INTRODUCTION
Crospondione is considered as a standard disintegrant in direct release tablet formulations. It is a mainly physically cross-linked, and thus insoluble, polyvinylpyrrolidone. Crospondiones are available in various grades, mainly varying in its particle size and water uptake capability (1–3). However, next to its regular feature (disintegration enhancer), fine and micronised crospondione grades can offer distinct dry binding capabilities (4–6). Therefore, those grades can be regarded as binding disintegrants.

The aim of this study was to investigate different directly compresstable tabletting formulations of crospovidone grades, distinctly varying in particle size. Tabletting and disintegration characteristics were investigated.

MATERIALS AND METHODS

Two different basic tabletting formulations were tested. Alpha-lactose monohydrate was chosen as main Binder (Table 1, Table 2). They were formulat- ed with 3.0% of one of the following crospovidone grades: Kollidon® CL, Kollidon® CL-F, Kollidon® CL-SF, or Kollidon® CL-M, each offering a distinctively different particle size distribution (Table 3).

In order to measure the particle size distribution of the disintegrants in a swollen state, the disintegrants were dispersed in water. The tabletting blends were prepared by passing all components through a sieve (w=0.8 mm). The main components were mixed in a Turbula® T2C mixing machine (BÜCHI). The tabletting blends were prepared by passing all components through a sieve (w=0.8 mm). The main components were mixed in a Turbula® T2C mixing machine (BÜCHI).

RESULTS AND DISCUSSION
The tensile strength values of Formulation 1 were found to be in general comparatively low. The particle size of crospovidone distinctly affected the strength of the tablets, whereas a decreasing particle size led to an increase in tensile strength (Figure 1).

This effect was caused by a poorer compressibility of the formulations contain- ing a coarser disintegrant. The compressibility plot shows, that energy (compression pressure) could less efficiently be transferred into powder solidification in the presence of larger crospovidone particles (Figure 4). Pre- sumably, the viscoelastic deformation of microcrystalline cellulose consumed this energy and the much more form-able crospovidone could not be compressed. Therefore, the inherent porosity of the particles remained unsati- isfied, increasing the overall porosity (lowering ejected solid fraction) of the tablet. Smaller particles additionally act as dry binders. This could be a sec- ond effect, supporting the tensile strength of those tablets containing small particles of crospovidone.

The bondability of all formulations were quite similar (Figure 5). Merely Kollidon® CL presented a slightly reduced bondability, still in the range of the other disintegrants, though.

Tablets of Formulation 1 disintegrated very quickly (Figure 6). Even with the mi- cronised grade Kollidon® CL, mean disintegration times below 0.05 s could be observed (due to micromixing, Kollidon® CL-M; dramatically less disintegra- tion form). This was caused by the microcrystalline celluloses, which provided some disintegration enhancing features by its own. Generally, disintegration characteristics were found to be independent of tablet's tensile strength.

Interestingly, the tabletability characteristics of Formulation 2 differed mark- edly from those of Formulation 1. Compactability of all formulations, but the crospovidone containing CL, was equal (Figure 2). Over the whole compres- sion pressure range, higher tensile strength values were achieved than with the formulation containing microcrystalline cellulose.

It seems that the main difference of Formulations 1 efficiently allowed the solidification of the crospovidone particles. The ejected solid fractions of all formulations (as a given compact pressure), were very similar (Figure 6). The same applies for bondability (Figure 6). Only Kollidon® CL showed slightly lower values, which was the reason for the lower tensile strength of the tablets containing this disintegrant.

Tablets of Formulation 2 containing Kollidon® CL-M disintegrated very slowly (Figure 4). This indicated that the micronisation process reduced the product’s capability to act as a strong disintegrant. All other grades accelerated drug release distinctly. Greatest disintegration times were found for the formulation containing Kollidon® CL, with results independent of tensile strength.

Without pointing out is the fact that a crospovidone content of merely 3.0% could decisively change tablet’s compressibility and bondability, eventually leading to very different tablet tensile strength values. In formulation development, it is therefore essential to select the most appropriate grade.

CONCLUSION
The individual crospovidone grades were added with a concentration of only 3.0% to the tabletting formulation. Nevertheless, a great impact of these in- gredients on tabletability, tensile strength, and disintegration time could be observed.

The effect of crospovidone on the tensile strength of the tablets depended on the additional ingredients present in the formulation. Microcrystalline crospovidone cellulose most likely consumed compression energy and prevented the solidification of crospovidone. As a result, tablet strength decreased with an increasing particle size of crospovidone. Therefore, grades of small particle size (Kollidon® CL-F or Kollidon® CL-SF) are recommended for those tablet- ing formulations.

In the present formulations containing mainly brittle ingredients, allowed a proper solidifi- cation of crospovidone during tabletting. As a result, tabletting characteristics become less affected by the particle size of crospovidone. However, fine grades (Kollidon® CL-F or Kollidon® CL-SF) led to tablets of slightly higher strength compared to coarse grades (Kollidon® CL). Nevertheless, all crospovidone grades can be recommended for this formulation.

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Figures 1-6: Bondability and disintegration time as a function of crospovidone particle size (single values and mean values).

Figures 7-8: Bondability and disintegration time as a function of crospovidone particle size (single values and mean values).