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Investigations on the residence time distribution of a three-chamber feed frame with special focus on its geometric and parametric setups

M. Dülle [a], H. Özcoban [b], C.S. Leopold [a,*]

[a] Division of Pharmaceutical Technology, University of Hamburg, Bundesstraße 45, 20146 Hamburg, Germany,
[b] Fette Compacting GmbH, Grabauer Strasse 24, 21493 Schwarzenbek, Germany

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ABSTRACT

The feed frame is one of the key elements of a rotary tablet press. It ensures a uniform flow rate of powder from the funnel to the compression dies. An experimental study was conducted to investigate the residence time distribution of a three-chamber feed frame system (Fill-O-Matic). For this study, a Fette 102i rotary tablet press was used to simulate the conditions of the manufacture of tablets. The Fill-O-Matic consists of distributing, filling, and dosing chamber which together provide a large volume. For this reason, the influence of a geometric setup (filling cam and inner/outer scraper) and a parametric setup (die disc speed, feed frame speed, and filling depth) on the residence time distribution were determined with regard to the continuous manufacturing of tablets, an approach to optimize the configuration of the Fill-O-Matic. The results showed that the outer scraper has an influence on the residence time of the powder in the feed frame. An interesting output of the study was that an increase of the feed frame speed did not lead to an influence of the mean residence time. Instead, the intermixing of the powder, described as mean centered variances, increased by an increasing feed frame speed.

1. Introduction

Tablet manufacture is nowadays the most widespread method to formulate active pharmaceutical ingredients (API) into a user-friendly dosage form [1,2]. >60% of the APIs are sold in the form of tablets [3]. One of the advantages of this dosage form is its simple manufacture. Nowadays, tablets are often manufactured with rotary tablet presses. The pharmaceutical industry is one of the few industrial branches that still mainly produces in batches. An advantage of the tablet batch manufacture is the precise control of the different production steps. After each production step, a quality check is carried out with subsequent approval for the following production steps. If quality problems arise, it is possible to take countermeasures quickly and effective [5]. However, there are also disadvantages of batch manufacturing. Withdrawal periods between the production steps as well as downtimes of the machines lead to an increase of production costs [2,6]. Moreover, customers demand tight deadlines from the pharmaceutical manufacturing companies, as well as consistently high quality at all stages of manufacture, such as tablet production [3]. To reduce the costs, some of the raw materials are imported from low-wage countries [7]. A further approach of cost reduction is to switch from batch manufacture to continuous manufacture. During continuous manufacture, the excipients and APIs are transferred directly and continuously to the next production step for further processing right through to final product [2]. Schaber et al. published an analysis of integrated continuous manufacturing in which he concluded that the `continuous manufacturing of pharmaceuticals is a viable way for the pharmaceutical industry to achieve substantial cost savings´ [8]. Further advantages of the continuous manufacture are a high utilization of the pharmaceutical equipment without long downtimes, automation requirements, and low storage capacities [7]. For this reason, extensive research is currently being conducted on continuous manufacturing to replace the traditional batch manufacture of pharmaceutical products. Despite the higher initial cost and the lower flexibility of the continuous manufacture, conversion from the batch to the continuous manufacture will occur in the future. Further industrial branches have already largely converted there production to the continuous manufacture. Examples from the chemical industry are catalysts manufacture [9], mineral processing [10], and also the food industry has switched to continuous manufacture [11,12]. The use of continuous manufacture in the pharmaceutical industry is still limited [13]. In addition, costs can also be reduced by more efficient machines, which increase the tablet production rate. Modern rotary tablet presses are able to produce tablets with a quantity of over 1.6 million tablets per hour [14]. It is important for the continuous production to have a well-balanced interplay between the individual components. Each production step of the manufacturing chain is interdependent.

The manufacture of tablets consists of several steps [16]: The powder flow through the hopper to the feed frame [17,18], the powder

* Corresponding author.
E-mail addresses: matthias.duelle@chemie.uni-hamburg.de (M. Dülle), hoezcoban@fette-compacting.com (H. Özcoban), claudia.leopold@uni-hamburg.de (C.S. Leopold).

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flow through the chambers of the feed frame [1,19], the filling of the dies [20,21], and the compaction of the powder. Previous studies showed that many processes in the feed frame could not be analyzed because of their complexity. To completely replace the batch manufacture to the continuous manufacture, it is important to understand the influence of varies parametric and geometric setups on the powder flow through the feed frame. A method to investigate the influence of these setups on powder flow is the residence time distribution. The residence time distribution describes how a filling material moves inside the operation unit of a continuous system. Each individual particle behaves differently in the feed frame, taking different paths through the system which requires in different periods of time. The distribution of these time periods is called the residence time distribution [22].

The residence time distribution has already been applied in the chemical and food industry to develop models, characterize mixing effects and design new equipment [23]. Lately the residence time distribution has also been introduced in the pharmaceutical industry. Efforts have been made to use residence time distribution for description of processes involving solid materials such as powder blending [24], powder extrusion [25], fluid bed granulation [26], twin screw granulation [27]. Also, the feed frame has been subject of research with regard to the residence time distribution. Mateo-Ortiz et al. described the relationship between residence time distribution and the force applied by the paddle wheel [23] and computationally simulated the powder movement in the feed frame by means of discrete element method [19]. Considering the different geometries of the feed frame, there is a wide variety of possible setups which resulting in numerous influencing factors on the residence time. For the further development of feed frames it is important to understand the relationships between the tableting setups and the resulting residence time of the powder, to ensure a high tablet quality. Potapov et al. simulated the particle attrition of a two dimensional shear cell containing composite, non-spherical particles by discrete element method [28]. It has been shown that the attrition is directly related to the overall shear stress in the system. A further quality loss of the particles may result from powder overlubrication. The lubricants present in the tableting mixture reduce the friction between the metal components of the feed frame and the powder particle. A too high concentration of lubricant as well as an increased of shear stress on the lubricant lead to an overlubricated state, which has a negative influence on the tablet quality [29,30]. For these reasons, it is important to optimize the tableting setup to reduce the residence time and to minimize the applied shear stress on the powder in the feed frame. Engisch et al. defined the continuous manufacture as a series of single batches with an interface region [5]. This interface region describes the intermixing effect between the batches.

Fette compacting has equip their rotary tablet presses with a three-chamber feed frame (Fill-O-Matic). The Fill-O-Matic ensures an accurate powder flow from the hopper to the dies. Because of the three chambers the Fill-O-Matic has a large volume, resulting in a high robustness against disturbances such as a brief stop of the powder flow from the hopper to the feed frame. Regarding the continuous manufacture, a large volume of the feed frame might also have negative consequences. Therefore, the aim of this study was to offer a more comprehensive knowledge of the powder behavior in the Fill-O-Matic and to analyze influences of various parameters such as the die disc speed and feed frame speed. Moreover, various configurations of the powder scrapers and the filling cam were investigated with regard to the residence time distribution. In view of the current trend towards the implementation of continuous manufacturing in the pharmaceutical industry, it is of particular importance to know the influence of the operating conditions and system geometry on the residence time distribution. For this reason, the experiments were carried out on a fully mounted rotary tablet press. Furthermore, this paper focuses on microcrystalline cellulose, which is a widely used pharmaceutical filling material for tablets. The obtained results are important for the scaling up and optimization of the corresponding tablet manufacture equipment. With this knowledge of the powder behavior, it is possible to reduce the residence time and to minimize the powder shear stress in the feed frame and to increase the quality of the resulting tablets.

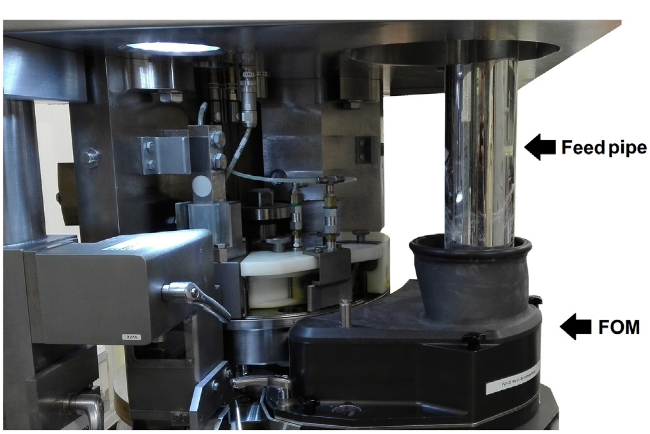

Fig. 1. Fette 102i tablet press mounted with a feed pipe and a Fill-O-Matic.

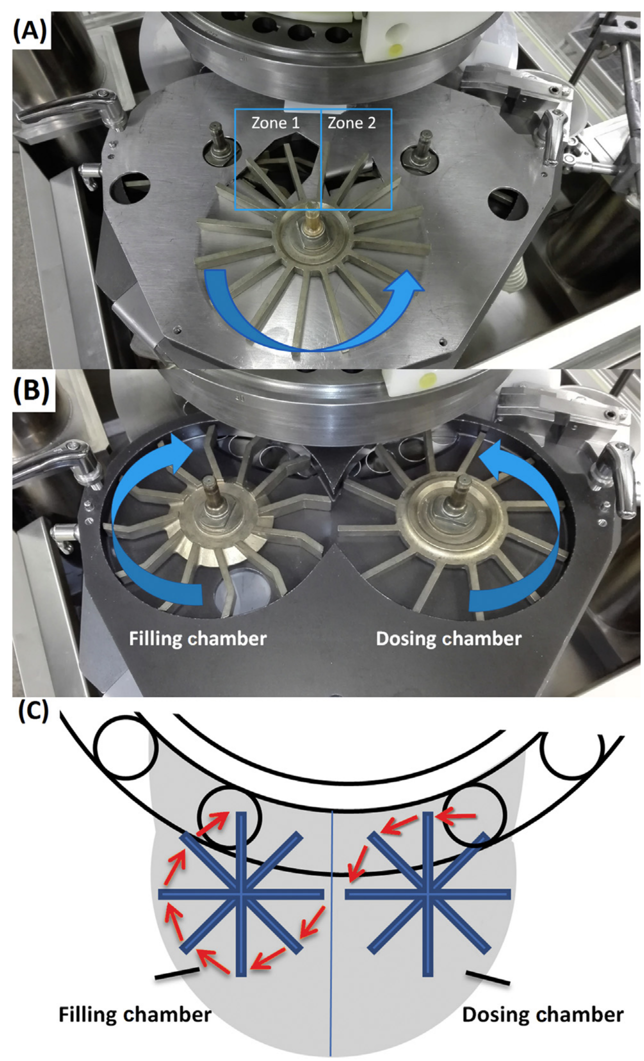

Fig. 2. (A) Distributing chamber with two exit zones to the filling chamber (Zone 1) and the dosing chamber (Zone 2); (B) Filling chamber (left) and dosing chamber (right); (C) path of dosing powder. Arrows depict the movement of the powder from the dosing chamber to the filling chamber.