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Note

Influence of scale-up on the abrasion of tablets in a pan coater

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Abstract

The purpose of this study was to examine the influence of batch size during scale-up on the abrasion and edge splitting of flat faced lactose tablets. The weight loss of white tracer tablets in a batch of blue coated tablets was investigated in a laboratory scale pan coater and a pilot scale pan coater as a function of different pan speeds and mixing times. It was observed that increasing batch size resulted in a decreased weight loss due to less edge damaging. The higher number of tablet impacts at the pan wall in the laboratory scale compared to the pilot scale might be the reason for this phenomenon. The common assertion that an increase in batch size in scale-up leads to a higher abrasion or tablet damaging was not supported in the current study.

Keywords: Scale-up; Film coating; Abrasion; Pan speed; Bohle Film Coater

1. Introduction

The film coating process in a pan coater can be divided into different operations steps. First the cores are warmed up. During this step the tablet cores are mixed gently in order to avoid abrasion and edge splitting. After a defined time and/or a defined bed temperature the spraying process starts. Due to the higher pan speed in the spraying process, the cores can erode or the edges are damaged, which can cause problems during the film coating process. Furthermore, ignoring the tablets weight loss due to abrasion will affect the calculation for the coating efficiency (based on weighing) and, consequently, the true results. In scale-up, the tablet bed depth is higher for larger coating pans.

An increase in friction and friability of tablets with increasing batch size in scale-up was reported [1,2]. Pondell [3] reported higher exerted forces with increasing pan size. The related effects cannot be predicted in work with a small-scale pan. However, there is a lack of experimental data and approaches to comprehend the acting strains on the tablets in scale-up.

The aim of this work was to investigate and to quantify the effect of batch size in the scale-up from the laboratory scale to the pilot scale on the abrasion and damaging of tablets. The influence of different mixing times up to 10 min and different pan speeds on the abrasion of tablets was investigated in the two scales. For the laboratory scale a Bohle Film Coater 5 (BFC 5) and for the pilot scale a BFC 40 were used.

2. Materials and methods

2.1. Tablets and tracer tablets

Flat faced lactose tablets (tracer tablets) were used to simulate damageable cores. The composition of the white tracer tablets was lactose monohydrate 99.5% and magnesium stearate 0.5%. The weight of the tracer tablets was approximately 368 mg. The bulk density of the tracer tablets was 696 kg/m^3. The tracer tablets had a diameter of 10.1 mm, a height of 3.6 mm, a crushing strength (Ph. Eur. 5) of 70.9 N (±6.0 N) and a friability (Ph.Eur. 5) of 0.32% (±0.01%). For each trial 30 tracer tablets were placed into a tablet bed of blue coated biconvex tablets.

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The tablets were coated with a polyvinylacetate film (Kollicoat SR 30D, BASF, Germany). The coated tablets had a diameter of 9.2 mm, a height of 3.7 mm, a tablet mass of approximately 290 mg, a bulk density ρ of 791 kg/m^3 and a crushing strength of 157 N (±5.3 N). The coated tablets showed no detectable abrasion in a conventional friability tester.

2.2. Determination of the abrasion in two different coater sizes

The tablets abrasion was investigated in two different coater sizes. For the laboratory scale a BFC 5 with a pan diameter d_{pan} of 316 mm and length l_{pan} of 356 mm and for the pilot scale a BFC 40 with a pan diameter of 660 mm and length of 743 mm were used. Fig. 1 shows a schematic depiction of a BFC.

The BFCs are equipped with integrated transport ribbons on the bottom of the pan and reverse running mixing ribbons.

Thirty tracer tablets were exactly weighted w_b and put into the bed of the blue coated tablets. After a defined mixing time (see Section 2.4) all white tracer tablets were carefully manually removed, dusted off and weighed back w_a. The abrasion A was calculated according to Eq. (1). For every trial 30 new tracer tablets were used.

$$A\ [\%] = \left(1 - \frac{w_a}{w_b}\right) \cdot 100 \tag{1}$$

w_b = weight of 30 tablets before mixing, w_a = weight of 30 tablets after mixing.

2.3. Scale-up of the pan speed and batch size

The tablets abrasion in the BFC 5 was investigated with three different pan speeds n_{pan} 10, 18 and 25 rpm. The use of same peripheral speeds in the laboratory coater and the production coater is a common approach for scaling up the pan speed [4–6] (Table 1). The peripheral speed v was calculated as follows:

Table 1
Calculated peripheral speed

BFC 5 (rpm)	BFC 40 (rpm)	Peripheral speed (m/s)
10	4.8	0.165
18	8.6	0.298
25	12.0	0.414

$$v = \pi \cdot d_{pan} \cdot n_{pan} \tag{2}$$

The batch size for the trials in BFC 5 was 4.5 L. The measured tablet bed depth in the BFC 5 was approximately 5.2 cm. The batch size for the BFC 40 was calculated based on a constant filling degree φ (Eq. (3)) of the pan. The volume of the cylindrical part of the pan was calculated from the diameter and the length of the pan.

$$\varphi = \frac{m_{batch}}{\frac{\pi}{4} \cdot d_{pan}^2 \cdot l_{pan} \cdot \rho_{tablets}} \tag{3}$$

The value of the filling degree in the BFC 5 was calculated to be 0.161. The batch size of the BFC 40 for the same filling degree was calculated as 32.40 kg. The tablet bed depth in BFC 40 was approximately 12 cm.

2.4. Experimental design

The influence of the mixing time and pan speed on the abrasion of the tracer tablets was investigated. For this study a full factorial design on three levels with two additional repetitions of every trial and ($n_{total} = 27$) runs was used for the BFC 5. Table 2 shows the levels for the experimental design in the BFC 5.

Table 2
Variables for the trials in BFC 5

Variable/level	−1	0	1
Mixing time [s]	60	330	600
Pan speed [rpm]	10	18	25

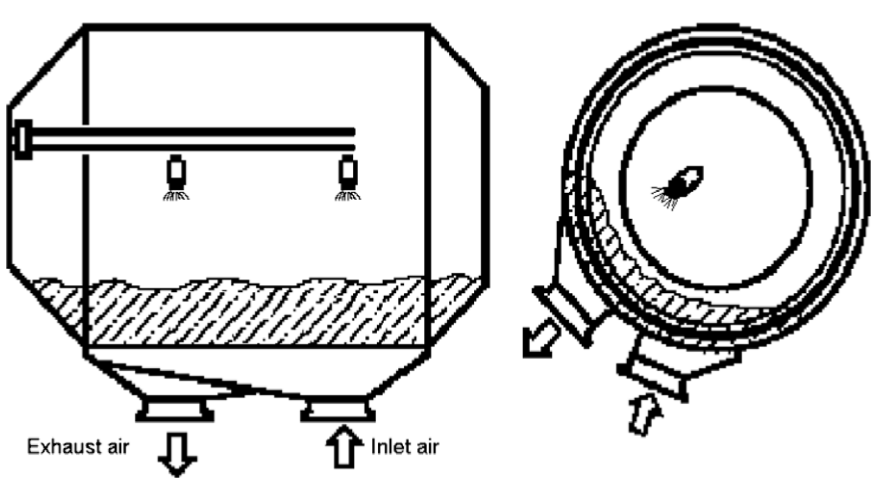

Fig. 1. Schematic diagram of Bohle Film Coater.

For the BFC 40 only two mixing times 330 and 600 s and three pan speeds 4.8, 8.6 and 12.0 rpm were investigated. Every trial was repeated two times ($n_{total} = 18$). The calculated peripheral speeds according to Eq. (2) are listed in Table 1.

The results were evaluated with Excel program and Modde 7, Umetrics. The response variable was the abrasion A (%). The regression model for the two independent variables (time, speed) can be presented in a general formula (Eq. (4)):

$$Y = \beta_0 + \beta_1 \text{time} + \beta_2 \text{speed} + \beta_3 \text{time} \cdot \text{speed} + \beta_4 \text{time}^2 + \beta_5 \text{speed}^2 \quad (4)$$

where $\beta_1, \ldots, \beta_5$ are the regression coefficients and β_0 is the regression constant. When the equation is presented with coded values, the magnitude of the coefficient specifies the change in response variable if the variable is altered from the lower level to zero or from zero to the upper level and the sign indicates the direction of the change. A coefficient plot is used for the graphical illustration of the results. The scaled and centred coefficients for the response variables are depicted in a coefficient plot.

3. Results and discussion

3.1. Effect of mixing time and pan speed in BFC 5

The mixing times were only investigated up to 10 min, because this time is critical at the beginning of the spraying process. All tablets should have a thin film after 10 min, which protects the cores from further abrasion. Fig. 2 shows the abrasion of the flat faced lactose tablets depending on mixing time and pan speed. The coefficient plot for the design of experiments is shown in Fig. 3.

As expected, the abrasion increased with increasing mixing time and pan speed. Mainly edge deterioration was observed. Also, a quadratic effect of the mixing time and an interaction between the mixing time and the pan speed was observed. With increasing mixing time the increase in abrasion was lower as indicated by the negative sign of the quadratic effect of the mixing time (Fig. 3, see also Fig. 2).

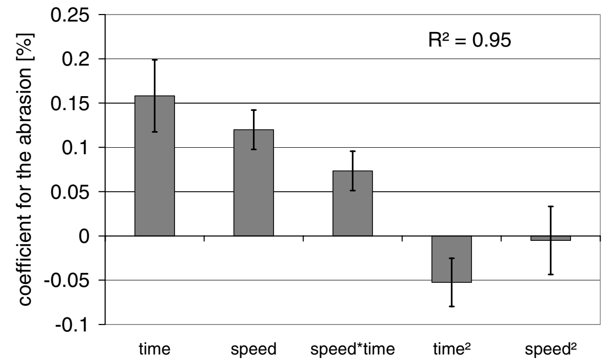

Fig. 3. Coefficient plot for the abrasion in BFC 5 (confidence level 95%).

3.2. Effect of mixing time and pan speed on the BFC 40

The results of the 18 trials in the BFC 40 are shown as stripped bars in Fig. 4. Increasing pan speed and mixing time in BFC 40 led in turn to an increase in the tablets abrasion. The comparison of the absolute abrasion of the tablets for 330 and 600 s showed that the abrasion in the BFC 40 was significantly lower ($p < 0.01$) than BFC 5.

The result was unexpected since the opposite behavior is reported in the literature. A plausible explanation for this fact could be provided by considering the tablets movement in the pan. A number of publications deal with the tablet motion in rotating drums [7–10]. Fig. 5 shows a simplified depiction of a flowing tablet bed in a pan coater.

When a tablet reaches point 1 in Fig. 5a, the tablet moves to point 2 on the surface of the tablet bed. The moving tablet impacts at the wall of the coating pan at point 2. For constant process time and equivalent peripheral speed the tracer tablets in the BFC 5 impact more frequently the pan at point 2. The chosen flat faced tracer tablets for this study were very sensitive to such impact. Consequently, the weight loss of the tablets in the BFC 5 was higher compared to the BFC 40 due to the higher number of tablet impacts at the pan wall.

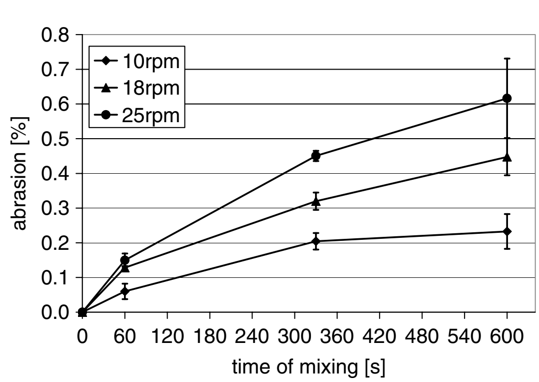

Fig. 2. Abrasion of flat faced tablets in BFC 5 ($n = 3$; av ± sd).

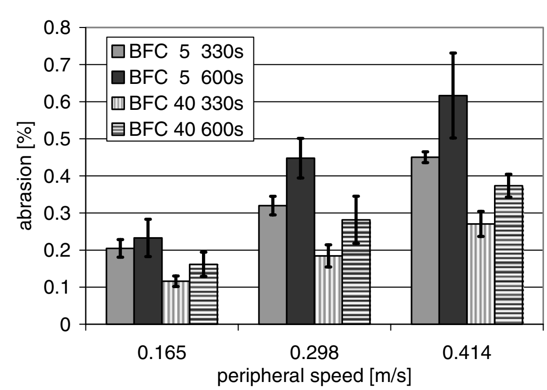

Fig. 4. Comparison of the tablet abrasion in BFC 5 and BFC 40 ($n = 3$, av ± sd).

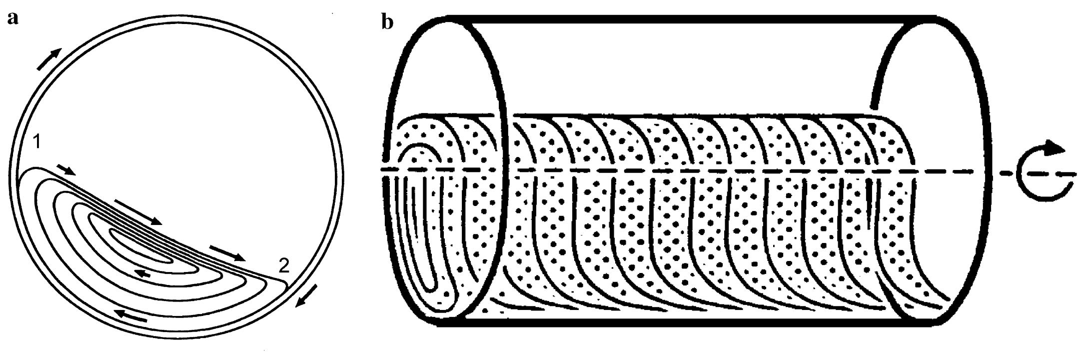

Fig. 5. Schematic motion of tablets in a pan coater.

3.3. Calculation of the number of tablet impacts at the pan wall

According to the statistical calculation of the number of passes through the spray zone [4], the number of impacts at the bottom of the pan could be calculated in the same way. Provided that each tablet on the surface of the tablet bed impact at the bottom of the pan, the impact area per time was calculated as the product of the pan length and the peripheral speed v according to Eqs. (2) and (5).

$$A_{\text{impact}}^{\text{min}}\left[\frac{\text{m}^2}{\text{min}}\right] = v \cdot l_{\text{pan}} \tag{5}$$

The number of tablets that impact per minute at the bottom of the pan $n_{\text{tabl.impact}}^{\text{min}}$ could be calculated by dividing this area through the impact area $A_{\text{tabl.impact}}$ of one tablet. The impact area of one tablet had not to be specified, because in both scales the same tablets were used.

$$n_{\text{tabl.impact}}^{\text{min}}\left[\text{min}^{-1}\right] = \frac{A_{\text{impact}}^{\text{min}}}{A_{\text{tabl.impact}}} \tag{6}$$

From the number of tablets that impact per minute at the bottom of the pan, the total number of tablets per batch $n_{\text{tabl.tot}}$ and the run time t_{process} the total number of impacts per tablet at the bottom of the pan $n_{\text{impact.tot}}$ could be determined for each scale.

$$n_{\text{impact.tot}_{\text{BFC}}} = \frac{t_{\text{process}} \cdot n_{\text{tabl.impact}_{\text{BFC}}}^{\text{min}}}{n_{\text{tabl.tot}_{\text{BFC}}}} \tag{7}$$

The ratio of tablet impacts in BFC 5 and BFC 40 could be calculated as follows:

$$\frac{n_{\text{impact.tot}_{\text{BFC5}}}}{n_{\text{impact.tot}_{\text{BFC40}}}} = \frac{\frac{t_{\text{process}} \cdot n_{\text{tabl.impact}_{\text{BFC5}}}^{\text{min}}}{n_{\text{tabl.tot}_{\text{BFC5}}}}}{\frac{t_{\text{process}} \cdot n_{\text{tabl.impact}_{\text{BFC40}}}^{\text{min}}}{n_{\text{tabl.tot}_{\text{BFC40}}}}} \tag{8}$$

For a constant process time in both scales Eq. (8) could be written as:

$$\frac{n_{\text{impact.tot}_{\text{BFC5}}}}{n_{\text{impact.tot}_{\text{BFC40}}}} = \frac{n_{\text{tabl.impact}_{\text{BFC5}}}^{\text{min}}}{n_{\text{tabl.tot}_{\text{BFC5}}}} \times \frac{n_{\text{tabl.tot}_{\text{BFC40}}}}{n_{\text{tabl.impact}_{\text{BFC40}}}^{\text{min}}} \tag{9}$$

With a constant filling degree φ according to Eq. (10)

$$\frac{m_{\text{batch}_{\text{BFC5}}}}{\frac{\pi}{4} \cdot d_{\text{pan}_{\text{BFC5}}}^2 \cdot l_{\text{pan}_{\text{BFC5}}} \cdot \rho_{\text{tablets}}} = \varphi = \frac{m_{\text{batch}_{\text{BFC40}}}}{\frac{\pi}{4} \cdot d_{\text{pan}_{\text{BFC40}}}^2 \cdot l_{\text{pan}_{\text{BFC40}}} \cdot \rho_{\text{tablets}}} \tag{10}$$

$$m_{\text{batch}} = n_{\text{tabl.tot}} \cdot m_{\text{tabl}} \tag{11}$$

By substituting Eq. (11) in Eq. (10) the total number of tablets in BFC 40 was calculated by Eq. (12).

$$n_{\text{tabl.tot}_{\text{BFC40}}} = \frac{n_{\text{tabl.tot}_{\text{BFC5}}} \cdot d_{\text{pan}_{\text{BFC40}}}^2 \cdot l_{\text{pan}_{\text{BFC40}}}}{d_{\text{pan}_{\text{BFC5}}}^2 \cdot l_{\text{pan}_{\text{BFC5}}}} \tag{12}$$

If filling degree, bulk density, tablet mass, impact area of one tablet and process time were the same in BFC 5 and BFC 40 the ratio of the number of impacts for the BFC 5 and BFC 40 could be calculated by putting Eqs. (5), (6) and (12) into Eq. (9) as follows:

$$\frac{n_{\text{impact.tot}_{\text{BFC5}}}}{n_{\text{impact.tot}_{\text{BFC40}}}} = \frac{d_{\text{pan}_{\text{BFC40}}}^2}{d_{\text{pan}_{\text{BFC5}}}^2} \tag{13}$$

Thus, the ratio of the number of impacts was calculated by the ratio of the square diameter of the BFC 40 and BFC 5. The calculated ratio was 4.36. The tablets impacted statistically 4.36 times more to the bottom of the pan in the BFC 5 than in the BFC 40. Since the tracer tablets were sensitive to impact, the strain on the tablets in the laboratory scale was higher than the pilot scale.

4. Conclusion

For the investigated tracer tablets, an increase in batch size from the laboratory scale to the pilot scale did not result in a higher abrasion or tablet damaging. For same peripheral speeds and mixing times a decrease in abrasion and edge splitting in the pilot scale compared to the laboratory scale could be observed. The higher number of tablet impacts at the pan wall in the laboratory scale compared to the pilot scale might be the reason for this phenomenon. Further work is required to study the abrasion in the production scale and to further explore the influence of tablet hardness.

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