Klucel™ HPC

in hot-melt extrusion applications / controlling drug solubility in immediate- and sustained-release tablets

Advantages of hot-melt extrusion (HME) over other processes include continuous processing efficiencies (high throughput, low cost, no solvents or water required), improved product uniformity, and enhanced solubility due to molecular dispersion of the active. HME can be used to make granules that are then tabletted or alternative dosage forms such as thin films (Figures 1 and 2).

In this application, molten thermoplastic polymers function as thermal binders during extrusion and upon cooling and solidification. Since most drugs are thermally sensitive, it is critical that the polymer can be processed at a relatively low temperature.

Klucel hydroxypropylcellulose (HPC) is the premier thermoplastic polymer for hot melt extrusion applications. This family of products is fully approved for pharmaceutical and food use and can be processed without plasticizers at significantly lower temperatures than other polymers (Table 1).

Low molecular weight grades such as Klucel EF and ELF can be used to enhance the solubility of low-soluble, Class II drugs. Klucel acts as a matrix in which drug molecules are immobilized and dispersed in a nanocrystralline or amorphous state.

Higher molecular weight grades (Klucel MF) can be used to make controlled-release tablets that are smaller, stronger, and less porous compared to those prepared via wet granulation. This allows a gel layer to be formed, retarding the dissolution of highly soluble drugs like Metformin (Figure 3).

Features and Benefits:

- Increased formulation stability – nonionic polymer that does not require plasticizer
- Low temperature processing
- Enhanced solubility of low soluble actives
- High molecular weight grades for sustained release of highly soluble drugs
- Stronger, smaller, and less porous tablets compared to wet granulation
- Widest pharmaceutical and food regulatory approval compared to other thermoplastic polymers

Figure 1. Extruded strands of nifedipine, Klucel and MCC which have been milled and compressed into tablets.

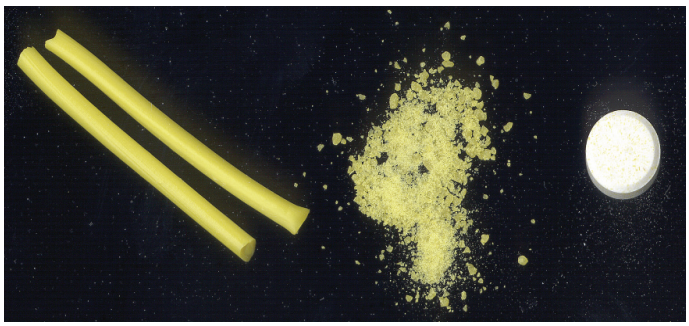


Figure 2. Extruded orange oil films using a flat die which have been cut into various shapes.

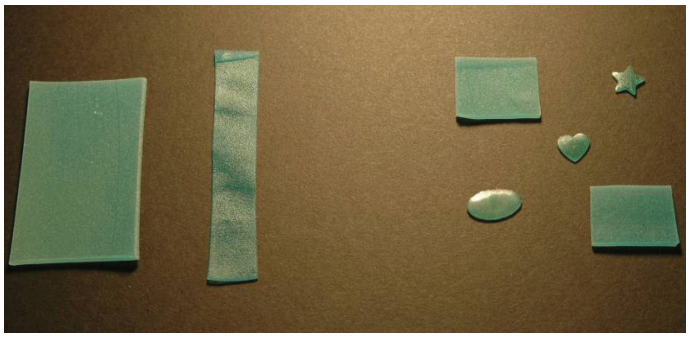


Table 1. Typical glass transition temperatures of polymers commonly used in hot-melt extrusion.

Polymer	Tg*
PVP	165°C
Methylcellulose	150°C
HPMC (USP 2910 Type)	140°C
HPMCAS	120°C
EC	120°C
Copovidone (PVA-PVP)	115°C
Methacrylic acid copolymer (E-type)	125-160°C 50°C
HPC	**0°C**
PEO	-30°C

The Ashland Research Center in Wilmington, Delaware is equipped with a Leistritz ZSE 18-mm twin-screw extruder that can be used for customer trials and new product development. We also have wide-ranging capabilities for thermal property analysis.

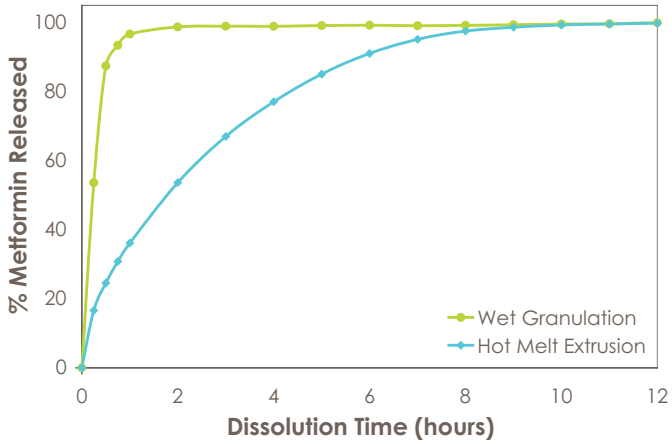
Please contact your local sales representative or visit us at ashland.com/pharmaceutical to learn more about Klucel HPC and its benefits in hot-melt extrusion.

Table 2. Klucel HPC – affects of molecular weight on thermoplasticity, processing temperature and mechanical properties.

Type	MW	Processing Temp. (°C)*	Melt Viscosity	Finished Product Properties	Solubility Rate
HF	1,150,000	205	Highest	Highest tensile strength Lowest modulus	Slowest
MF	850,000	190			
GF	370,000	176			
JF	140,000	160			
LF	95,000	150			
EF	80,000	137			
ELF	40,000	120	Lowest	Lowest tensile strength Highest modulus	Fastest

* approximate: no plasticizers or other additives

Figure 3. Dissolution profile of extruded and wet granulated 75% Metformin / 25% Klucel MF tablets.



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