Comparison of the Performance of Single Punch and Rotary Tablet Presses from Different Vendors

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Abstract
As tablets are the most common dosage form for drug delivery, many different rotary presses are available on the market in order to produce tablets with a high throughput. Single punch presses are used for pharmaceutical development or to simulate the compaction process using small material quantities. In this study, 5 different rotary presses and 4 single punch presses were utilized using 3 different model formulations. Tablet masses and tensile strengths were investigated as a function of compaction force and process time. The corresponding force-time profiles were analyzed as well. In general, significant differences between the presses were observed even if the deviations were rather small from a practical point of view. The lowest variations of tablet properties were found using the plastically deforming formulation, while the elastic formulation was more challenging. High throughput with comparable high tablet tensile strength can be achieved by the brittle formulation. By analyzing representative force-time diagrams it was found that dwell times varied considerably between the different machines.

Introduction
Tablets are solid single unit dosage forms made from dry powder blends or granules using high compression forces [1]. They are the most common drug delivery systems today: According to the International Association for Pharmaceutical Technology (APV) about 80% of the produced dosage forms are solid [2]. Tablets offer a number of advantages: They have a high level of patient compliance. In addition, tablets are typically of excellent dosing accuracy, easy to pack, to store, and to transport [3]. A high production rate is realized on rotary presses, where the maximum output of a single tablet machine may be up to 1.6 million tablets/h [2].

The practical environment for the experiments was a workshop. Suppliers of 5 rotary presses and 3 single punch devices were invited to present their machines. To ensure comparability, all machine suppliers used the same materials, as far as possible the same type of punches and performed the same trials during the workshop. Due to different die types tablet throughput could vary even though the rotary tablet presses have a similar pitch circle diameter. The compressed tablets were analyzed regarding their mass, dimensions and breaking force immediately after the experiments.

The following rotary presses were involved in this study: “TPR 500” (Bosch, Gerlingen, Germany), “102i” (Fette Compacting, Schwarzenbek, Germany), “PREXIMA 300” (IMA Pharma, Ozzano dell’Emilia, Italy), “KTP 420X” (Romaco Kilian, Köln, Germany) and “XL 400 MFP” (Korsch, Berlin, Germany). The “TPR 500” provided by Bosch was the rotary press with the largest pitch circle diameter and the highest number of press stations resulting in the machine with the highest nominal throughput of more than 400 000 tablets/h (table 1). For rotary tablet...
presses the pitch circle diameter directly correlates with dwell time. The pitch circle diameter of Fette’s “102i” was the smallest one (280 mm) which thus accompanies smaller dwell times of this galenic machine compared to high performance production machines with larger turrets. In order to support a realistic galenic trial scenario, where a high accuracy of the measurements is of high importance, 4 punches were removed and the related dies were blinded in order to avoid potential inaccuracy of punch force measurements by signals from neighboring punches during recording of typical force-time diagrams. The maximum output of IMA’s “PREXIMA 300” was 237 600 tablets/h with 33 press stations. The rotary presses of Kilian and Korsch featured almost the same pitch circle diameter. The maximum output of the Kilian press was 324 000 tablets/h and of the Korsch press 252 000 tablets/h due to a different number of press stations. In addition to the rotary presses, 3 single punch presses were considered in this study: “Series D” (Gamlen Instruments, London, United Kingdom), “Styl’One Evolution” (Medelpharm, Beynost, France) and ”FlexiTab XL” (Röltgen, Solingen, Germany). When using the “Series D”, the tableting material had to be weighed manually. However, it was the smallest and cheapest device in this study. The “Styl’One Evolution” mimicked the “KTP 420X” by Kilian and was operated with a gravity feeder. The dwell time can be chosen from several seconds to 2 ms (~ rotary press of 400 000 tablets/h). Röltgen’s “FlexiTab XL” is a hydraulic press and offers a high flexibility. In addition, the “EK 0” (Korsch, Berlin, Germany) was used for preliminary tests when designing the study. This type has been widely used in tablet development for many years and served as a reference in this study.

The aim of this study was to compare the performance of different tablet presses based on tablet properties (mass and tensile strength or breaking force). Therefore, 3 different model formulations were chosen in order to challenge the machines.

Powder compression can be attributed to 3 different mechanisms: plastic and elastic deformation and brittle fracture [2]. The first formulation mainly consists of lactose monohydrate and microcrystalline cellulose (table 2). Microcrystalline cellulose is considered to be a plastically deforming material [4;5]. The second formulation contains microcrystalline cellulose and starch. Starch is used as a pharmaceutical excipient with predominantly elastic deformation characteristics [6;7]. The third formulation is composed of dicalcium phosphate anhydrate, which is known for its brittleness [7;8]. In all formulations magnesium stearate was used as a

Table 1

<table>
<thead>
<tr>
<th>Manufacture</th>
<th>Press type</th>
<th>Number of press stations</th>
<th>Pitch circle diameter</th>
<th>Pre-main compaction force (max.)</th>
<th>Output (max.)</th>
<th>Punch diameter</th>
<th>Punch curvature radius</th>
<th>Punch/die type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosch TPR 500</td>
<td>56</td>
<td>470</td>
<td>100/100</td>
<td>406 000</td>
<td>8</td>
<td>12</td>
<td>XDF/BBS</td>
<td></td>
</tr>
<tr>
<td>Fette 102i</td>
<td>30*</td>
<td>280</td>
<td>80/80</td>
<td>216 000</td>
<td>8</td>
<td>12</td>
<td>FS19/BB</td>
<td></td>
</tr>
<tr>
<td>IMA PREXIMA 300</td>
<td>33</td>
<td>380</td>
<td>100/100</td>
<td>237 600</td>
<td>8</td>
<td>10</td>
<td>B/B</td>
<td></td>
</tr>
<tr>
<td>Kilian KTP 420X</td>
<td>45</td>
<td>416</td>
<td>100/100</td>
<td>324 000</td>
<td>8</td>
<td>12</td>
<td>B/BB</td>
<td></td>
</tr>
<tr>
<td>Korsch XL 400 MFP</td>
<td>35</td>
<td>410</td>
<td>100/100</td>
<td>252 000</td>
<td>8</td>
<td>12</td>
<td>B/B</td>
<td></td>
</tr>
<tr>
<td>Gamlen Series D</td>
<td>1</td>
<td>–</td>
<td>–/5</td>
<td>–</td>
<td>5</td>
<td>Flat</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Korsch EK 0</td>
<td>1</td>
<td>–</td>
<td>–/30</td>
<td>3 600</td>
<td>8</td>
<td>12</td>
<td>B/B</td>
<td></td>
</tr>
<tr>
<td>Medelpharm Styl’One Evolution</td>
<td>1</td>
<td>–</td>
<td>50/50</td>
<td>1 650</td>
<td>8</td>
<td>12</td>
<td>B/BB</td>
<td></td>
</tr>
<tr>
<td>Röltgen FlexiTab XL</td>
<td>1</td>
<td>–</td>
<td>–/100</td>
<td>900</td>
<td>8</td>
<td>12</td>
<td>B/B</td>
<td></td>
</tr>
</tbody>
</table>

*4 punches were removed to simulate single-punch mode. The used number of punches is 26.
lubricant. These 3 model formulations were chosen due to their widely different compression and compaction behaviors in order to evaluate the performance of the machines.

Materials and Methods

Materials
All materials were used as received. The materials used in this study included colloidal silicon dioxide (AEROSIL® 200, Evonik, Parsippany, USA), dicalcium phosphate anhydride (DI-CAFOS® A150, Chemische Fabrik Budenheim, Budenheim, Germany), microcrystalline cellulose (EMCOCEL® 90M, JRS, Rosenberg, Germany), starch (Starch 1500®, Colorcon, Dartford, United Kingdom), lactose monohydrate (Tablettose® 80, Meggle, Wasserburg, Germany) and microcrystalline cellulose (VIVAPUR® 102, JRS, Rosenberg, Germany). Magnesium stearate (LIGAMED®, Peter Greven, Venlo, Netherlands) was used as a lubricant. All substances were donations of the material suppliers.

Formulation preparation
The 3 formulations were prepared in a drum mixer (BM 125S, ATIKA, Burgau, Germany) in batches of 30 kg each. The powder mixtures were blended at 28 rpm for 15 min. Afterwards, magnesium stearate was added and the blends were mixed for another 3 min. The formulations were stored in sealed tin-plate containers.

Tableting on rotary and single punch presses
For each formulation 2 different studies were performed. The first test series was a compression study. Convex-faced tablets with a target mass of 250 mg and a diameter of 8 mm were compressed at four different compaction stresses (50, 100, 200, 400 MPa) with an output of 100 000 tablets/h for the rotary presses (table 3). Sampling was done after 15 min. of equilibration at each applied level of compaction stress. Tablet masses and tensile strengths (n = 20) were determined. Representative force-time profiles for each compaction stress level were recorded by the respective built-in data acquisition systems. The single punch presses were run under comparable conditions. However, dwell time at Korsch’s “EK 0” and the single punch device of Gamlen could not be adjusted. Furthermore, Gamlen produced flat tablets with a diameter of 5 mm and a mass of 55–60 mg.

In the second test series, a stability study was performed at high production rates. Therefore, the tablet properties were investigated with respect to the process time for all rotary tablet presses. Targets for all tablets were a mass of 250 mg and a breaking force of 100 N. The process conditions were chosen according to the machine suppliers’ recommendations (table 4). Samples were taken after 25 000, 50 000, 75 000 and 100 000 compressed tablets and tablet masses and breaking forces (n = 20) were determined. The single punch presses were not included in the stability study, since these machines are not intended to be used for long term production.

Tablet characterization
All samples were collected and analyzed directly after they were taken. Mass, diameter, thickness and breaking force of 20 tablets were tested by a semi-automatic tablet testing system (ST50, Sotax, Aesch, Switzerland). The tensile-strength of the tablets was calculated using the US-Pharmacopeia (USP)-equation for convex-faced (1) [9; 10] or for flat-faced tablets (2) [11].

\[
\sigma = \frac{10F}{\pi DH} - \frac{2.44}{D} \left( \frac{D}{2} - \frac{h}{2} \right) \left( \frac{W}{D} + 0.01 \right)^{-1}
\]

or

\[
\sigma = \frac{2F}{\pi DH}
\]

The parameter F describes the tablet breaking force, D, H and W represent the tablet diameter, the tablet thickness and the central cylinder thickness, respectively.

Results and discussion

Compression Study
In a first series of experiments the different presses were tested using the 3 formulations at varying compaction stress. These experiments were done at a throughput of 100 000 tablets/h for the rotary presses. If possible, dwell time of the single punch presses was adjusted accordingly (see Materials and Methods). Tablet mass correlates with the drug content in homogeneous blends. Therefore, it is a highly relevant processing parameter. The uniformity of mass was tested for all
formulations for all presses and in all cases the requirements of the European Pharmacopeia (Reference 2.9.5: Uniformity of mass of single-dose preparations) were met [12]. The scaling of the mass axes in fig. 1 is over-discriminative in order to visualize the differences. The “EK 0” shows the largest deviations of tablet mass from the set value (250 mg). This fact may be attributed to the filling principle using an oscillating hopper, which causes densification of the powder in the feeder over time based on the motion. This observation was made using the plastic formulation and was compensated in the later experiments by adjusting the mass for each stress level for the elastic and brittle formulation separately. Additionally, mass variations are listed as mean values of the coefficients of variation in table 5. Almost all tablet mass deviations were below 1% of the average tablet mass which is excellent and far below the requirements of the European pharmacopoeia of 5% (Reference 2.9.5) [12]. It should be kept in mind that 4 punches had been removed from the Fette machine for a more accurate determination of the force-time profiles, which is assumed to be the reason for the slightly higher mass variation for the elastic formulation due to its poor flowability.

The radial tensile strength of tablets describes the breaking force normalized on the tablet size. It is a relevant parameter in terms of handling and further processing and is typically highly correlated to the compaction stress. In general, higher compaction stresses led to higher

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**Table 3**

Compression study: Process conditions for the plastic, elastic, and brittle formulation, respectively (manufacturer’s data). The speed of the main feeder is listed.

<table>
<thead>
<tr>
<th></th>
<th>Plastic formulation</th>
<th>Elastic formulation</th>
<th>Brittle formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Revolutions per minute</td>
<td>Dwell time</td>
<td>Feeder speed</td>
</tr>
<tr>
<td></td>
<td>[rpm]</td>
<td>[ms]</td>
<td>[rpm]</td>
</tr>
<tr>
<td>Bosch</td>
<td>29</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Fette</td>
<td>56</td>
<td>15</td>
<td>55</td>
</tr>
<tr>
<td>IMA</td>
<td>50</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Kilian</td>
<td>37</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Korsch</td>
<td>48</td>
<td>10</td>
<td>24</td>
</tr>
</tbody>
</table>

**Table 4**

Stability study: Process conditions for the plastic, elastic, and brittle formulation, respectively (manufacturer’s data). The speed of the main feeder is listed.

<table>
<thead>
<tr>
<th></th>
<th>Plastic formulation</th>
<th>Elastic formulation</th>
<th>Brittle formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Output</td>
<td>Pre-/main compaction force</td>
<td>Feeder speed</td>
</tr>
<tr>
<td></td>
<td>[tabl./h]</td>
<td>[kN]</td>
<td>[rpm]</td>
</tr>
<tr>
<td>Bosch</td>
<td>300 000</td>
<td>2.0/9.3</td>
<td>37</td>
</tr>
<tr>
<td>Fette</td>
<td>100 000</td>
<td>1.4/8.5</td>
<td>55</td>
</tr>
<tr>
<td>IMA</td>
<td>178 200</td>
<td>5.0/10.0</td>
<td>16</td>
</tr>
<tr>
<td>Kilian</td>
<td>240 000</td>
<td>2.6/8.1</td>
<td>77</td>
</tr>
<tr>
<td>Korsch</td>
<td>210 000</td>
<td>3.5/8.5</td>
<td>38</td>
</tr>
</tbody>
</table>
tensile strengths for all formulations (fig. 1). Laminating or capping was not observed in any of the trials. Comparably weaker tablets were found for the elastic formulation, which is assumed to be related to elastic recovery after compression. The Gamlen machine produced in all cases tablets with higher tensile strengths with respect to stress. This may be caused by the different tablet geometry or by a calibration issue of the stress cell, which could not be verified within this study. The tabletability profiles of the plastic formulation were closer to each other compared to the elastic or brittle formulations due to the excellent tableting behavior of this formulation [4; 5]. Producing tablets with the elastic formulation was much more challenging in manufacturing by reason of poor powder flowability and the compression behavior. Significant differences were seen at higher compaction pressures; however, these differences are irrelevant at common stresses used in production. Therefore, this issue was not studied further. The differences in the tabletability plots for the brittle formulation are remarkable (fig. 1). At compaction stresses of 400 MPa a broad scattering of tablet tensile strengths of the different machines could be identified. The values range from 3.56 MPa (IMA) to 4.74 MPa (Kilian) on the rotary tablet presses. The single punch device of Korsch showed a tablet tensile strength of 2.96 MPa, which was even below the value of IMA. This was unexpected since the brittle formulation (dicalcium phosphate anhydrate) is known for its time independent compaction mechanism [7; 8]. IMA’s comparable low tensile strength could be explained to some extent with a lower punch curvature radius. A reason for the remaining variation was not found within this study as mass variation as a reason could be excluded (fig. 1).

**Stability Study**

In a second series of experiments the stability of the compression process over the running time was investigated at a high throughput. A drift in tablet properties was expected due to systematic effects of the machine. Examples of such systematic effects might be warming up due to friction or settling of the tableting mass in the feeder. Therefore 100 000 tablets were compressed and samples were taken after 25 000, 50 000, 75 000 and 100 000, respectively. Variations in tablet mass and breaking force over time were studied. The machine parameters were chosen based on the recommendations of the machine suppliers (table 4). Fette conducted the stability study (plastic formulation) 2 times, where the second data set was produced with a higher throughput.

![Figure 1: Compression study: Tablet mass and tensile strength as a function of stress (mean ± CI, α = 0.05, n = 20) for the plastic, elastic and brittle formulation, respectively. The graphs of the single punch and of the rotary tablet presses are shown (source of all figures: Department of Biochemical and Chemical Engineering, TU Dortmund University, Dortmund (Germany)).](image-url)
The results for the rotary presses are given in fig. 2. The tablet masses fulfill the requirements of the European Pharmacopeia regarding the uniformity of mass (Reference 2.9.5) [12]. Systematic trends with respect to time could not clearly be seen. The mass variations tend to slightly increase during the stability study in many cases (fig. 2). It is concluded that the control routines of the machines work very well over time. The particularly high tablet masses of the Fette machine for the elastic formulation at the time point of 75 000 compressed tablets was caused by a manual refilling issue by the operator (fig. 2).

For the evaluation of the mechanical resistance the radial breaking force was used where a tablet breaking force of 100 N was aimed at. The corresponding tablet tensile strengths differed for each machine due to different geometries (heights) of the tablets. Therefore, the conversion of tablet breaking force into tensile strength was not useful. In this evaluation, the absolute breaking force difference is less important than its fluctuation over time. This test seems to be quite challenging: Especially but not only when handling the elastic formulation nearly each rotary press had some issues and either a slight variation in tablet breaking force over time or single outliers are observed (fig. 2). These deviations may be caused by systematic effects or result from the action of a controller compensating these systematic effects. As the fluctuations over time are small the variations are not crucial from the practical point of view: Kilian’s rotary press produced the maximum outlier (almost 10% of the actual mean value) in tablet breaking force for the elastic formulation at the time point of 50 000 compressed tablets while tablet mass and height remained in the same range as at the other time points. Similar to the slight variations over time this deviation is of little significance to practical production, since the test specification was re-met after a short period of time.

**Force-time profiles**

Representative force-time profiles of the compression study for different formulations at 200 MPa and an output of 100 000 tablets/h are presented in fig. 3 and 4. There was no force-time diagram provided for the Bosch machine, since it was not equipped adequately. The profiles were adjusted to each other by the onset of the functions (t = 0 ms). As Fette removed 4 punches in order to achieve measurements with a high accuracy distinct starting and ending points are visible. Different lengths of dwell times can be seen in which dwell times of Korsch and IMA were shorter than dwell times of Fette and Kilian for all formulations. The comparable long dwell times of Bosch and Fette (table 3) are due to the use of different punch types (table 1). Unexpectedly, longer
Dwell time did not lead to a higher mechanical strength of the tablets (fig. 1).

Force-time profiles of single punch devices are shown in fig. 4 for the same conditions as for the rotary presses. As expected, the diagrams are quite similar for the different formulations within one press. The rank order of time for reaching the maximum force may vary due to different settings of the zero-points and different upper punch speeds when reaching the powder. The Röltgen press delivered a slightly different shape for the curves due to hydraulic compression. In summary, no significant differences between the graphs of the different formulations are observed.

Conclusion
The performance of 5 different rotary presses and 4 single punch presses were studied using 3 formulations of different compaction behaviors. The aim was the investigation of differences in tablet properties (mass and tensile strength or breaking force) subject to compaction force (compression study) and number of compressed tablets (stability study).

Table mass is a relevant parameter for the tableting process as it correlates with the dosing. In both the compaction study as well as in the stability study all formulations on all considered presses met the requirements of the European Pharmacopeia for uniformity of dosage units with respect to mass variation. The observed marginal deviations were due to manual feeding difficulties or sub-optimum machine settings. Radial tensile strength is relevant for handling and further processing of tablets. In general, higher compaction forces led to higher tablet tensile strengths. As expected, the tablets compressed of the elastic formulation were weaker compared to the plastic and the brittle formulation. Differences between the tabletability profiles of the machines...
were observed. In the case of the plastically deforming formulation the differences were smaller than in the case of the other formulations because this formulation did not challenge the machines as much as the elastic and the brittle formulations did. Unexpectedly, the differences in the tabletability plots for the brittle formulation were significant. A stability study was conducted to investigate drifts in tablet properties over the processing time. Certain increasing or decreasing trends in tablet properties as well as single outliers were observed. Nevertheless, the variations in the tabletability profiles in both the compression study and the stability study were not relevant for practical applications as they were rather small. In addition, typical force-time profiles were analyzed. Different dwell times were represented. No significant differences were recognized due to different formulations. There was no obvious link between the force-time profiles and the tablet properties either.

It can be concluded that all the studied production presses handled the challenges without a problem, and the single punch devices appear to be useful tools for tablet development.

### Acknowledgement

This study was performed during the APV Expert Workshop Tableting which was hosted by the University of Dortmund in Apr. 2017. The experiments were sponsored by Boehringer Ingelheim, the City of Dortmund as well as Invite. Several material excipient suppliers donated more than 2 500 kg of material in order to make this study possible as there are Chemische Fabrik Budenheim, Colorcon, Evonik, JRS Pharma, and Meggle. The equipment was provided by Bosch, Fette, Gamlen, IMA, Korsch, Medelpharm, Röltgen, Romaco Kilian and Sotax. The organizers would like to thank all companies for their generous support.

### References