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Investigating the impact of particle size and content of cross-linked PVP onto the resulting tablet characteristics

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INTRODUCTION

Disintegration properties are one of the most important features of an instant release tablet. Therefore, dedicated excipients (disintegrants) are typically added to the formulation to facilitate quick drug release. For this purpose, a huge variety of different excipients can be employed. One product group is the mainly physically cross-linked insoluble poly(vinyl pyrrolidone) or crospovidone, respectively.

Crospovidone is a standard disintegrant, which is frequently employed to enhance the disintegration characteristic of a tablet. The product is available in different grades, mainly varying in particle size and water up-take capabilities [1–3].

The aim of this study was to investigate the impact of these different grades on tensile strength and disintegration time of a placebo tablet holding different levels of disintegrant.

MATERIALS AND METHODS

Four different grades of cross-linked poly(vinyl pyrrolidon) or crospovidone (Kollidon® CL, CL-F, CL-SF, and CL-M; all BASF) were used for this investigation (Figure 1–4). Each individual grade was added at three different concentration levels to the tabletting formulation (1.5, 3.0, and 5.0%). The tabletting formulation was kept simple, containing merely 0.5% magnesium stearate (Bärlocher) as lubricant, and some direct compressible lactose based filler (Ludipress® LCE, BASF). Each formulation was passed through a screen (w=0.8 mm) and mixed in a Turbula® T2C blender (20 + 2 minutes).

The compression was done employing a Korsch XP 1 single punch press using flat faced punches with a diameter of 12.0 mm. Compression forces of 5 to 15 kN (compression pressure 44.2 to 132.6 MPa) were applied at a tabletting speed of 25 tablets per minute.

Dedicated tablets of each formulation (individual compression forces recorded) were examined by a tablet tester (Sotax HT100) allowing the calculation of tensile strength with respective standard deviation (n=20). Additionally, disintegration time (n=6) was tested (ERWEKA ZT74) in demineralised water (37°C ±1 K).

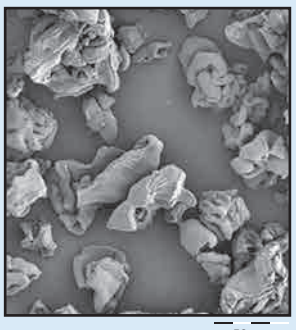

Figure 1. Scanning electron microscopy (SEM) image of Kollidon® CL (SE, 5 kV).

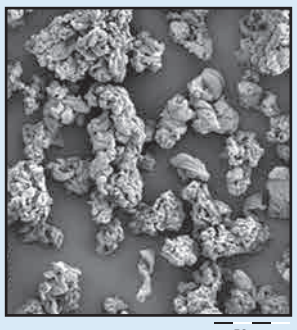

Figure 2. Scanning electron microscopy (SEM) image of Kollidon® CL-F (SE, 5 kV).

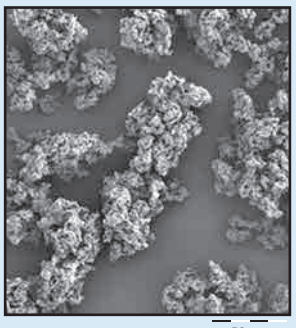

Figure 3. Scanning electron microscopy (SEM) image of Kollidon® CL-SF (SE, 5 kV).

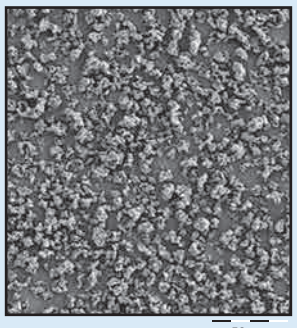

Figure 4. Scanning electron microscopy (SEM) image of Kollidon® CL-M (SE, 5 kV).

RESULTS AND DISCUSSION

All formulations tested during this study showed a marked dependency of the tablet's tensile strength value on compression pressure applied (Figure 5, 7, 9). Firstly considering the formulation with no disintegrant, sufficient tablet strength (>1.5 N/mm²) could be achieved with moderate compression pressures (about 85 MPa). This observation, in combination with the low variation of the tensile strength values, suggests both proper flowability and excellent compressibility features of the lactose based filler. Yet, without any further additive, disintegration characteristics were poor (Figure 6).

When adding excipients of the same chemical and physical nature to a tabletting blend, a dependency of tablet strength on the additive's particle size can be observed. Whereat, a smaller particle size typically leads to higher tensile strength values. This effect is described for crospovidone as well [2, 4–6].

Interestingly, the addition of fine crospovidone grades to the tabletting formulation did not lead to a higher strength of the tablets in general. Actually, the presence of crospovidone seemed to disturb the integrity of the tablet resulting in a tendency for lower tensile strength values in particular for concentrations of 5.0% (Figure 9).

1.5% crospovidone content in the tabletting formulation hardly affected the tensile strength features at all. There seemed to be a trend for smaller grades (CL-M and CL-SF) leading to stronger tablets whereas the coarser grade (CL) led to weaker tablets, but the differences were barely pronounced (Figure 5). 3.0% crospovidone content clearly indicated a lower tensile strength for the formulation containing the coarse crospovidone grade (Figure 7) and 5.0% crospovidone content separated the formulations clearly (Figure 9). The two very fine grades (CL-M and CL-SF) were still very similar in their performance and barely affected the tablet strength. The slightly coarser grade (CL-F) decreased the tensile strength value distinctively whereas the coarse grade (CL) showed lowest tensile strength values (Figure 9).

Employing disintegration time as discriminating parameter allowed distinguishing the performances of the different grades. Due to micronisation, CL-M lost most of its power and hardly acts as a disintegrant anymore. The coarse grade (CL) showed almost no dependency of disintegration time on its concentration, suggesting that low concentrations are already sufficient for high performances. CL-F and CL-SF presented disintegration times depending on particle size and content. Interestingly, at contents of 5.0% disintegrant in the formulation all three grades offered the same disintegration time independent of the tensile strength value of the tablet (Figure 6, 8, 10).

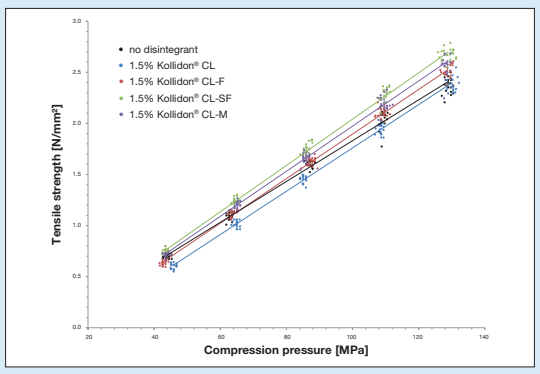

Figure 5. Tensile strength of individual tablets (n=20) containing none or 1.5% cross-linked PVP plotted as function of compression pressure (5 levels).

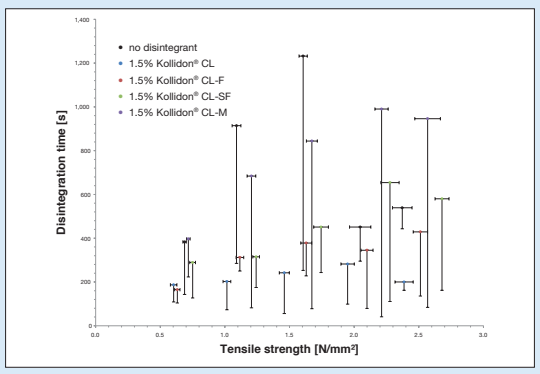

Figure 6. Maximum disintegration time (n=6; -min) of tablets containing none or 1.5% cross-linked PVP plotted as function of tensile strength (n=20; ±SD).

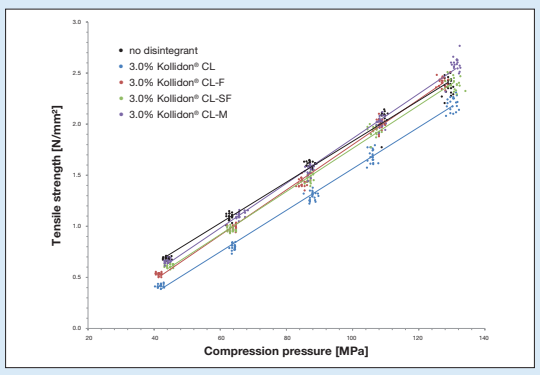

Figure 7. Tensile strength of individual tablets (n=20) containing none or 3.0% cross-linked PVP plotted as function of compression pressure (5 levels).

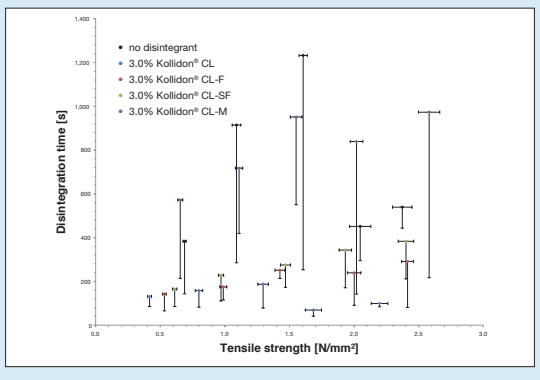

Figure 8. Maximum disintegration time (n=6; -min) of tablets containing none or 3.0% cross-linked PVP plotted as function of tensile strength (n=20; ±SD).

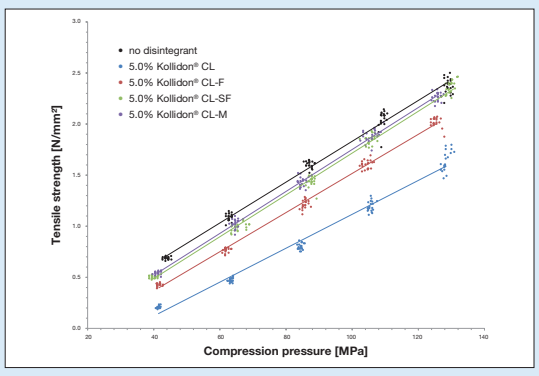

Figure 9. Tensile strength of individual tablets (n=20) containing none or 5.0% cross-linked PVP plotted as function of compression pressure (5 levels).

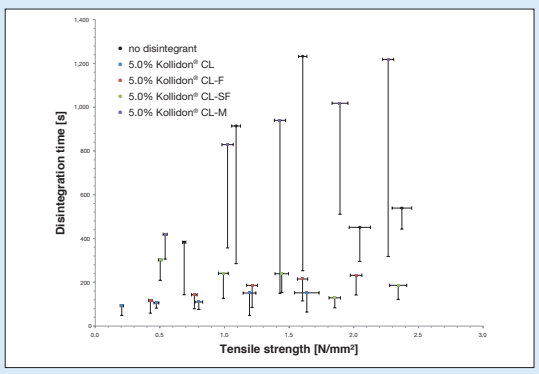

Figure 10. Maximum disintegration time (n=6; -min) of tablets containing none or 5.0% cross-linked PVP plotted as function of tensile strength (n=20; ±SD).

CONCLUSION

The particle size of crospovidone distinctly affects both strength and disintegration time of the final tablet. Due to micronisation, Kollidon® CL-M lost most of its disintegration power. Kollidon® CL-SF provides high tensile strength values; yet similar to Kollidon® CL-F it needs to be used in higher concentrations (3.0 – 5.0%) to achieve quick disintegration. The coarse particles of Kollidon® CL markedly affected tablet strength when added in high concentrations (5.0%), but a similar disintegration performance could also be achieved with low contents (1.5%), while maintaining high tensile strength values.

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Presented at:
42nd CRS Annual Meeting & Exposition, July 26–29, 2015;
Edinburgh, Scotland
Pharma Ingredients & Services | G-ENP/ET453

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