This method continues to become more popular because it needs no water and, thus, requires no drying step. Furthermore, it can easily be scaled up since the output of granulated material is only dependent on the roller speed settings. In order to achieve uniform granules, it is of utmost importance to use highly compactible binders of constant quality.

Different MCC-based excipients were evaluated for their suitability for roller compaction. They were used in combination with a brittle fracturing material (dicalcium phosphate dihydrate, EMCOMPRESS®) in order to obtain the best compaction results [1].

The cellulosics used for this study were traditional MCC (VIVAPUR® 101) and two grades of silicified MCC (PROSOLV® SMCC 50 and PROSOLV® SMCC 50LD). All three grades exhibit very similar particle size distributions as determined by laser diffraction. PROSOLV® SMCC 50 was used as the reference material because the effect of silicification on VIVAPUR® 101 and the effect of bulk density in comparison to PROSOLV® SMCC 50LD could be analyzed.

Dicalcium phosphate dihydrate (EMCOMPRESS®) was added as a filler with a purely brittle deformation mechanism.

In order to obtain the best individual compaction results, different compaction forces were tested during roller compaction. All resulting compacts were compressed into tablets and compared regarding their hardness.
The Effect of Silicification on the Roller Compaction Performance of Microcrystalline Cellulose

Materials and Methods

The powder blends used consisted of 75 % of the cellulosic compound (either MCC or SMCC) and 25 % dicalcium phosphate dihydrate. Materials were blended in a drum hoop mixer for 10 minutes. The ingredients are listed in Table 1.

Different roller compaction forces were adjusted and the compacts were milled using the Hosokawa sieve mill. The resulting powder was tested for particle sizes and flowability. Furthermore, placebo tablets containing 0.5 % of the lubricant, sodium stearyl fumarate (PRUV®), were compressed (400mg, round, biplane, 13mm diameter) and their hardness, as well as disintegration time, was analyzed.

All tests were performed in triplicate.

Roller Compactor Details

The roller compactor was equipped with interlocking serrated rolls and was used as follows:

<table>
<thead>
<tr>
<th>Diameter of rolls</th>
<th>200 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working width</td>
<td>50 mm</td>
</tr>
<tr>
<td>Roller speed</td>
<td>6 rpm</td>
</tr>
<tr>
<td>Preload force</td>
<td>9 kN</td>
</tr>
<tr>
<td>Screw speed</td>
<td>Variable</td>
</tr>
</tbody>
</table>


Results

Graph 1 shows the particle size (expressed as D50) of milled compacts made from PROSOLV® SMCC 50.

The average particle size became higher as compaction forces increased. Even the particles obtained at the lowest compression forces were in a range suggesting passable to good flow.

Flow properties

<table>
<thead>
<tr>
<th>Flow characteristics</th>
<th>Speed of flow</th>
<th>Angle of repose [°]</th>
<th>Hausner ratio</th>
<th>Flowability acc. Jenike (FF1-2C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremely bad</td>
<td>No flow</td>
<td>&gt; 66</td>
<td>&gt; 1.60</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Very bad</td>
<td>Low</td>
<td>56 - 65</td>
<td>1.46 - 1.59</td>
<td>1 - 2</td>
</tr>
<tr>
<td>Bad</td>
<td>46 - 55</td>
<td>1.35 - 1.45</td>
<td>2 - 4</td>
<td></td>
</tr>
<tr>
<td>Sufficient</td>
<td>36 - 45</td>
<td>1.19 - 1.34</td>
<td>4 - 10</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>31 - 35</td>
<td>1.12 - 1.18</td>
<td>&gt; 10</td>
<td></td>
</tr>
<tr>
<td>Very good</td>
<td>High</td>
<td>25 - 30</td>
<td>1.00 - 1.11</td>
<td></td>
</tr>
</tbody>
</table>

Graph 1: Particle size of PROSOLV® SMCC 50 compacts as a function of compression force during roller compaction.
The flowability of the roller compacted substances was determined either with the Schulze shear cell (FF1-2C value) or using the Hausner ratio (Graph 2). To obtain flow index (FFC) values indicating good flow, a minimum of 25 kN compaction force during roller compaction was needed. At the same time, all samples exhibited good flowability according to the Hausner ratio.

Hard tablets could be obtained even at the lowest compression forces, irrespective of the compaction force used during roller compaction. At higher tableting forces, it became evident that the final compactibility was affected by the primary compaction forces during roller compaction. Granules produced at a lower roller compaction force (18 kN) yielded harder tablets than those pre-compact at 31 kN.

**Comparison between PROSOLV® SMCC 50, PROSOLV® SMCC 50LD and VIVAPUR® 101**

Based on the findings for PROSOLV® SMCC 50, corresponding tests were performed with PROSOLV® SMCC 50LD and VIVAPUR® 101.

Table 5 displays the fundamental powder properties of the three excipients. A roller compaction force of 25 kN was selected for the comparison study.
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Graph 4 shows that the highest average particle sizes for the milled compacts was obtained if PROSOLV® SMCC 50 was used.

PROSOLV® SMCC 50 also exhibited better flow than both VIVAPUR® 101 and PROSOLV® SMCC 50LD compacts (Graph 5).

By comparison, the compacts based on PROSOLV® SMCC 50LD exhibited on average a 30% higher hardness yield (Graph 6).

In terms of tableting performance, the compacts made from VIVAPUR® 101 and PROSOLV® SMCC 50 showed nearly identical tablet hardness values over the entire range of compression forces.

Discussion

Formulations that contain both plastically deforming and brittle fracturing materials are known to yield hard compacts due to the synergistic combination of these different deformation mechanisms [1]. Furthermore, it has been demonstrated that the particle size of the starting material used for roller compaction has a significant influence on the hardness of the resulting tablets [2]. Consequently, a formulation containing primarily plastically deforming microcrystalline celluloses and brittle fracturing dicalcium phosphate dihydrate was studied. In order to avoid interfering influences due to different particle sizes, the chosen microcrystalline celluloses exhibited the same particle sizes. Thus, the influence of the silicification of microcrystalline cellulose, as well as the influence of different bulk densities, could be investigated.

In our study, PROSOLV® SMCC 50 was tested in comparison to traditional MCC (VIVAPUR® 101).

PROSOLV® SMCC is a microcrystalline cellulose, which has been treated with colloidal silicon dioxide during the manufacturing process in order to increase the surface area.
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Thus, more area for binding interactions between the individual particles is available. Larger binding surfaces result in harder compacts. This has been proven for roller compacted SMCC before [3] and was verified in this study.

When PROSOLV® SMCC grades of different bulk densities were compared, the lower bulk density grade (PROSOLV® SMCC 50LD) resulted in a particle size smaller than the grade with the normal bulk density (PROSOLV® SMCC 50). Due to their smaller particle size, the flow of the PROSOLV® SMCC 50LD granules was reduced compared to the flow of the particles made from PROSOLV® SMCC 50. While the flowability of the milled compacts was better for PROSOLV® SMCC 50, the hardness of tablets made with PROSOLV® SMCC 50LD was higher than for PROSOLV® SMCC 50.

Conclusion

The silicification of MCC has been shown to significantly influence the hardness and the flowability of compacts, as well as the hardness of tablets made from these materials. If the overall target in tablet production is the highest possible tablet hardness the use of PROSOLV® SMCC 50LD in combination with EMCOMPRESS® is recommended. If both, the particle flow, and the tablet hardness, must be optimized PROSOLV® SMCC 50 is the best choice.

Acknowledgement:
We would like to thank Prof. Dr. Ingrid Müller, Albstadt-Sigmaringen University, and her team for carrying out the roller compaction work and the shear cell measurements.

References
[3] B.N. Chukwumezie, S. Katpally, A. Vargas-Perez, B.E. Sherwood, M.C. Addeeye, Roller compaction studies and granule characteristics of silicified microcrystalline cellulose