Comparative Study of Different Binders for Roll Compaction/Dry Granulation

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Purpose
Tablets produced from granules, which were obtained by roll compaction/dry granulation show reduced tensile strength compared to tablets produced by direct compression or after wet granulation. This emphasizes the importance of binders for this application besides their general relevance for the tablet formulation. In previous studies different binders were compared in a formulation in which they could not be well distinguished [1]. In this study, different binders were compared in a formulation containing an active pharmaceutical ingredient with a poor binding capacity and the effects on the tensile strength after roll compaction and tableting were assessed. Additionally the suitability of a new hydroxypropyl cellulose grade (HPC-SSL-SFP) should be evaluated.

Methods
Tablets containing acetaminophen (70 % w/w) with a weight of 200 mg were produced. Dicalcium phosphate anhydrate (20 % w/w) (DiCafos A150, Chemische Fabrik Budenheim) was applied as filler. The following binders (10 % w/w) were compared: HPC-L fine, HPC-SSL, HPC-SSL-SFP (Nippon Soda), Klucel EXF (Ashland), Avicel PH 101 (FMC Biopolymer) and Pharmacoat 603 (Shin-Etsu) as cellulose derivatives and Kollidon VA 64 fine and Kollidon CL-SF (BASF) as povidone derivatives. One binder free formulation with 30 % w/w filler was analysed as reference. All powder mixtures were dry granulated on an instrumented roll compactor (Mini-Pactor, Gerteis) with a specific compaction force of 5 kN/cm. Rolls with rim roll sealing were used at a rotation speed of 2 rpm. A star granulator was equipped with a sieve with 1 mm mesh size. The granules were compressed with 8 mm flat faced punches on a rotary tablet press (IMA Pressima, Kilian) at various compaction pressures. External lubrication with magnesium stearate (Parteck MST Lub, Merck) was performed by using an eyeshadow applicator. To calculate the tensile strength, breaking force of the tablets was determined with a tablet tester Typ TBH 210 (Erweka). Height and width were measured with a micrometer screw (Mitutoyo).

Particle size distributions (PSD) of the binders were analysed by laser diffraction (Mastersizer 3000, Malvern). The PSDs of granules were measured via dynamic image analysis (CamsizerXT, Retsch).

Results
The resulting particle size distributions of the granules after roll compaction differ significantly. The x50-value (Q3) of granules with Pharmacoat 603 was lowest with 203 ± 24 µm. The largest granules were obtained in the formulation with HPC-SSL-SFP with a size of 696 ± 12 µm. This HPC grade had the smallest particles in comparison to the other HPCs and this might explain the larger granules due to the higher specific surface area of small particles or due to a better distribution in the powder blend. Formulations with binders of small particle sizes predominantly lead to larger granules [2]. By same reason the amount of fines were lower with binders of small size. This is an additional important point, as in dry granulation fines are typically present which in turn affects the flowability. Correlating the x50-values of the binders with the amount of granule particles smaller than 180 µm leads to a coefficient of 0.854. The effect of larger particles and a better flowability could also be shown by a strong correlation of Hausner ratios to the x50-values of the granules (R = -0.976).

Furthermore the compactibility profiles of the different formulations were evaluated. Tablets with HPC-SSL-SFP and Kollidon VA 64 fine achieved the highest tensile strength exceeding 2.5 MPa at a compaction pressure of 350 MPa. HPC-SSL, which differs to HPC-SSL-SFP only in particle size, is less effective as expected. This might be again due to larger particles and lines up in its compactability with Klucel EXP and Kollidon CL-SF. Without binder the tablet strength increased up to a compaction pressure of 150 MPa. Increasing compaction pressures further led to weaker tablets, which is caused by capping of tablets. A similar observation was made for Avicel PH 101, whose binding properties were weak. Here capping appeared above 250 MPa. Formulations with Pharmacoat 603 and HPC-L fine were less effective regarding to compactibility but capping was prevented. Tensile strength values of approximately 1.5 MPa were achieved.

Conclusion
Generally, binders of small particle sizes performed better regarding granule size and compactibility. This comparative study showed, that HPC-SSL-SFP is a suitable binder for dry granulation beside Kollidon VA 64 fine. Formulations with the new HPC grade showed the lowest amount of fines, the lowest Hausner ratio and an improved tablet tensile strength.