

benecel™ PH DC hypromellose (HPMC)

benecel™ DC HPMC is a surface-modified, co-processed excipient designed for improved performance over benecel™ CR HPMC in direct compression and continuous manufacturing controlled-release applications.

key features and benefits

- Improved powder flow
- Improved content uniformity
- Improved compactibility
- Dissolution profiles comparable with controlled-release grades of HPMC
- Reduced processing time and production costs

direct compression

Direct compression is a preferred process for manufacturing tablets because it is simple and cost effective. However, direct compression of controlled-release formulations has traditionally been a challenge due to limitations of controlled-release excipients which are used at high levels and can result in poor compressibility and low final product content uniformity.

Typical controlled-release polymers have a fibrous nature, small particle size, strong inter-particle cohesion and surface charge, which may lead to poor flow in pharmaceutical unit processes. Formulators often use a granulation step to overcome these challenges. The improved powder flow of Benecel™ DC HPMC allows for the production of formulations without the use of an extra granulation step.

improved powder flow

Improved powder flow for Benecel™ DC HPMC was shown using an annular shear-cell that measures the flow rate of a sample. A higher flow rate index indicates a freer flowing material. The shear cell testing predicts that formulations containing Benecel™ DC HPMC will flow better than formulations containing Benecel™ CR HPMC (figure 1).

figure 1: improved powder flow of formulations with low and high drug loading (formulation 1 = 5% metformin, formulation 2 = 50% metformin)

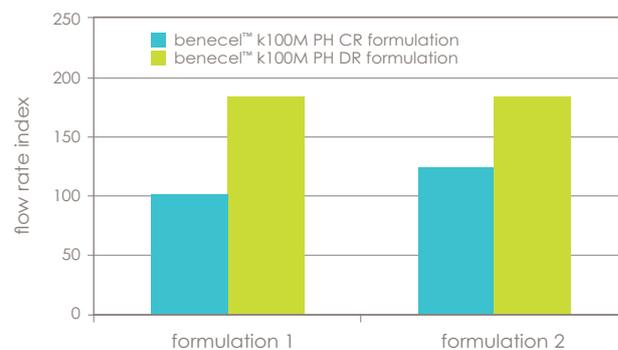


figure 2: improved compactibility of metformin formulation with low drug loading (5%)

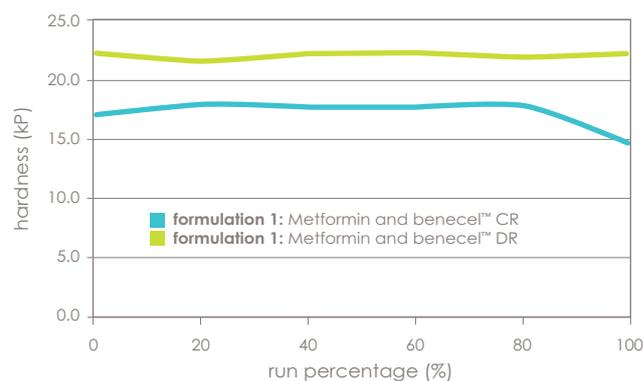


figure 3: improved compactibility of formulation with high drug loading (50%)

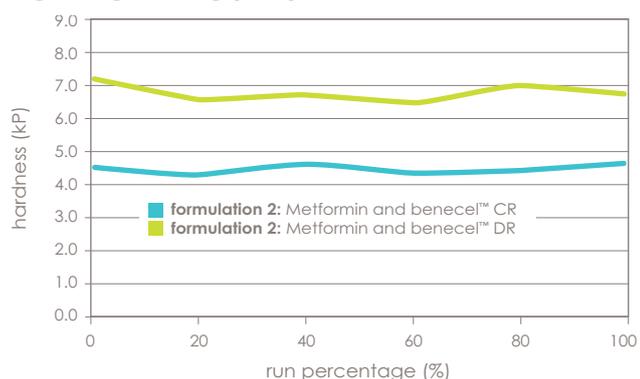
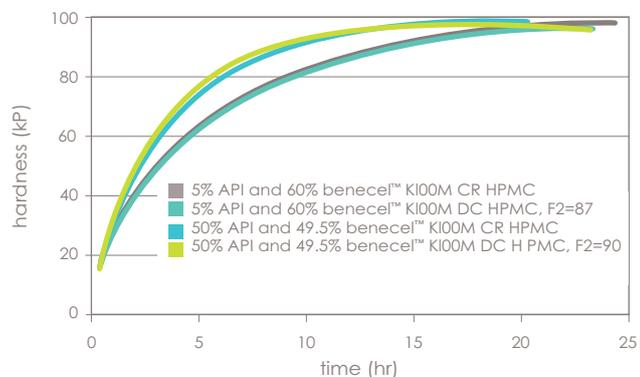


figure 4: Similar release profiles as HPMC CR grades in direct compression applications with low and high drug loading create the opportunity for drop-in replacement.



cost savings

Using these grades in direct compression applications can provide a significant cost savings over traditional wet-granulation applications because of the simplified manufacturing process.

continuous manufacturing

Continuous manufacturing of pharmaceutical products is increasingly gaining in importance in the pharmaceutical industry. Unit operations such as blending, granulation, tableting, and film coating which would have been separate in traditional batch processing are merging to form a single line, enabling a higher degree of production flexibility and lower production costs. There are some challenges with this method related to material processing including powder flow/flow stagnation in hoppers/bins/bulk containers, and segregation. Ashland has the solution to your continuous manufacturing challenges, BeneceI™ DC HPMC.

improved powder flow

Typically, poor flow can pose significant challenges to a continuous manufacturing process, such as starving downstream equipment, production delays, and the requirement for frequent operator intervention to reinitiate flow.

Since precise and reliable powder feeding is required to attain the critical quality attributes of pharmaceutical products, loss-in-weight feeders are typically employed. A lower drive command (CMD) indicates how much of the controller output is used to deliver in percentage. The lower the percentage, the better the flow of the material in the hopper. Flow results (figures 5 and 6) using a K-Tron loss-in-weight feeder (LIW) demonstrate the improved feeding performance of BeneceI™ DC HPMC as indicated by a lower CMD% at both feed rates of 2 kg/h and 12 kg/h. Additionally, BeneceI™ DC HPMC had a lower standard deviation at both feed rates indicating a more consistent feed compared with BeneceI™ CR HPMC.

figure 5: CMD% versus net weight in hopper at 2 kg/h

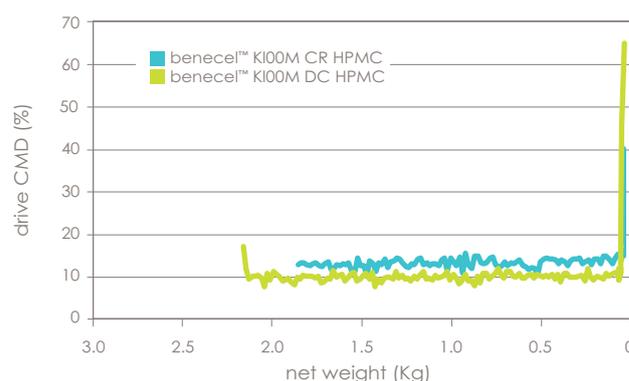
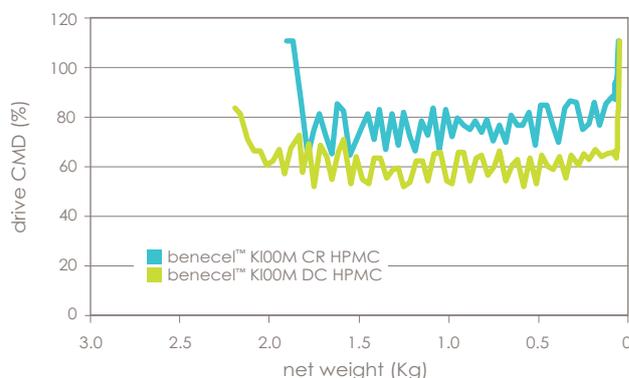


figure 6: CMD% versus net weight in hopper at 12 kg/h



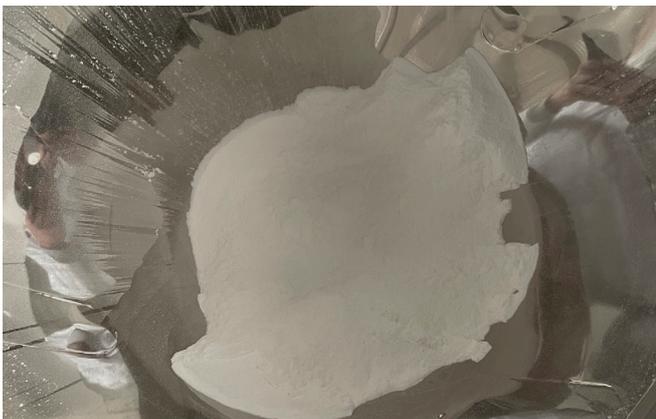
At both 2 kg/h and 12 kg/h BeneceI™ DC HPMC demonstrated lower average CMD% and CMD standard deviation indicating improved feeding performance.

Improved powder flow is also important for refill processes, especially in continuous manufacturing. Having to stop and manually refill material that bridges or creates a rathole can be extremely problematic for a continuous process that is designed to run constantly without any interruption or where accessing the powder would be very challenging because of the sealed and contained nature of the equipment. Overall, the better flowability of Benecel™ DC HPMC also applies to more consistent refills of gravimetric feeders, avoiding the complications of acquiring a “rathole” in the powder inside the bulk container and is eventually a significant advantage by itself (images 1 and 2).

images 1 and 2: vacuum assisted powder refill from intermediate bulk containers (IBC) in a continuous manufacturing process.



Benecel™ CR HPMC shows erratic flow and forms a rathole quite soon.

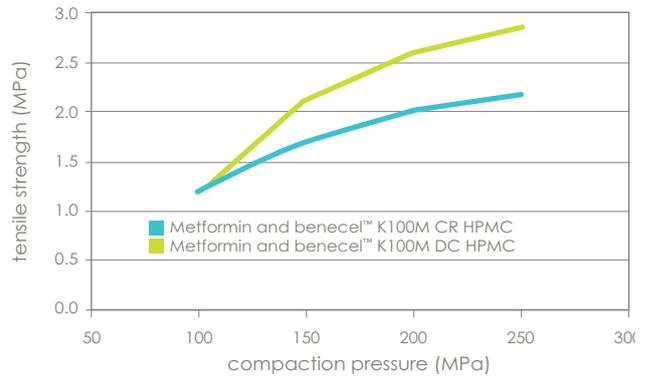


Benecel™ DC HPMC exhibits significant powder flow improvements and does not show any flow issues at all.

improved compactibility

Figure 7 shows the results from an application study of a metformin HCl (METF) formulation, produced using continuous wet granulation. Formulations containing Benecel™ DC HPMC show a significant increase in tablet tensile strength, especially at higher compaction pressures.

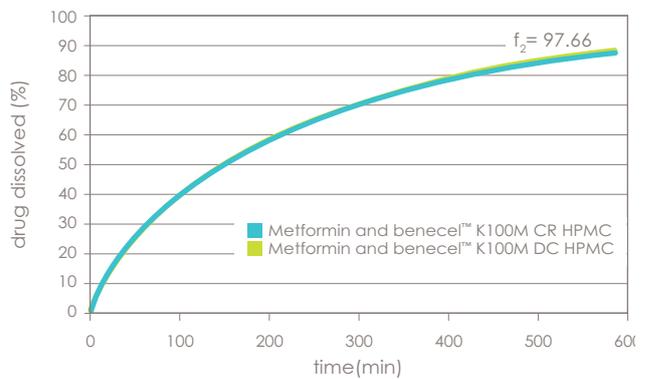
figure 7: tableability plots for formulations of metformin HCl and 35% Benecel™ HPMC (CR or DC). Tablets with higher than 1 MPa tensile strength were considered as robust and strong.



dissolution profile consistent with standard CR grades

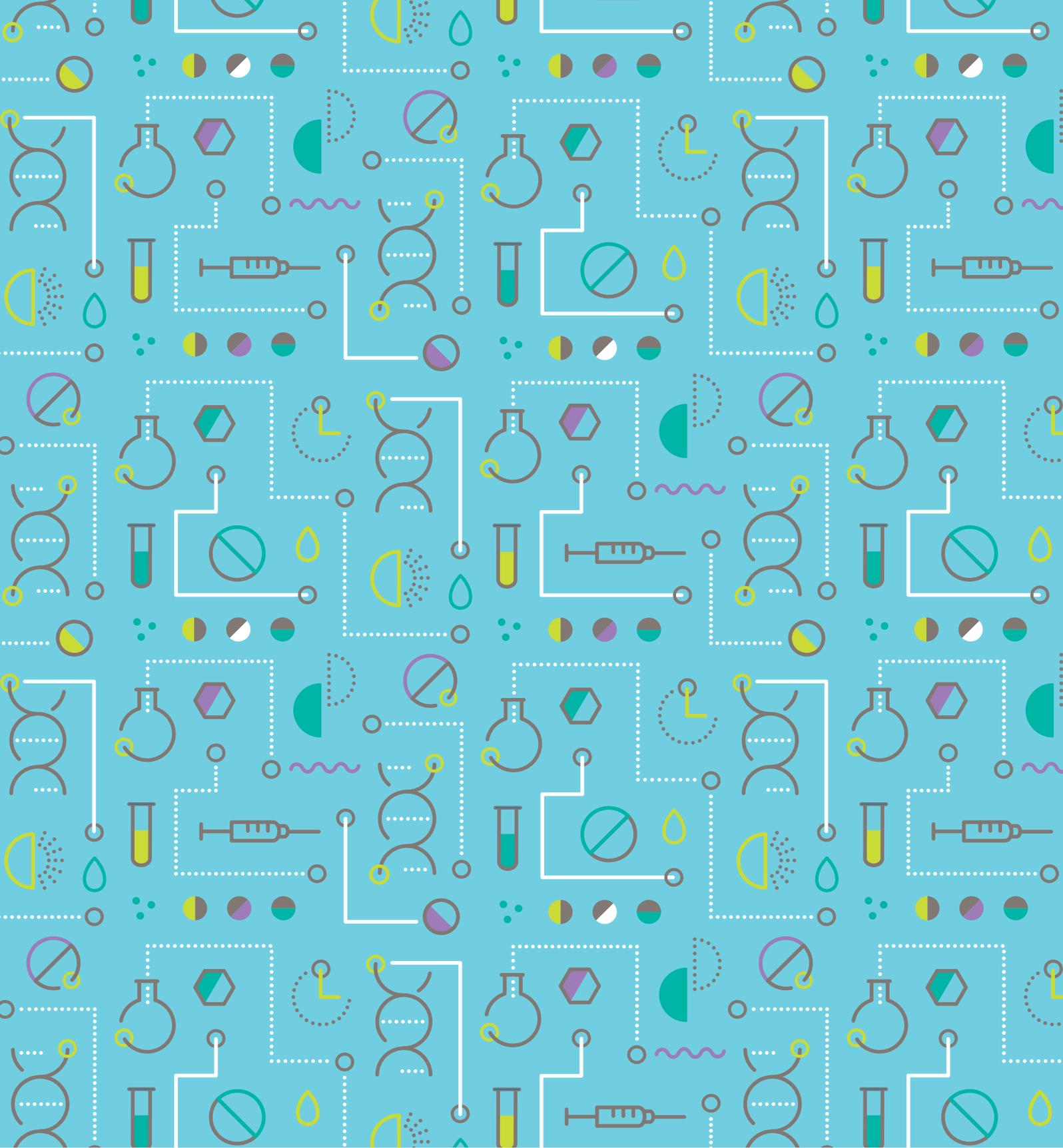
Replacing Benecel™ CR HPMC with Benecel™ DC HPMC (of the same molecular weight) has no influence on drug dissolution and can be considered as similar as indicated by an f_2 factor of 97.66 (figure 8). The f_2 factor measures the closeness between two dissolution profiles. FDA has set a public standard of f_2 value between 50–100 to indicate similarity between two dissolution profiles.

figure 8: Consistent drug dissolution. Example formulation: Metformin HCl (METF) with 35% Benecel™ DC or Benecel™ CR HPMC (among other excipients). dissolution similarity was confirmed using the similarity factor, f_2 , that measures the closeness between two dissolution profiles.



summary

Benecel™ PH DC grades of HPMC are controlled-release excipients that offer better powder flow and compaction properties than Benecel™ CR HPMC grades for direct-compression and continuous manufacturing applications. These grades are an ideal choice for high-quality dosage forms.



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