cellulosic dry binders in direct compression and roll compaction: effect of particle size and mechanical properties on tablet performance

Amol Batra[1], Ronald Deeter[1], Michael Kogan[1], Anthony Sosnowik[1], Vivian Bi[1], Daniel Sieber[2], Christian Muehlenfeld[2], Tom Dürig[1]
[1]Ashland Specialty Ingredients, Wilmington, DE 19808, USA; [2]Ashland, Pharmaceutical R&D, Düsseldorf, Germany

introduction

Dry binders play a crucial role in ensuring an acceptable tablet hardness and low friability in direct compression (DC) and roll compaction / dry granulation (RCDG) processes. Dry binders are often cellulosic polymers, e.g. hydroxypropylcellulose (HPC). HPC behavior is dominated by high levels of plastic deformation and high axial recovery (i.e., HPC is a visco-elastic material). It's compactibility and plasticity increase with lower molecular weight (MW) and particle size[1]. This study was performed to investigate the suitability of Klucel EXF ultra HPC in DC and RCDG, a recently launched highly compressible dry binder, with a very fine particle size and low MW.

materials and methods

Low molecular weight Klucel™ EXF HPC and Klucel™ EXF Ultra HPC with fine and ultrafine particle size, respectively, were manufactured by Ashland Specialty Ingredients, G.P., Wilmington, USA. Avicel PH 102 (MCC PH 102) was received from DuPont™ Nutrition and Health, Kansas, USA, and Nisso SSL SFP (HPC SSL SFP), was obtained from Nippon Soda Co., Japan.

laser diffraction particle size analysis

Particle size analysis was performed using a Mastersizer 3000 (Malvern Panalytical, UK) laser diffractometer.

tablet fracture test

Force-displacement curves for pure polymer tablets were obtained with an Instron® 5965 Universal Testing System (Instron®, Massachusetts, USA) using a 5 kN load cell with a crosshead speed of 0.5 inch/min.

direct compression

For direct compression formulation, acetaminophen (80% w/w) was blended with MCC PH 102 (18% w/w) and the selected binder (1.5% w/w) in a V-blender for 10 minutes. Magnesium stearate (0.5% w/w) was added to the blend as a lubricant and blended for 2 minutes. 400 mg tablets were compressed at four different compaction forces of 10, 15, 20, and 25 kN using a STYL'one compaction simulator (Medelpharm®, France) simulating a Manesty Beta press operating at 67 rpm.

roll compaction

For the dry granulation formulation, metformin HCl (75.8% w/w) was blended with mannitol (17.8% w/w) and binder (6% w/w) for 10 min in a GMX-Lab Mini high shear mixer (Freund-Vector® corporation, USA). Roll compaction was performed using a TFC Lab Micro roll compactor (Freund-Vector® corporation, USA) at a feed screw speed of 30 rpm, a roll speed of 2 rpm, and a roll pressure of 30 bar. Ribbons were milled through an 850 µm sieve and granules blended with 0.4% w/w magnesium stearate before compaction. Tablets with a weight of approx. 660 mg were compressed using a STYL'One® compaction simulator (Medelpharm®, France) simulating a Manesty Beta Press operating at 37 rpm.

tablet breaking force and friability

After storage for 48h, breaking force of tablets was evaluated using diametrical tablet hardness tester and friability was determined using USP method.

results & discussion

mechanical properties of polymers

HPC SSL SFP and Klucel™ EXF Ultra HPC have a comparable particle size distribution. The median (D_{50}) particle size measured by laser diffraction is an important distinctive parameter of a dry binder, which is also an indication of the to the specific surface area.

table 1. Particle size distribution for cellulosic binders.

binder	D_{10} [µm]	D_{50} [µm]	D_{90} [µm]
Klucel™ EXF Ultra HPC	6	23	55
Klucel™ EXF HPC	23	68	200
HPC SSL SFP	8	20	50
MCC PH 102	35	110	225

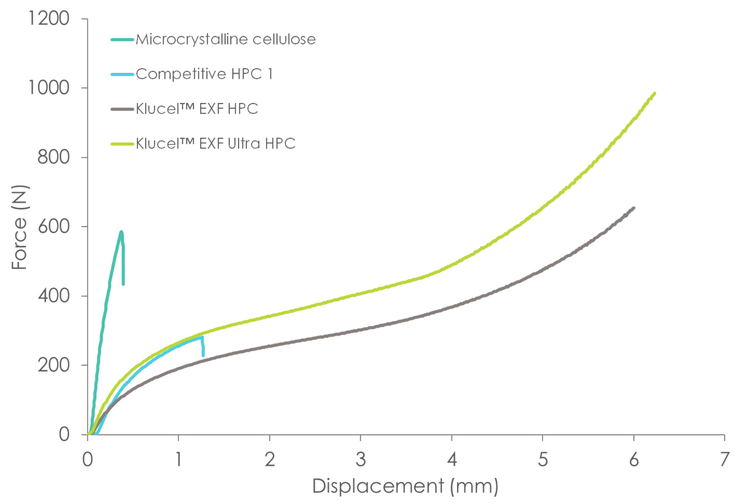

Figure 1. Force-displacement curves.

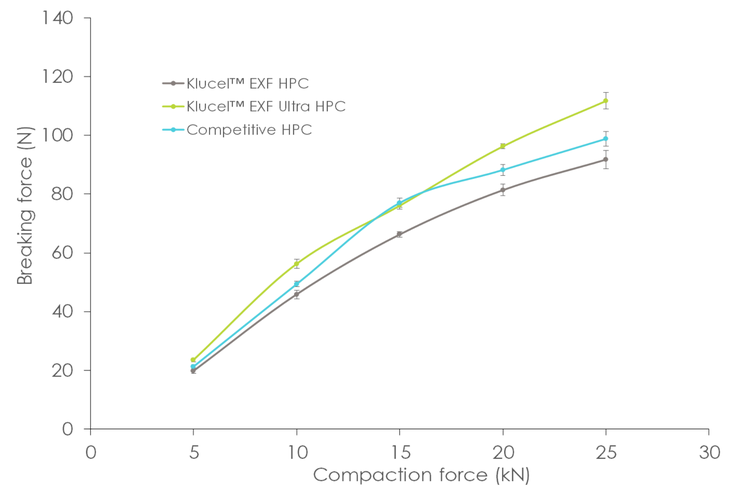

Figure 2. Tablet breaking force of cellulosic polymers with different particle size.

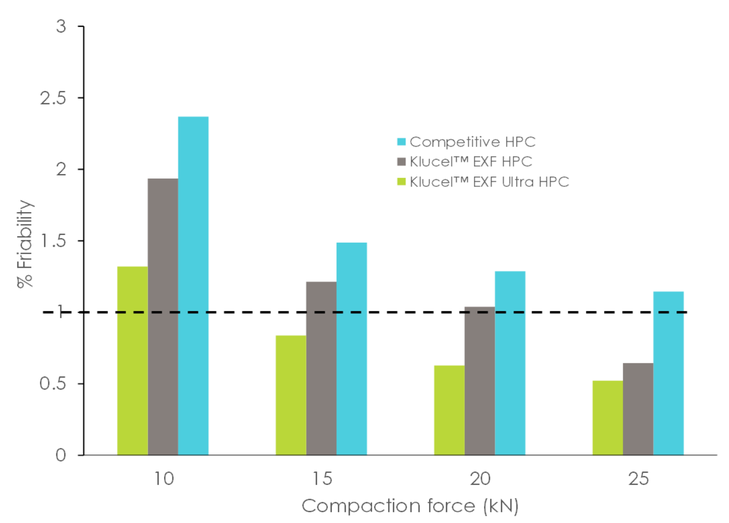

Figure 3. Friability of tablets using different cellulosic binders.

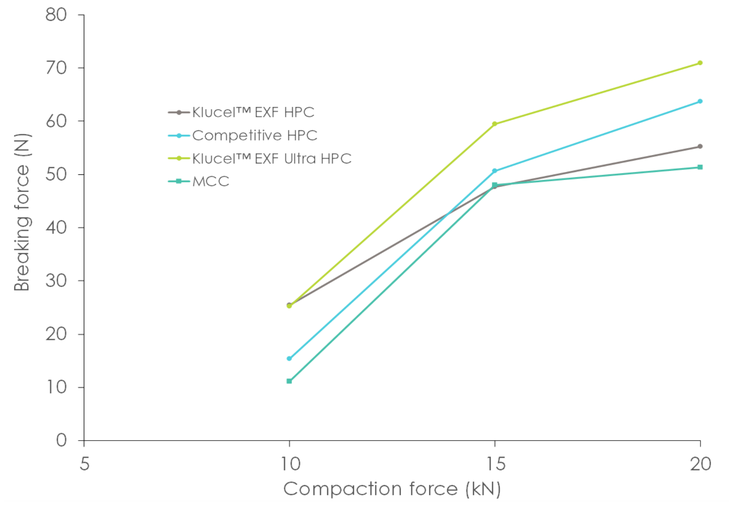

Figure 4. Tablet breaking forces of roll compacted tablet formulations.

Binders should also show substantial plastic deformation[2]. The force displacement curves for the pure polymer tablets show, that despite the comparable particle size of HPC SSL SFP and Klucel™ EXF Ultra HPC, Klucel™ EXF Ultra HPC has higher plasticity and toughness, indicated by the AUC of the force displacement curve (figure 1).

direct compression

The effect of different binders on tablet breaking forces can be seen in figure 2. Klucel™ EXF Ultra HPC provided the highest tablet strength at all four compaction forces and provided the lowest friability at all four compaction forces (figure 3). Tablets with HPC SSL SFP did not pass the friability test at all compaction forces.

roll compaction

The effect of different binders on tablet breaking forces can be seen in figure 4. All binders provided acceptable tablet breaking forces in the range of 15 kN and 20 kN compaction forces, however, Klucel EXF ultra HPC gave the highest tablet breaking force.

Friability values were below 1% for Klucel EXF ultra HPC at all compaction forces, while other dry binders resulted in more friable tablets (data not shown).

conclusion

This work demonstrates that among all cellulosic dry binders evaluated, Klucel™ EXF Ultra HPC led to highest tablet breaking forces and lowest friabilities. The increase in compactibility and plasticity can be correlated with the finer particle size compared to other grades of HPC.

references

1. Picker-Freyer, K.M. and Dürig, T. AAPS PharmSciTech 8 (4), Article 92 (2007).

2. Kristensen, HG. Binders. In: Swarbrick J, Boylan JC, eds. Encyclopedia of Pharmaceutical Technology. vol. 1. New York, NY: Marcel Dekker Inc; (1988)

Ashland™ always solving