extent of lubrication using the discrete element method. The extent of lubrication given in Eq. (2) can readily be seen to approximate the mean distance a particle has traveled in the feed frame. In the present work, this approach is extended to track the distance each particle has traveled in the feed frame throughout the DEM simulation. This approach is used in lieu of directly modeling the lubrication process in the DEM simulations for two reasons. First, the very small size of the magnesium stearate particles requires a prohibitively large number of particles to be modeled and, second, the complexities of the deagglomeration and spreading of the magnesium stearate particles are not well represented by current DEM contact models.

Similar to the approach to assess attrition potential described in Section 1.2, the total distance traveled is useful to gauge how certain process and equipment decisions may impact the extent of lubrication for a given formulation. However the specific relation between the distance traveled by particles and the rate at which lubrication adversely affects blend properties such as tensile strength and dissolution are material specific (see parameters $\beta$ and $\gamma$ in Kushner and Moore [31]) and dependent on properties of the particular formulation, such as the specific surface areas of the lubricant and the non-lubricant (API and excipient) particles. Furthermore, lubrication effects are dependent on the quantity of lubricant in the formulation. Therefore, this approach is used only for comparison of the effects of process parameters and equipment design alternatives for a fixed formulation.

### 1.4. Objectives

The recent experimental work of Mendez et al. [22–24] has begun to shed light on the variety of effects feed frames have on powders during tableting operations and others, such as Blackwood et al. [34], have begun to quantify the extent of lubrication in the feed frame. There remain, however, a variety of unanswered questions that call for further work to develop a more complete picture of powder flow in feed frames. In the present work, a DEM model is developed for a lab-scale Korsch XL100 rotary tablet press feed frame with a single paddle wheel. The objective of this work is to better understand the effect of paddle wheel shape and rotation speed and direction on the powder flow patterns, residence time distributions, and die fill weight and the variability thereof. Additionally, measurements of the work done on the particles and the total distance traveled by the particles are proposed to give some indication of the level of particle attrition and the extent of lubrication, respectively. The underlying goal of the work is to virtually assess the real world impact of processing decisions made in the lab