Evaluating various disintegrants regarding their performance in orally disintegrating tablet formulations

Thorsten Agnese[1], Florian Bang[1], Thorsten Cech[1], Maureen Mistry[2]

[1]Application Lab Pharma Ingredients & Services Europe, BASF SE, Ludwigshafen, Germany
[2]Pharma Ingredients & Services, Sub-Sahara Africa, BASF West Africa Ltd., Ikoyi, Nigeria
Corresponding author: thorsten.cech@basf.com

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INTRODUCTION

In regard to line extensions or improving administration convenience, orally disintegrating tablets (ODTs) have become a popular dosage form over the last years [1]. Even though formulators have some ready-to-use aids on hand, allowing quick and simple drug formulation [2], some active pharmaceutical ingredients raise the need to employ customised formulation development.

An ODT administration calls for fast disintegrating dosage forms offering a pleasant mouth sensation to gain patient's compliance. Hence, the selection of the disintegrant is crucial for the success of the final product. The aim of this study was to compare the performance of various disintegrants in a set ODT formulation [3].

MATERIALS AND METHODS

Lactose (GranuLac® 230, Meggle Pharma) was agglomerated (wet granulation) with native maize starch (C*PharmGel™, Cargill) to be used as filling material. The wet granulation process was conducted in a high shear mixer (Diosna P 1/6) applying an impeller speed of 200 rpm and a chopper speed of 2,000 rpm. The binder (2.0% w/w final granules) was added as aqueous paste within 120 s, followed by a granulation time of 180 s [3].

The wetted agglomerates were passed through an oscillating sieving machine (w=1.6 mm, AR400, ERWEKA), dried on a tray (ambient conditions), and finally passed through a sieve (w=0.8 mm) [3].

The following disintegrants were investigated with a concentration of 5.0% in the tabletting blend: six grades of cross-linked poly(vinyl pyrrolidone) differing in particle size (Kollidon® CL, Kollidon® CL-F, Kollidon® CL-SF, Kollidon® CL-M, all BASF; Polyplasdone® XL, Polyplasdone® XL-10, both Ashland), croscarmellose sodium (Ac-Di-Sol®, FMC) and sodium starch glycolate (Explotab®, JRS).

Eventually, 0.5% magnesium stearate (Bärlocher) was added as lubricant to the tabletting blend.

The compression was done using a single punch press XP 1 (Korsch) equipped with flat faced, faceted punches with a diameter of 8.0 mm. Compression forces of 2 to 8 kN were applied at a tabletting speed of 20 tablets per minute.

The tablets were characterised (n=20) using a multi-tester (HT100, Sotax). The disintegration time (n=6) was determined (ERWEKA ZT 74) in demineralised water (37°C ±1 K).

RESULTS AND DISCUSSION

Generally, the characteristic of a tablet is strongly impacted by the disintegrant. Tensile strength and friability for instance (as essential features) are markedly influenced by particle size of the disintegrant chosen whereas smaller particles tend to lead to tablets of higher strength [4]. As regards to the ODT application, the texture of the disintegrated tablet presented to the tongue is worth noting [2].

In this regard, the latter characteristic is influenced by the wetted and swollen material whereas tensile strength is impacted by the particle size of the dry powder.

According to this, Kollidon® CL-M appears to be a promising candidate. But this grade is micronised and thereby lost most of its power to act as a disintegrant. Therefore, Kollidon® CL-SF was selected for this investigation (Figure 1).

As second cross-linked poly(vinyl pyrrolidone) grade Polyplasdone® XL-10 was chosen, since it also presented smaller particles compared to the regular Polyplasdone® XL grade. Furthermore, Ac-Di-Sol® and Explotab® were used, even though both products presented very uncomfortable sand in the mouth sensation due to the size of the swollen particles (Figure 2).

The visual appearance of all investigated disintegrants is shown in the SEM images (Figures 3-10).

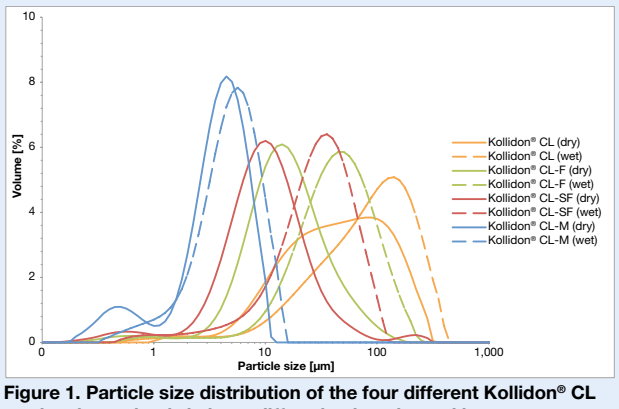

Figure 1. Particle size distribution of the four different Kollidon® CL grades determined via laser diffraction in a dry and in a wet state (Mastersizer 2000, Malvern Instruments).

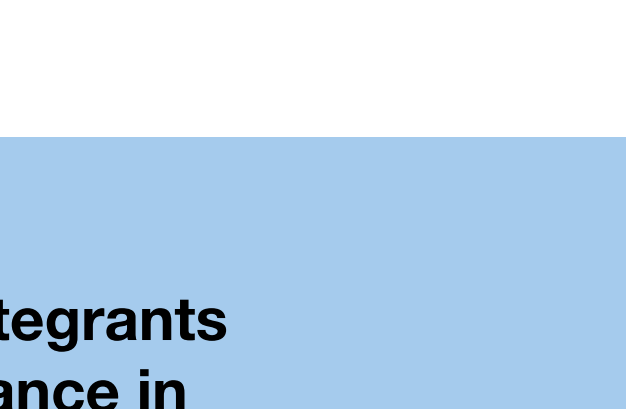

Figure 2. Particle size distribution of four different disintegrants determined via laser diffraction in a dry and in a wet state (Mastersizer 2000, Malvern Instruments).

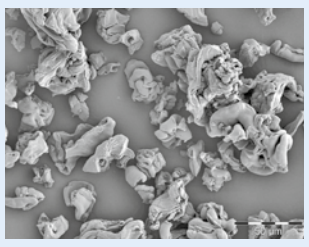

Figure 3. Scanning electron microscopy (SEM) image of Kollidon® CL (SE, 5 kV).

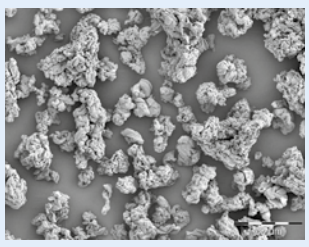

Figure 4. Scanning electron microscopy (SEM) image of Kollidon® CL-F (SE, 5 kV).

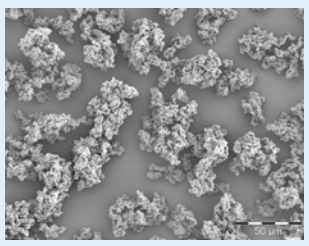

Figure 5. Scanning electron microscopy (SEM) image of Kollidon® CL-SF (SE, 5 kV).

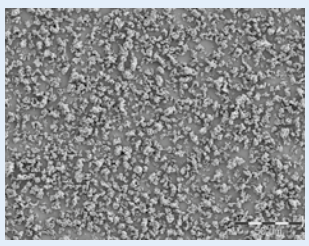

Figure 6. Scanning electron microscopy (SEM) image of Kollidon® CL-M (SE, 5 kV).

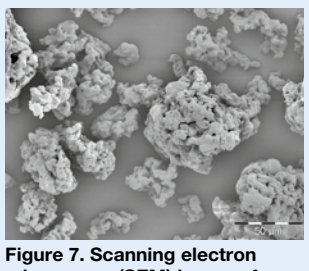

Figure 7. Scanning electron microscopy (SEM) image of Polyplasdone® XL (SE, 5 kV).

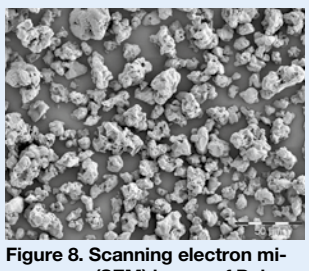

Figure 8. Scanning electron microscopy (SEM) image of Polyplasdone® XL-10 (SE, 5 kV).

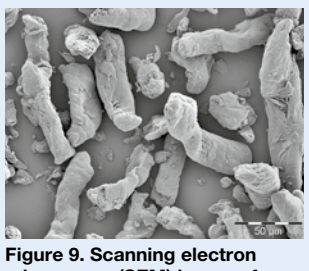

Figure 9. Scanning electron microscopy (SEM) image of Ac-Di-Sol® (SE, 5 kV).

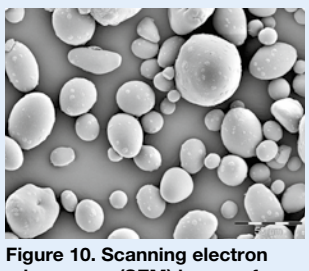

Figure 10. Scanning electron microscopy (SEM) image of Explotab® (SE, 5 kV).

When compressing the different tabletting blends to ODTs, a clear functionality of tensile strength on compression force could be found. Interestingly, adding a disintegrant to the tabletting formulation hardly changed or even decreased the strength of the ODT. However, this was decisively different for Kollidon® CL-SF. Resulting tensile strength for formulations containing this particular excipient were distinctly higher compared to the disintegrant-free formulations; particularly at high compression forces (Figure 11).

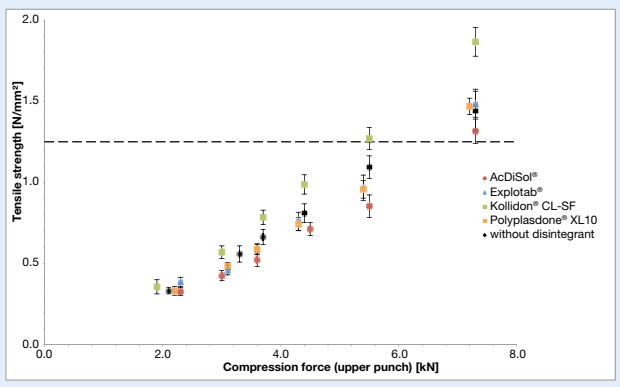

Figure 11. Tensile strength of ODTs containing different disintegrants (or no disintegrant) as function of compression force (mean values (n=20), ±SD).

Although tensile strength was found to be high, these tablets offered the shortest disintegration time of all formulations. And even more interesting, latter values were always found at merely about 10 s independent of the compression force applied (Figure 12).

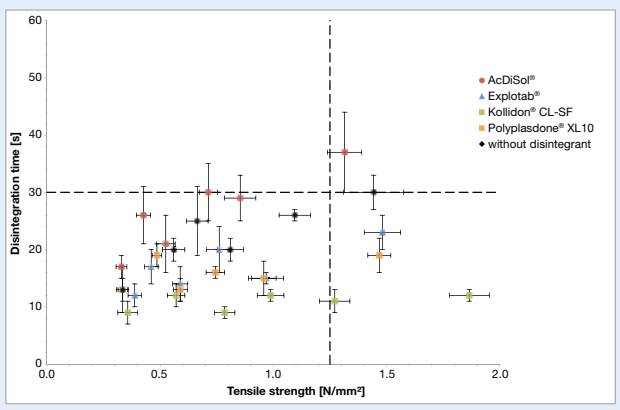

Figure 12. Disintegration time of tablets, containing 10% of disintegrant (mean value (n=6), ±SD).

CONCLUSION

Several advantages can be utilised when employing Kollidon® CL-SF as disintegrant in ODT tabletting formulations: firstly, it presents a superior mouth sensation due to its small particle size, secondly, it leads to tablets of high tensile strength, and thirdly, it allows very fast disintegration independent of compression force applied.

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