Determining the minimum amount of Kollidon® SR required in a tabletting blend to obtain a matrix tablet

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Introduction

Kollidon® SR-based matrix formulations are well known for obtaining strong sustained release functionality [1]. Depending on the solubility of the active ingredient and the required dissolution profile, pore formers need to be added for adjusting drug release [2].

This work was to investigate the maximum amount of excipients that can be added to PVAc still leading a 'non-disintegrating' tablet matrix in the dissolution test. Three filling materials were tested, representing the groups of 'stone like', swellable and soluble excipients or actives.

Materials and Methods

Materials

The poly(vinyl acetate) [PVAc] based matrix former, Kollidon® SR (consisting of 80% poly(vinyl acetate) and 20% poly(vinyl pyrrolidine) K 30) from BASF, was investigated.

As fillers, dicalcium phosphate anhydrous (DI CAFOS A60, CFB), micro-crystalline cellulose [MCC] (Avicel® PH-102, FMC), gran. lactose monohydrate (Ludipress® LCE, BASF) and as lubricant, magnesium stearate (Baerlocher) were used.

Methods

Binary blends of Kollidon® SR and one of the filling materials were produced whereas the individual content of each filler was varied in the range of 20 to 80%. Before tableting, 0.5% magnesium stearate was added.

The compression was done using a single punch press XP 1 (Korsch) assembled with a set of flat faced, bevelled edge punches with a diameter of 10 mm. The compression forces applied were 5, 10 and 20 kN.

The crushing force of the tablets was determined by using a multi-tester HT-TMB-CI-12 FS (Kraemer). Based on this result, tensile strength was calculated according to equation given in Figure 1:

$$\sigma = \frac{2 \cdot F_c}{\pi \cdot h \cdot d}$$

Figure 1. σ: Tensile strength [N/mm²]; F_c crushing force [N]; h: tablet height [mm]; d: diameter [mm].

As indicator for the mechanical stability of the tablet, a disintegration tester according to Ph. Eur. was used (ZT74, Erweka). Tablets which did not show any disintegration after 120 minutes were regarded as 'non-disintegrating'.

Results and Discussion

Kollidon® SR is a spray dried product showing the typical spherical particles characteristic for such kind of excipient (Figure 2) whereas the used fillers differ in shape and particle size (Figure 3–Figure 5).

Independent of the nature of the filling material, all formulations containing the amount of Kollidon® SR necessary for the formation of non-disintegrating matrix tablets, yielded high strength.

However, a clear dependency of tablet hardness on compression force could be found (Figure 6) whereas MCC generally offered the highest value.

During the first days after compression a lot of tablet formulations show a change in tablet strength, such as 'post-curing' effects (increasing tablet strength). Interestingly, this could not be seen for all the formulations tested in this investigation. Compared to the initial values, a subsequent measurement after 8 days of storage hardly showed any change in tablet strength.

According to tablet strength, the resistance of the tablets to disintegration was found to follow the same dependency: the higher the compression force, the less the tablet was prone to disintegration. In this connection, a higher mechanical stability led to higher quantities of filling material that could be incorporated into the tableting formulation.

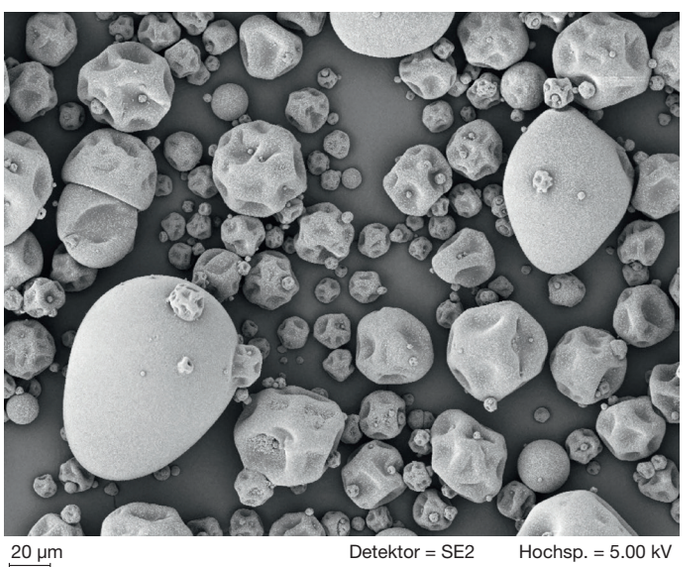

Figure 2. SEM image of Kollidon® SR.

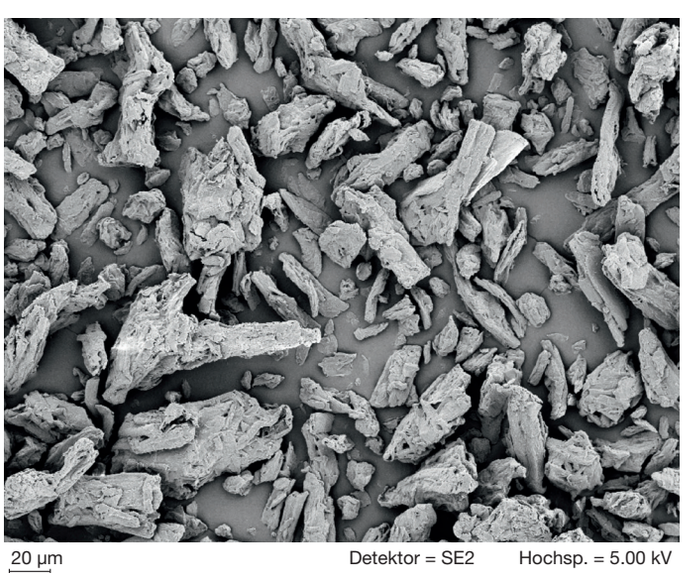

Figure 3. SEM image of Avicel® PH-102.

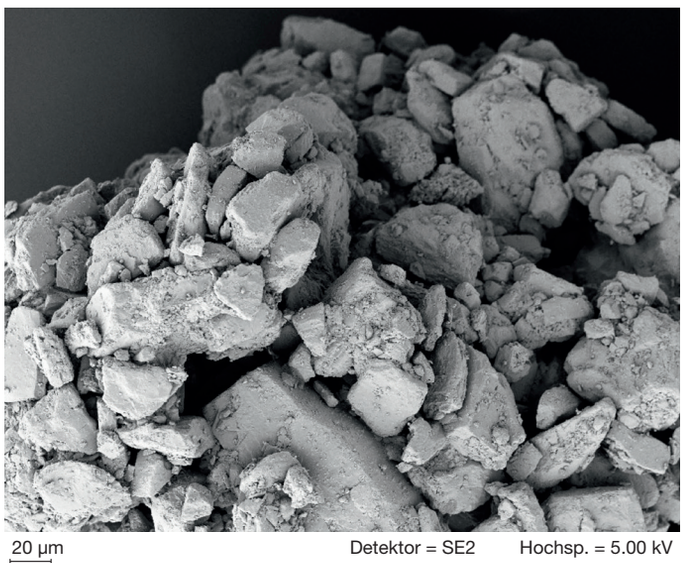

Figure 4. SEM image of Ludipress® LCE.

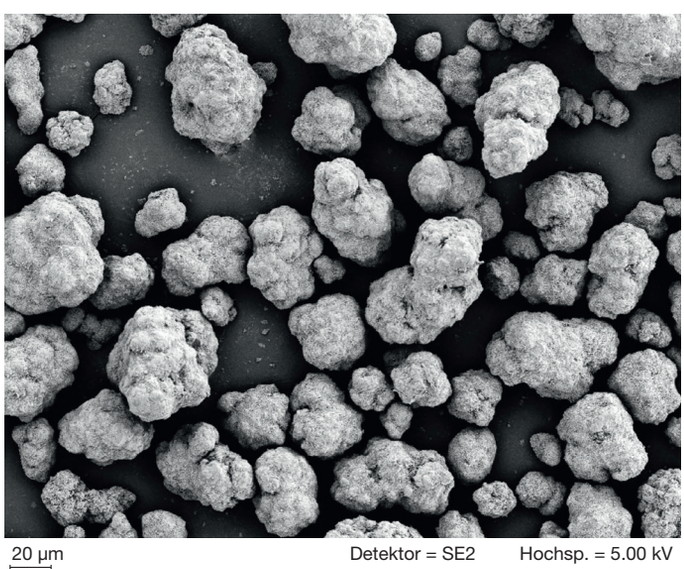

Figure 5. SEM image of DI CAFOS A60.

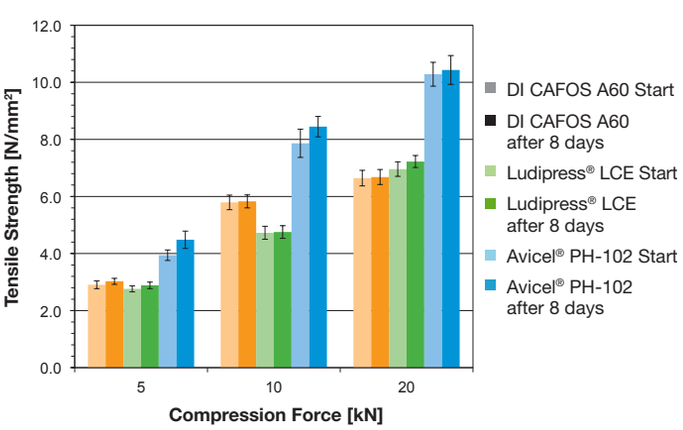

Figure 6. Tensile strength directly after compression and after 8 days of storage as function of compression force.

Interestingly, at compression forces of 5 or 10 kN this was found to be independent of the type of filler. At 5 kN, at least 75% Kollidon® SR have to be added to MCC (Figure 7), Ludipress® LCE (Figure 8) or DI-CAFOS A60 (Figure 9) to obtain a non-disintegrating matrix tablet. On the other hand, the amount of matrix former could be reduced to about 50% as soon as 10 kN were applied.

However, at high compression forces such as 20 kN, the nature of the filling material influenced the characteristics of the tablet. 45% Kollidon® SR was required to obtain a matrix tablet holding MCC as filling material whereas with Ludipress® LCE about 40% was needed.

Best results could be found for DI-CAFOS A60 where just 30% of matrix former had to be added to form a non-disintegrating matrix tablet.

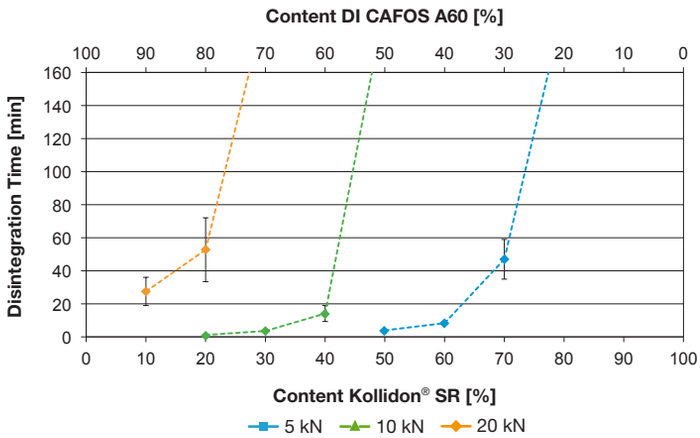

Figure 9. Disintegration time as function of DI CAFOS A60 content in the formulation.

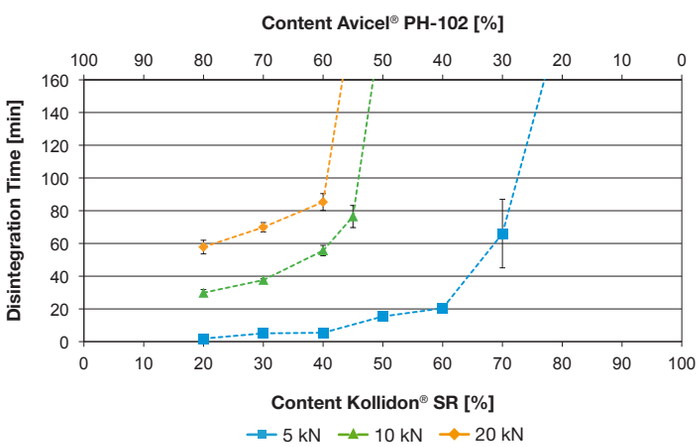

Figure 7. Disintegration time as function of Avicel® PH-102 content in the formulation.

Conclusion

The disintegration tester was found to be a good indicator for characterising the strength of a matrix tablet. Consequently, the results could be used to determine the amount of Kollidon® SR that had to be added to filling materials of different nature to yield a non-disintegrating matrix formulation.

Independent of the formulations tested, it was found that there is hardly any change in tablet strength within 8 days after compression.

Regarding the mechanical stability of the matrix tablets, no dependency on the nature of the filling materials could be found for compression forces of 5 or 10 kN.

The type of filler influenced the stability at compression forces of 20 kN in the following order: DI-CAFOS A60, Ludipress® LCE and Avicel® PH-102. However, DI-CAFOS A60 resulted in the highest concentration which led to a non-disintegrating matrix tablet.

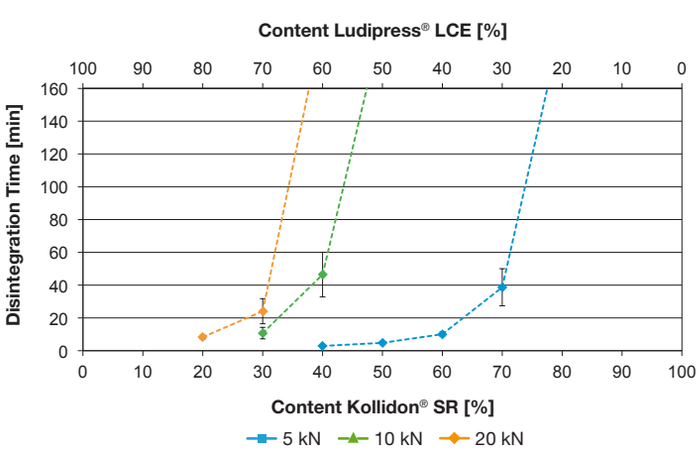

Figure 8. Disintegration time as function of Ludipress® LCE content in the formulation.

References

[1] Bühler, V.; Kollidon® Polyvinylpyrrolidone excipients for the pharmaceutical industry; 9th edition; 2008; BASF SE, Ludwigshafen, Germany.

[2] Agnese, T.; Cech, T.; Geiselhart, V.; Investigating the effect of various pore formers on the dissolution characteristics of a matrix tablet based on polyvinyl acetate; Innovation in Drug Delivery; October 3–6, 2010; Aix-en-Provence, France.

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