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Correction

Correction to: Designing Robust Tablet Formulas Resilient to Raw Material and Equipment Variations with the Aid of Design of Experiment (DOaE) Method

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The authors would like to correct an error in the original publication.

In the originally published version of this article, the positions and captions for **Figure 8** and **9** were reversed. The corrected Figure 8 and 9 are shown below:

To address the particle size impact on compressibility, we intentionally separated a complete tablet blend into three fractions of different particle size ranges using Ro-tap equipment. While this approach of sieving an entire tablet blend is not practically employed during tablet manufacture and may result in some composition differences among the sieve fractions collected, it was used to quickly understand the impact of particle size by creating drastic changes to the overall blend. The compression profiles of these three fractions are shown in Figure 8. For the high and medium particle size ranges, the compression profiles are very similar within the compression force range 5 to 35 kN. These results indicate that the compression profile may not change if the particle size of the whole formula is above 170 microns. However, once the particle size is below 149 microns, the blend becomes less compressible and requires greater compression force to achieve the same harness compared to the blends produced with larger particles. Figure 8 demonstrates that particle size variation could potentially shift the compression profile, resulting in unexpected changes to tablet properties.

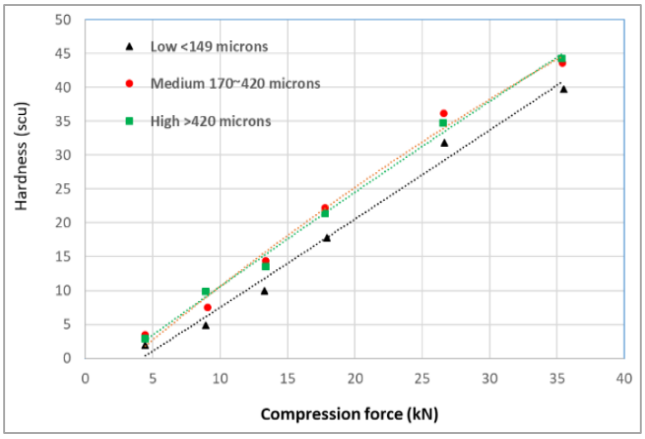

Figure 8. *The compression profiles of the same formula but containing different grades of microcrystalline celluloses (MCC) from Asahi Kasei.*

To ensure consistent compressibility of tablet formulations, particle size of all ingredients should be controlled in an acceptable range and an adequate amount of a binder material like microcrystalline cellulose (MCC) may be added to compensate for variation of raw materials. MCC is available in many grades with different physical properties. Three grades

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of MCC with different particle sizes, bulk densities, and morphologies from Asahi Kasei were evaluated and their physical characterization is shown in Table 2. UF-711 and KG-1000 grade MCCs have a similar particle size about 50 μm, but they have different bulk densities and particle morphologies. KG-1000 are needle-shaped particles and expected to show a relatively poor flowability in comparison with UF-711, which is more spherical with a porous structure. PH-102 has a relatively large particle size of about 90 μm and the highest bulk density. The particles of PH-102 are spherical and hard, which may contribute to higher bulk density. Each grade was evaluated with the same concentration of MCC in a tablet formulation. The compression profiles of the formulas are shown in Figure 8. The formula with UF-711 MCC is the most compressible, followed by KG-1000 and PH-102, respectively. The compressibility differences are induced by the particle size and particle morphology differences among the grades of MCCs. PH-102 has been widely used in various formulas due to its lower cost and good flowability; however, its capability for enhancing compressibility is limited in comparison with the smaller particle sized MCC. Although both UF-711 and KG-1000 are more compressible than PH-102, the compressibility improvement observed with PH-102 was sufficient in this formulation and thus it was chosen for further evaluation of MCC concentration impact on compressibility. The compression profiles generated with the Carver press are shown in Figure 10, including the original formula, the optimized formula described in section 3.1, and the further enhanced formulas with 10 wt% and 20 wt% PH-102 MCC. The optimized formula is very compressible in comparison with the original formula, and they contain the same ingredients with slightly different concentrations. The compressibility was further improved with the addition of MCC to the optimized formula. The compression data demonstrate the power of the optimization process through DOE, as compressibility was dramatically improved without adding new ingredients. Addition of MCC as a dry binder resulted in even further improvements to the product.

Table 2. *Microcrystalline Cellulose (MCC) used in the study [12].*

Grade	Average particle size (μm)	Bulk density (g/cm^3)	Particle morphology
UF-711	50	0.22	Porous, spherical
KG-1000	50	0.12	Needle-shaped
PH-102	90	0.30	Spherical, hard

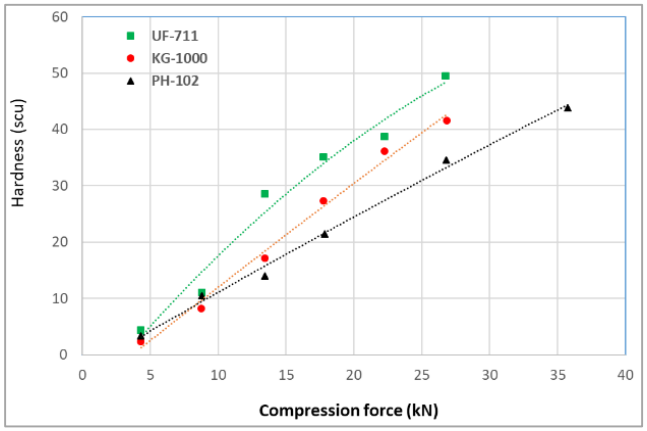

Figure 9. *The compression profiles of the same formula blend sieved into three fractions of different particle size ranges.*