Klucel™ hydroxypropylcellulose

Physical and chemical properties

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1. Introduction

Klucel hydroxypropylcellulose (HPC) is a nonionic water-soluble cellulose ether with a remarkable combination of properties. It combines organic solvent solubility, thermoplasticity, and surface activity with the aqueous thickening and stabilizing properties characteristic of other water-soluble cellulose polymers available from Ashland. Klucel HPC films are flexible without plasticizers and non-tacky at high humidity.

The information presented here describes the physicochemical and material properties of Klucel HPC, specific for pharmaceutical applications, as developed in our research and plant facilities. Also included is information about the behavior of Klucel HPC in a number of common pharmaceutical applications. A guide to regulatory status and toxicological studies is provided for convenient reference. The Appendix gives information about the methods used for analytical processes described in this document.

To help the reader identify some of the versatile uses for this water-soluble polymer, a representative listing is presented in Table 1. Many of these uses for Klucel HPC are discussed in detail in this document. Additional technical literature is available from your Ashland sales representative by request, or from our website at ashland.com/pharmaceutical.

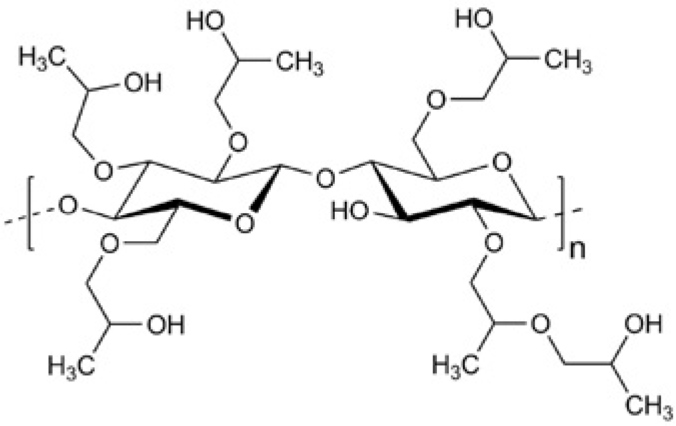
Table 1. Typical pharmaceutical uses for Klucel HPC

Klucel HPC grade	Immediate-release binder (use level, w/w)	Controlled-release matrix (use level, w/w)	Film coating (use level, w/w)
ELF Pharm	2-6%		5%
EF Pharm	2-6%		5%
LF Pharm	2-6%		5%
JF Pharm		15-35%	
GF Pharm		15-35%	
MF Pharm		15-35%	
HF Pharm		15-35%	

2. Chemistry

Klucel HPC is manufactured by reacting alkali cellulose with propylene oxide at elevated temperatures and pressures. The propylene oxide can be substituted on the cellulose through an ether linkage at the three reactive hydroxyls present on each anhydroglucose monomer unit of the cellulose chain. An idealized structure for a portion of a hydroxypropylcellulose molecule with a degree of substitution (DS) of 2.5 is given in Figure 1.

Figure 1. Chemical structure of Klucel hydroxypropylcellulose



The etherification takes place in such a way that hydroxypropyl substituent groups contain almost entirely secondary hydroxyls. The secondary hydroxyl present in a side chain is available for further reaction with the oxide, and chaining out may take place. This results in formation of side chains containing more than one mole of combined propylene oxide. The added hydroxypropyl group contains a hydroxyl group that also can be etherified during preparation of hydroxypropylcellulose. When this occurs, the number of moles of hydroxypropyl groups per glucose ring, or moles of substitution (MS), can be higher than 3.

3. Grades and Viscosity Types

Klucel HPC is produced in several grades. Seven viscosity types are available, designated as EL, E, L, J, G, M and H. Product designation is a combination of viscosity type followed by particle size and market segment designation, for example: Klucel HF Pharm HPC; in which the H designates the grade and the F Pharm designates the market as Pharmaceutical. Fine particle size is indicated by an X (e.g., Klucel MXF Pharm). Some typical viscosity and molecular weight values are given in Table 2.

Table 2. Klucel HPC Viscosity and Molecular Weight

Grade	Concentration in Water/ Brookfield Viscosity (25°C, LVF, Moisture Free; mPa·s)				Molecular Weight (Daltons)
	1%	2%	5%	10%	
HF Pharm	1500–3000				1,150,000
MF Pharm		4000–6500			850,000
GF Pharm		150–400			370,000
JF Pharm			150–400		140,000
LF Pharm			75–150		95,000
EF Pharm				300–600	80,000
ELF Pharm				150–300	40,000

*Measured by GPC-size exclusion chromatography.

4. Physical Properties

Klucel HPC is a white to slightly yellow colored, odorless and tasteless powder. Some selected physicochemical properties for Klucel HPC are listed in Table 3.

Table 3. Selected Physicochemical Properties for Klucel HPC.

Test	Plant Specification
Particle size	**Regular grades**, total through 595 µm: 85 to 100%; on 841 µm and above: <1%; on 595 µm and above: <15%. **Fine grades**, total through 250 µm: 99.9%; through 177 µm: <90%; through 149 µm: <80%.
Moles of substitution	2 to 4.1
pH	5 to 8
Residue on ignition, %	≤0.8
Softening temperature, °C	100 to 150
Burnout temperature, °C in N_2 or O_2	450 to 500
T_g*, °C	0 and 120
Lead, ppm max	10
Heavy metals, ppm max	20
Silica, %	≤0.6
Assay of hydroxypropoxy groups, %	53.4 to 80.5

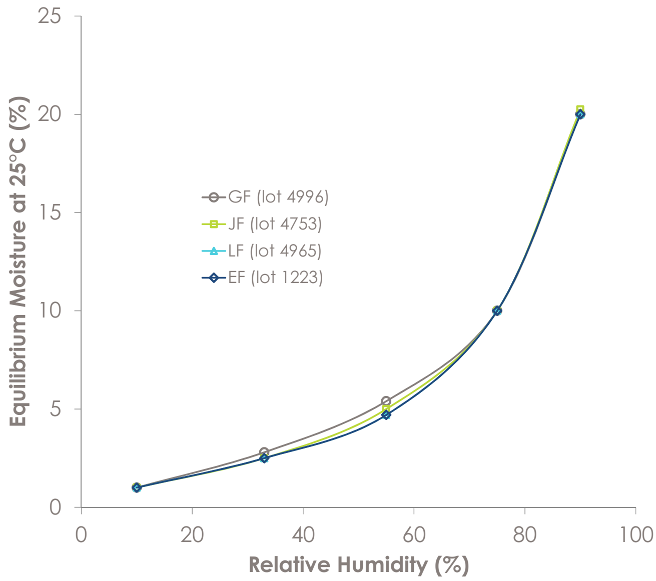
* Klucel HPC is a special polymer that can show dual T_g because it has a beta transition.

4.1 Moisture Absorption

Klucel HPC absorbs moisture from the atmosphere, as do other water-soluble materials. The amount absorbed depends on relative humidity and temperature of the environment. As packed, moisture content of all grades does not exceed 5% by weight, and is generally between 2% and 3%. It is suggested that Klucel HPC be stored in tightly closed containers to prevent any increase in moisture content.

Klucel HPC has a low affinity for water. At any given relative humidity (RH), it has a lower equilibrium moisture content than most other water-soluble polymers. Typical values for Klucel HPC are shown in Figure 2.

Figure 2. Equilibrium Moisture Contents of Selected Grades of Klucel HPC



4.2 Dispersion and Dissolution

Klucel HPC is soluble in water at room temperature. It is insoluble in water above 45°C. It is readily soluble in many organic solvents, hot or cold. The best methods for preparing solutions of Klucel HPC in water or organic solvents are described in the following paragraphs. Note: As a general aid to preparation of solutions, the following points should be kept in mind:

- Wherever possible, Klucel HPC should be put into solution before adding other soluble ingredients. Other dissolved materials compete for the solvent and slow the solution rate of Klucel HPC. In this regard, soft water is preferred to hard water for solution preparation.
- Klucel HPC is less soluble in hot water than in cold. In organic solvents, application of heat speeds the solution rate.

4.2.1 In Water

Most soluble polymers have a tendency to agglomerate, or lump, when the dry powder is first wet with solvent. Hydration of the outer surface of a particle, or an agglomeration of particles (lump), results in the formation of a viscous gel layer that inhibits wetting of the inside materials. The faster the rate of hydration of the polymer, the more quickly the gel layer will be developed, and the greater the tendency for lumping as the dry powder is added to the solvent.

Klucel HPC hydrates somewhat slowly, and lumping can be avoided during solution preparation if the recommended procedures are followed. Lump formation should be avoided, as this can greatly increase the time required to prepare homogeneous solutions. To prepare lump-free, clear solutions of Klucel HPC in the shortest time, specific methods are recommended. The preferred method involves pre-slurrying the powder in a nonsolvent, such as hot water or glycerin, prior to addition to the main volume of water.

In the first step, prepare a high-solids slurry by adding dry Klucel HPC powder to 6 times (or more) its weight of well agitated hot water at a temperature of 50° to 60°C. Temperature should not exceed the 60°C maximum indicated. The hot slurry must be maintained above 50°C during this presoak to ensure that there is no premature dissolving of the particles that would result in the formation of a gelatinous mass. The slurry should be stirred for a few minutes before addition to the main volume of cold water. This presoak results in a faster dissolving of particles in the second step.

In the second step, the hot slurry is diluted with cold water (room temperature or lower). Agitation is continued until all particles are dissolved and solution is completely free of gels. High-shear agitation is not necessary, and may be undesirable because of the tendency for foaming and air entrainment. In this dissolving step, the time factor is more important than high shear when it comes to ensuring complete solution of all gel particles.

Dissolving periods of 10 minutes or more may be required, depending on solution concentration and viscosity type being used. Solutions of lower viscosity Klucel HPC types at low solids concentrations require the shortest time for preparation.

Additional dispersion and dissolution methods are listed in the Appendix (Methods 2 and 3). Typical viscosities of various grades of Klucel HPC in selected organic solvents are listed in Table 4.

4.2.2 In Organic Liquids

All types of Klucel HPC have excellent solubility in a wide range of polar organic liquids and give clear, smooth solutions at ambient or elevated temperatures. Klucel HPC does not precipitate in hot organic solvents; this is in contrast to its behavior in water solutions. Generally, the more polar the liquid, the better the solution. Methanol and ethanol, propylene glycol and dioxane are some of the best organic solvents for all types of Klucel HPC.

The molecular weight of the type of Klucel HPC can have a marked effect on solution quality in an organic liquid that is a borderline solvent for Klucel HPC. G viscosity types are intermediate in viscosity (i.e., molecular weight) between high viscosity H types and very low viscosity E types. In comparison with G viscosity types, lower viscosity types are more readily soluble and may give better solutions. The higher viscosity types may give slightly inferior solutions in some of the liquids listed in Table 4. For example, acetone gives excellent solutions with the E viscosity types, but acetone solutions of the G viscosity types are hazy and somewhat granular.

Solution quality in borderline solvents often can be greatly improved through the use of small quantities of cosolvents. Water, methanol, and ethanol function as excellent cosolvents and, in many cases, are effective in relatively small quantities (5% to 15%). (See Table 4.) For example, methylene chloride is a borderline solvent for high H viscosity types, and solutions are granular. Addition to the system of 10% methanol results in a smooth solution of nominal viscosity (5,000 mPa·s at 1% solids).

Elevated temperatures improve the solvent power of organic liquids for Klucel HPC. Heating of solvents will (a) reduce viscosity, (b) increase rate of solution, and (c) improve solution quality in the case of borderline solvents.

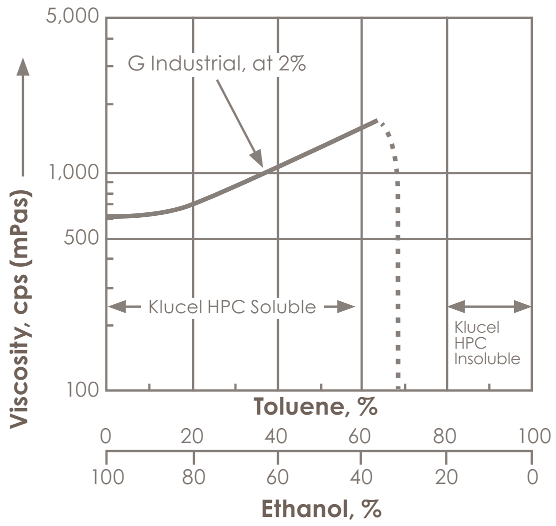
Aliphatic and aromatic hydrocarbons and petroleum distillates are nonsolvents for Klucel HPC. However, relatively large quantities of these nonsolvents can be tolerated in a solution if Klucel HPC is first dissolved in a solvent that is miscible with these nonsolvents. Figure 3 shows the effect of solvent composition on viscosity of a solution of G type in a toluene:ethanol system.

Table 4. Typical Viscosities for Various Klucel HPC Grades in Selected Solvents

	Viscosity[a] by Grade of Klucel™ HPC and Concentration (mPa·s)			
Solvent	H at 1%	G at 2%	L at 9%	E at 10%
Water	2,100	270	80	275
Methanol	800	85	25	75
Methanol:water (3:7 by weight)	–	360	–	–
Ethanol	1,600	210	65	255
Ethanol:water (3:7 by weight)	–	500	–	–
Isopropyl alcohol (99%)	[b]	[b]	145	570
Isopropyl alcohol (95%)	–	–	130	420
Acetone	[b]	[b]	50	175
Methylene chloride	4,500[b]	–	1,240[b]	14,600[b]
Methylene chloride:methanol (9:1 by weight)	5,000	–	400	–
Chloroform	–	–	2,560[b]	17,000[b]
Propylene glycol	6,000	6,640	5,020	>10,000
Ethylene chlorohydrin	470	430	310	1,110

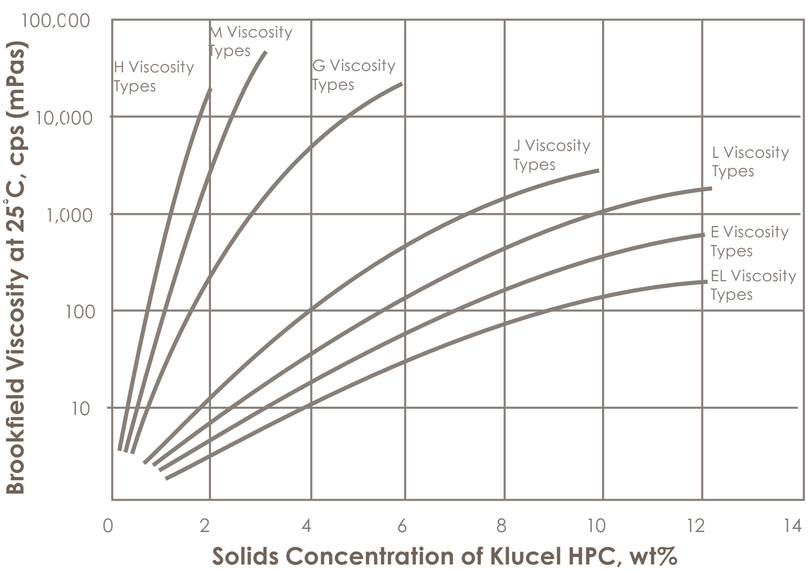
[a] Viscosities shown are presented only as typical values. Some variation in these viscosities will be obtained from lot to lot of each grade of Klucel HPC.
[b] Borderline solvent for the particular grade of Klucel HPC. Solutions are granular and may be hazy.

Figure 3. Viscosity of Klucel G HPC Dissolved in Toluene-Ethanol



In general, principles discussed for preparing water solutions apply when using organic solvents to make solutions of Klucel HPC. The methods described for preparing water solutions can therefore be used to prepare solutions of Klucel HPC in organic solvents. The preslurry method for preparation of aqueous solutions can be employed with nonsolvents such as glycerin, aliphatics, aromatics, and others. In aqueous-organic systems, the proportion of organic solvent will determine whether elevated temperature will speed or slow the rate of solution of Klucel HPC.

Figure 4. Viscosity Ranges for Various Grades of Klucel HPC



4.3 Properties of Solutions

4.3.1 Aqueous Solutions

Klucel HPC has excellent solubility in water and in many polar organic solvents. Solutions are clear, smooth, and visually free from gels and fibers. Solutions are non-Newtonian in flow, because they change in viscosity with rate of shear. However, solutions display little or no thixotropy. Because Klucel HPC is used extensively to modify viscosity of solutions, dispersions, emulsions, and suspensions involving water and/or organic solvents, a discussion of some of the factors that affect solution viscosity follows.

4.3.1.1 Effect of Concentration and Viscosity Type

The viscosity of aqueous solutions of Klucel HPC increases rapidly with concentration and becomes almost a straight-line relationship when plotted on a semi-log basis (see Figure 4). The bands in Figure 4 indicate the viscosity range within which each type is supplied. (See also Table 2, page 6)

At room temperature, solutions of Klucel HPC can be prepared in a wide range of viscosities, depending on concentration and viscosity type used. Because solutions are non-Newtonian, it is essential to standardize viscosity determination methods. The method used in the control laboratory at Ashland is described in the Appendix. Also refer to the USP <911> method for details.

4.3.1.2 Rheology

Solutions of Klucel HPC are smooth flowing and exhibit little or no structure or thixotropy. However, solutions are pseudoplastic under conditions of high rates of shear and will show a temporary decrease in viscosity while under shear. Viscosity returns to the original value when shear is removed. The lower the molecular weight of Klucel HPC and the lower the shear rate, the less this decrease in viscosity experienced under shear will be.

4.3.2 Effect of Temperature on Viscosity

Viscosity of an aqueous solution of Klucel HPC decreases as temperature is increased. This effect is normal for polymers in solution. This change in viscosity is illustrated in Figure 5 for H and J viscosity types. As shown, viscosity drops by about 25% as temperature is raised through 15°C. This effect is uniform up to the cloud point (precipitation temperature; 40° to 45°C).

4.3.3 Cloud Point

As already stated, Klucel HPC will precipitate from aqueous solutions at temperatures between 40° and 45°C. This precipitation is completely reversible. The polymer redissolves upon cooling the system below 40°C with stirring, and the original viscosity is restored. As the temperature reaches 40° to 45°C, this precipitation phenomenon is evidenced by cloudiness in the aqueous solution and by a marked reduction in viscosity. These effects are due to separation of the polymer as a highly swollen precipitate. The transition from dissolved to precipitated polymer takes place without the formation of a gel. The only apparent viscosity change is one of a rapid decrease, as shown in Figure 5.

4.3.3.1 Cloud Point Versus Molecular Weight

The form in which Klucel HPC precipitates from aqueous solutions depends not only on the molecular weight of the polymer, but also on other materials present in solution and whether or not stirring is employed. Low-viscosity types tend to separate as highly swollen and finely divided precipitates. High-viscosity types, particularly under agitation, may agglomerate on heating and form a stringy, rather than a finely divided, precipitate.

The precipitation temperature of Klucel HPC is increased or eliminated through the addition of organic liquids that are solvents for the polymer. This is discussed in more detail on page 15.

The precipitation temperature is lower in the presence of relatively high concentrations of other dissolved materials that compete for the water in the system. The magnitude of the lowering is dependent on the nature and concentration of the other dissolved ingredients. The data in Table 5 illustrate this effect.

Figure 5. Effect of Temperature on Viscosity of Aqueous Solutions of Klucel HPC

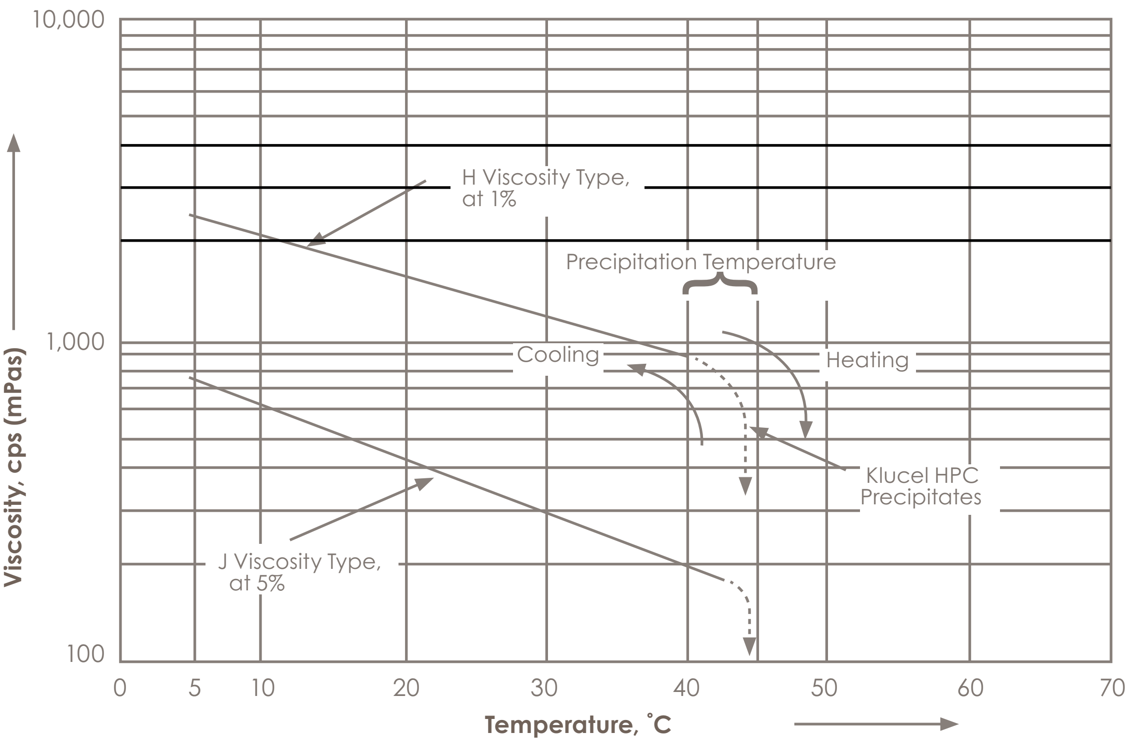


Table 5. Precipitation Temperature of Various Solutions of Klucel H HPC in Water

Ingredients and Concentration	Precipitation Temperature, °C
1% Klucel™ H HPC	41
1% Klucel™ H HPC + 1% NaCl	38
1% Klucel™ H HPC + 5% NaCl	30
0.5% Klucel™ H HPC + 10% Sucrose	41
0.5% Klucel™ H HPC + 20% Sucrose	36
0.5% Klucel™ H HPC + 30% Sucrose	32
0.5% Klucel™ H HPC + 40% Sucrose	20
0.5% Klucel™ H HPC + 50% Sucrose	7

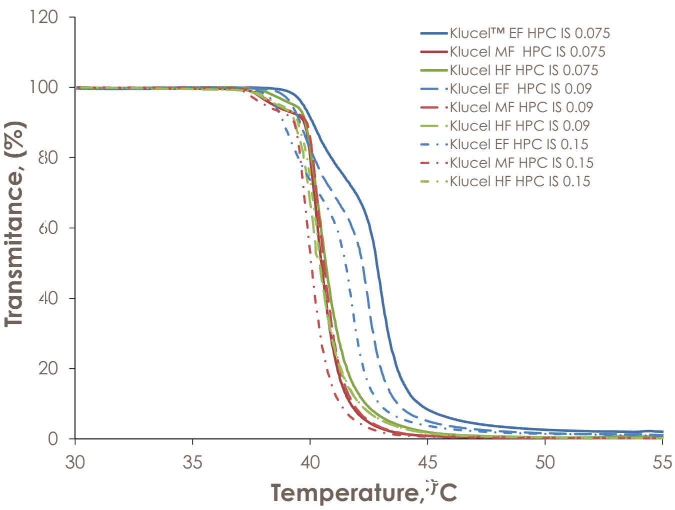
4.3.3.2 Effect of pH on Cloud Point

There was no effect of pH on the cloud point of Klucel HPC grades, as shown by Table 6 and Figure 6.

Table 6. Effect of pH on Cloud Point of Klucel HPC

Cloud Point		CP @ 96% (°C)	
Polymer	Solids	pH 1.2	pH 6.8
Klucel™ HF HPC	1%	40.5	40.2
Klucel™ MF HPC	1%	39.6	39.6
Klucel™ EF HPC	1%	40.8	40.9

Figure 6. Effect of pH on Cloud Point for Klucel EF, MF and HF HPC



4.3.4 Polymer Hydration

4.3.4.1 Effect of pH on Hydration

Klucel HPC is a nonionic polymer, and viscosity of water solutions is not affected by changes in pH (see Table 7 and Figure 7). The viscosity of solutions remains unchanged as pH is varied over the range of 2 to 11. However, where long-term solution stability is required, the solution pH is an important consideration because of degradation that can occur under highly acid or alkaline conditions, as described in the section titled Viscosity Stability, page 14.

Table 7. Effect of pH on Hydration of Klucel HPC

	Polymer	Klucel HF HPC	Klucel MF HPC	Klucel EF HPC
	Solids	0.75%	1%	4%
pH 1.2 (0.1N HCL)	Time to 90% Viscosity (min)	25.5	16.47	3.7
	Final Viscosity (mPa•s)	421.1	476.2	245.4
pH 6.8 (phosphate buffer)	Time to 90% Viscosity (min)	31.32	17.68	4.1
	Final Viscosity (mPa•s)	443.5	471.9	258.3

Figure 7. Effect of pH on Hydration for Klucel EF, EF,EF,MF and HF HPC

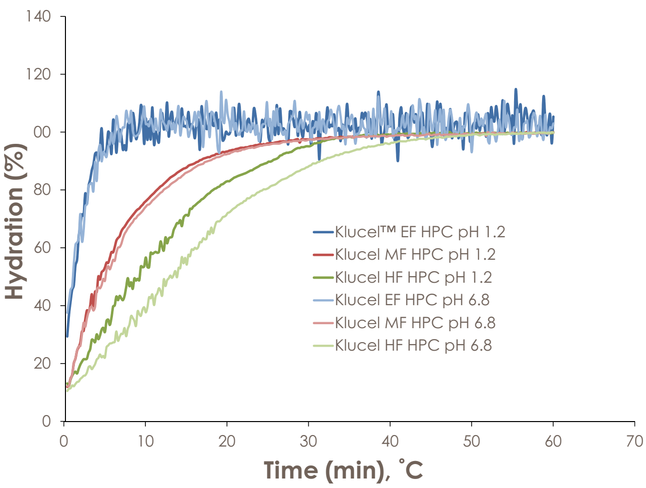
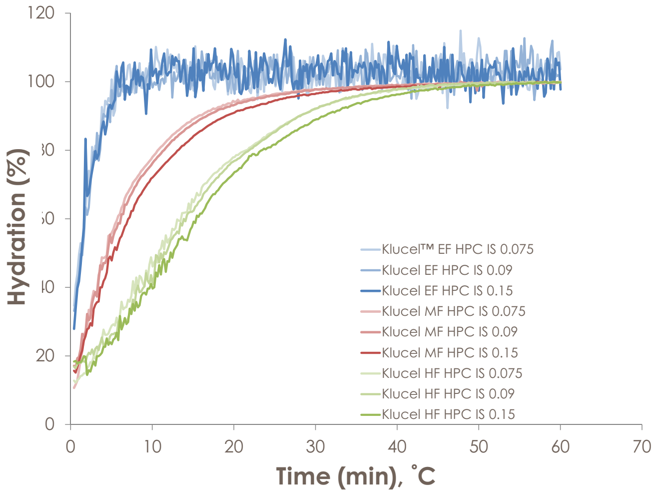


Figure 8. Effect of Ionic Strength on Hydration for Klucel EF, MF and HF HPC



The hydration/viscosity development times are very similar for all polymers at pH 1.2 and pH 6.8, with the exception of Klucel HF HPC. These data support the fact that Klucel has pH independent release profiles.

4.3.4.2 Effect of Ionic Strength on Hydration

The hydration/viscosity development times, although very similar, tend to increase with the increase in ionic strength, as shown in Table 8 and Figure 8, while cloud point tends to drop. These data also support the fact that Klucel has pH independent release profiles.

4.3.5 Aqueous Solution Compatibilities

4.3.5.1 Inorganic Salts

The compatibility of Klucel HPC with dissolved inorganic salts in aqueous solution varies according to the salt. If relatively high concentrations of dissolved salts are used, there is a tendency for the Klucel HPC polymer to be "salted out" from solution as a finely divided and highly swollen precipitate. This salting-out phenomenon generally results in some decrease in viscosity and in the appearance of cloudiness in the solution. In borderline cases, this salting out may not be immediately apparent,

Table 8. Effect of Ionic Strength on Hydration

		Ionic Strength 0.075M		Ionic Strength 0.09M		Ionic Strength 0.15M	
Polymer	Solids	Time to 90% Viscosity (min)	Final Viscosity (mPa·s)	Time to 90% Viscosity (min)	Final Viscosity (mPa·s)	Time to 90% Viscosity (min)	Final Viscosity (mPa·s)
Klucel™ HF HPC	0.75%	27.11	444.4	27.91	444.8	30.92	440.9
Klucel™ MF HPC	1%	15.47	427.86	16.68	425.52	18.86	430.11
Klucel™ EF HPC	4%	3.7	271.3	4.03	263.5	4.5	258.3

but may occur upon standing. The compatibility of G viscosity types with a number of selected salts is illustrated in Table 9.

Table 9. Compatibility of Klucel G HPC with selected salts

Salt	Salt Concentration, % by Weight			
	2	5	10	50
Aluminum sulfate	C	I	I	I
Ammonium nitrate	C	C	C	I
Ammonium sulfate	C	I	I	I
Calcium chloride	C	C	C	I
Disodium phosphate	I	I	I	I
Ferric chloride	C	C	C	I
Potassium ferrocyanide	C	C	I	I
Silver nitrate	C	C	C	I
Sodium acetate	C	C	I	I
Sodium carbonate	C	I	I	I
Sodium chloride	C	C	I	I
Sodium nitrate	C	C	C	I
Sodium sulfate	C	I	I	I
Sodium sulfite	C	I	I	I
Sodium thiosulfate	C	I	I	I
Sucrose	C	C	C	I

Key: C = compatible; I = incompatible

Tests were conducted by adding a 2% solution of Klucel G HPC to salt solutions of various concentrations. The salt concentration in the system is indicated, and the final concentration of Klucel G HPC was approximately 0.19% by weight in all cases.

4.3.5.2 Organic Materials

Klucel HPC has a wide range of compatibility with organic materials. The dual solubility of Klucel HPC permits its admixture with water-soluble, as well as solvent-soluble, resins, polymers, and organic liquids. In spite of this wide compatibility, the Klucel HPC polymer, when used in aqueous systems, may not tolerate high concentrations of other dissolved materials. The balance of hydrophilic and lipophilic properties of the polymer, which is required for dual solubility, reduces its ability to remain hydrated in the presence of high concentrations of other dissolved materials. Klucel HPC may precipitate or salt out under these conditions.

A detailed discussion of compatibility with natural and synthetic polymers follows.

Water-soluble polymers

Klucel HPC is compatible with most natural gums and synthetic water-soluble polymers. Solutions in water are homogeneous, and films cast from these solutions are uniform. The following have been tested and found to be compatible:

- Aqualon™ sodium carboxymethylcellulose (CMC)
- Natrosol™ hydroxyethylcellulose (HEC)
- Benecel™ methylcellulose (MC)
- Gelatin
- Sodium caseinate
- Polyethylene oxide
- Polyvinyl alcohol
- Sodium alginate
- Locust bean gum

Effect of blending with other water-soluble polymers

The effect on solution viscosity of blends of Klucel HPC and other water-soluble polymers varies, depending on the ionic nature of the copolymer. To illustrate, blends of Klucel HPC with Natrosol™ 250 HEC and Aqualon™ CMC were studied. The blends were prepared at a 1:1 ratio of the two polymers. The results of this work are given in Table 10. Solution viscosities of blends of nonionic polymers Klucel HPC and Natrosol 250 HEC were essentially in agreement with calculated values. This was true for all viscosity types studied. When solutions of blends of Klucel HPC and an ionic polymer, Aqualon CMC, were prepared, the resultant viscosities were greater than the calculated values. The synergism of this combination increased with increasing molecular weight of the polymers. The data shown in Table 10 were obtained with solutions prepared in distilled water or tap water. The synergistic effect may be drastically reduced in the presence of low levels of dissolved salts or if pH is below 3 or above 10.

Table 10. Effect of Polymer Blends on Solution Viscosity

Polymer Blend (1:1)	Concentration (%)	Solution Viscosity, mPa·s		
		Expected	Initial	After 24 Hours
Klucel J HPC and Natrosol 250 J HEC	5	235	240	235
Klucel M HPC and Natrosol 250 M HEC	2	6250	5900	5600
Klucel H HPC and Natrosol 250 H HEC	1	2320	2440	2440
Klucel H HPC and Aqualon 7H CMC	1	2220	4400	3860

Water-insoluble polymers

Klucel HPC is compatible with many natural and synthetic latexes available as emulsions in water. Klucel HPC is soluble in the aqueous phase, and uniform films and coatings are obtained upon drying. Using common solvents, Klucel HPC has been incorporated with water insoluble polymers such as zein, shellac, Aqualon ethylcellulose, and cellulose acetate phthalate. Films and coatings prepared from these systems are homogeneous and of good quality.

4.3.5.3 Surfactants

Compatibility of Klucel HPC with surface-active agents will vary according to the particular agent and concentration, as well as to the grade and concentration of Klucel HPC used. Because of its hydroxypropyl substitution, Klucel HPC is more lipophilic in nature than other water-soluble cellulose derivatives. Accordingly, it is compatible with a wide range of anionic, nonionic, cationic, and amphoteric surfactants.

Studies with Klucel HPC using certain ionic surfactants have aided the development of technology to permit thickening at temperatures in excess of the normal cloud points for Klucel HPC. Aqueous solutions of M viscosity type and sodium lauryl sulfate, at a surfactant to Klucel HPC ratio of 1:3 or greater, result in cloud points in excess of 70°C. At some ratios, cloud points greater than 95°C may be achieved. Included in these studies were the following ionic surfactants, which proved to be effective:

- Sodium lauryl sulfate
- Ammonium lauryl sulfate
- Lauryl alcohol ether sulfate
- Trimethylcoco ammonium chloride

The nonionic surfactants studied were not effective in raising the cloud points.

4.3.6 Viscosity Stability of Solutions

Water solutions of Klucel HPC possess best viscosity stability when pH is held between 6.0 and 8.0, and when the solutions are protected from light, heat, and action of microorganisms. Klucel HPC in water solution, like other water-soluble polymers, is susceptible to both chemical and biological degradation. This degradation generally results in reduction of molecular weight of the dissolved polymer, with an accompanying decrease in viscosity of the solution. Some loss of solution clarity may occur in cases of severe biological degradation. Klucel HPC has demonstrated greater resistance to chemical and biological degradation than other cellulose ethers. Techniques to minimize degradation mechanisms are discussed in the following two sections.

4.3.6.1 Hydrolysis and Oxidation

Klucel HPC in solution is susceptible to acid hydrolysis, which causes chain scission and loss of viscosity of the solution. The rate of hydrolysis increases with temperature and hydrogen ion concentration. Solutions should be buffered to pH 6.0 to 8.0 and maintained at low temperature to minimize acid hydrolysis. Alkali-catalyzed oxidative degradation will also degrade the polymer and result in decrease in viscosity of solution. The degradation can result from presence of dissolved oxygen or oxidizing agents in the solution. Peroxides and sodium hypochlorite under alkaline conditions cause rapid degradation. For best stability on storage, pH should be maintained between 6.0 and 8.0 and antioxidants should be used if oxidative degradation is likely to occur. Ultraviolet light will degrade the cellulose, and solutions of Klucel HPC will undergo some decrease in viscosity if exposed to light for several months.

4.3.6.2 Biological Stability

The high level of substitution of Klucel HPC improves resistance of this polymer to degradation by cellulase enzymes produced by molds and bacteria. However, water solutions are susceptible to degradation under severe conditions, and a viscosity decrease may result. If prolonged storage is contemplated, a preservative is recommended. Certain enzymes, produced by microbial action, will degrade Klucel HPC in solution. If microbial contamination is present in makeup water, it is important that sterilization techniques effective against enzymes as well as against microorganisms be employed prior to preparing the solution of Klucel HPC. Solutions of Klucel HPC in organic solvents do not generally require preservatives.

4.3.7 Preservatives

Listed below are some of the preservatives that are effective in preserving solutions of Klucel HPC. It is recommended that the preservative manufacturer be consulted regarding kind, amount, and rate of use for the preservative to be added.

- Dowicil 100 n-(3-chloroallyl)-hexaminium chloride
- Formaldehyde
- Phenol
- Omadine

Note: Solutions of Klucel HPC have demonstrated some incompatibility with a number of preservatives based on substituted phenol derivatives.

4.3.8 Surface and Interfacial Tension

Klucel HPC is a surface-active polymer. Water solutions display greatly reduced surface and interfacial tension. The reduction in surface and interfacial tension of water solutions containing Klucel HPC is illustrated in Table 11. All viscosity types have essentially the same effects, and a concentration of Klucel HPC as low as 0.01% produces close to the maximum reduction in surface tension.

Table 11. Surface and Interfacial Tensions of Klucel HPC Solutions at 25°C

Klucel™ HPC, wt %	Surface Tension, mN/m
0 (water)	74.1
0.01	45
0.1	43.6
0.2	43

4.3.9 Organic Solvent Solutions

4.3.9.1 Effect of Concentration and Viscosity Type

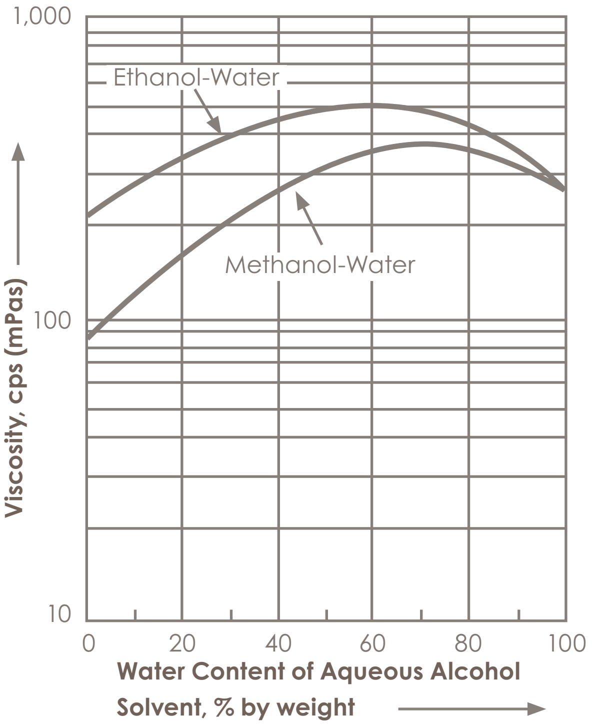
The viscosity-vs-concentration curves for Klucel HPC dissolved in organic liquids, which are good solvents for the polymer, show the same general pattern as those for Klucel HPC dissolved in water (Figure 4, page 9). The viscosity rises rapidly as the concentration of polymer is increased. The curves for viscosity in ethanol and methanol parallel those for viscosity in water, but are displaced toward somewhat lower viscosity values.

Where organic liquids that are borderline solvents for Klucel HPC are used, unusual viscosity effects can be observed. Viscosity may be abnormally high or abnormally low, depending on the degree of solvation of the polymer (see Table 4 on page 8). For example, the H viscosity type in methylene chloride gave a poor solution with reduced viscosity. The L viscosity type, which was better solvated, gave a solution with unusually high viscosity with the same solvent. In both cases, the addition of a small amount of cosolvent (10% methanol) gave solutions with normal viscosities (see Table 4).

4.3.9.2 Viscosity and Precipitation Temperature

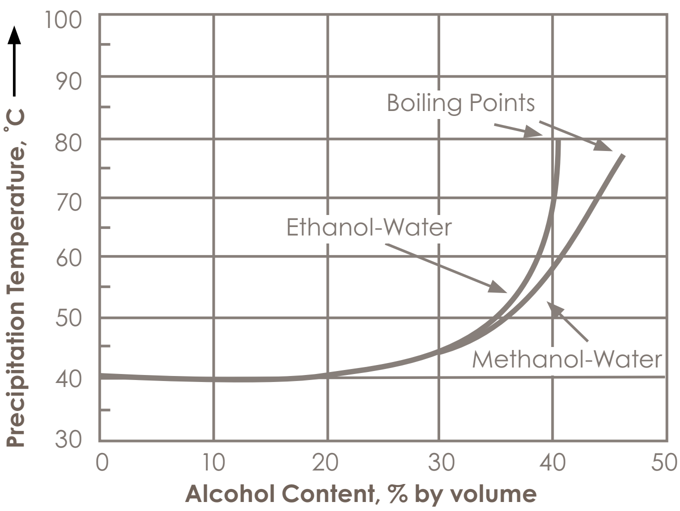
The viscosity of solutions of Klucel HPC in aqueous alcohols varies with composition of the solvent. The viscosity goes through a maximum value at a solvent composition of 7 parts water: 3 parts alcohol by weight. This is illustrated in Figure 9. This type of viscosity curve is obtained when Klucel HPC is added directly to aqueous alcohol or when it is first dissolved in either water or alcohol with subsequent addition of the second solvent. These viscosity curves mimic a scaled version of the binary solvent mixture viscosity curves.

Figure 9. Viscosity of aqueous alcohol solutions (G viscosity types at 2% concentration by weight).



Addition of alcohol to a water solution of Klucel HPC increases the temperature at which the polymer will precipitate from solution. Temperature elevation is dependent on type and concentration of alcohol. The effect obtained with methanol and ethanol is detailed in Figure 10. As shown, solutions of Klucel HPC containing 45% (by volume) of ethanol or methanol can be heated to the boiling point of the solution without precipitation of Klucel HPC.

Figure 10. Precipitation temperature of Klucel HPC in aqueous alcohols.



Propylene glycol performs similarly to methanol, and elevation of precipitation temperature falls on the same curve. Other water-miscible organic liquids, which are good solvents for Klucel HPC, will also elevate the precipitation temperature of the polymer in the system.

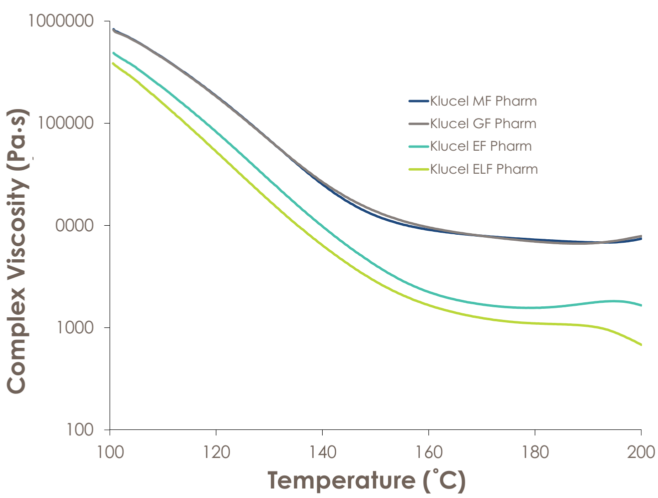
4.3.10 Recommended Defoamers

The low surface tension of water solutions containing Klucel HPC tends to promote foaming and air entrainment. If this presents a difficulty, a water-dispersible defoamer or antifoam agent can be used and should be added to the water prior to solution preparation. Defoamer concentrations generally run 25 to 200 ppm, but it is suggested that the manufacturers be consulted for their recommendations for the particular system involved.

4.4 Melt Rheology

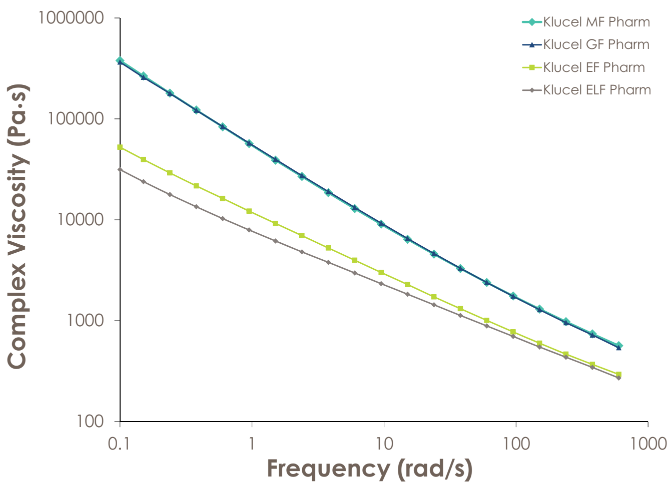
All molecular weight types of Klucel HPC are thermoplastic and can be readily molded and extruded. Melt flow behavior is dependent on the molecular weight, especially in pharmaceutical extrusion where thermolabile compounds are involved. Lower MW grades such as Klucel ELF and EF HPC are therefore recommended. See Figures 11 and 12. The methods for these tests are described in the Appendix.

Figure 11. Temperature Sweep Curves for Klucel HPC grades



5. Applications

Figure 12. Frequency Sweep Curves for Klucel HPC Grades



Klucel HPC is widely used in oral and topical pharmaceutical formulations. In oral products, Klucel HPC is primarily used as a film former or in tableting as a binder, film coating, and extended-release-matrix former. Concentrations of 2–6% w/w may be used as a binder in either wet-granulation or dry, direct-compression tableting processes. Concentrations of 15–35% w/w may be used to produce tablets for controlled release applications, including through extrusion granulation. The release rate of a drug increases with decreasing viscosity of Klucel HPC in immediate-release formulations. Blends of Klucel HPC and other cellulosic polymers have been used to improve wet granulation characteristics and tableting characteristics, as well as to achieve better control and manipulation of the rate of drug release. As an alternative technology to wet granulation, dry granulation and direct compression of Klucel HPC formulations have been reported to exhibit exceptional tableting and flow characteristics for application in extended-release matrix tablets. Klucel HPC is an excellent film former and due to its elastic nature, it does not require addition of plasticizers to the film coatings. For typical use levels in the most common applications of Klucel HPC, see Table 1 on page 4. Klucel HPC is also used in microencapsulation processes and as a thickening agent. In topical formulations, Klucel HPC has been used in transdermal patches and ophthalmic preparations.

5.1 Tablet Binding

The excellent thermoplastic and mechanical properties of Klucel HPC make it a binder of choice. In dry processing such as direct compression or dry granulation, finer particle size provides the best performance. Binder mechanical properties are important for dry processing. In wet processing, i.e., relationships between drug hydrophobicity and binder surface tension. A thorough study of the behavior of various Ashland cellulosic and vinyl pyrrolidone based binders in an array of wet granulated and direct compressed formulations with hydrophilic or hydrophobic active pharmaceutical ingredients (APIs) is available from your Ashland sales representative.

5.2 Modified-release Matrix Former

In the formulation of modified release matrix systems, fine particle, medium to high molecular weight (MW) Klucel HPC is well known for its controlled release, compactability, and binder efficiency. Among the useful attributes of Klucel HPC are demonstrated robustness under different processing conditions, such as wet granulation, roller compaction and direct compression. Reduction of particle size reduces drug release rates. This effect has been attributed to more rapid hydration, leading to more rapid formation of the diffusion-controlling gel layer around the dry tablet core. The role of Klucel HPC MW in controlled release matrix formation was investigated in the following case study, focusing on erosion-dependent systems. Low, medium, and high MW grades were tested in drug models differing in diffusion and erosion dependence.

High MW, fine-particle size Klucel HXF HPC is well known for creating swellable controlled-release matrices[1-4]. At use levels of 20 to 30%, Klucel HXF HPC forms strong gel matrices that are minimally affected by variation in hydrodynamic conditions. Drug release from such systems is mediated by swelling and diffusion control. Low MW, fine particle size Klucel EXF HPC is a tough, efficient thermoplastic tablet binder. However, the use of low and intermediate MW Klucel HPC in modified-release matrix systems has not been well studied.

Klucel HXF and EXF HPC and three intermediate MW grades were studied in diverse model systems where erosion may be of importance. The matrix formulations included a BCS class I soluble drug (theophylline) in wet-granulation formulations that varied in drug load; a low-dose, pH-dependent drug (papaverine) that was also wet granulated and a low-dose poorly soluble drug (nifedipine) that was directly compressed. Results indicated that use of different MW grades of Klucel HPC allowed the release profiles of the studied drugs to be optimized. A complete description of the study is available from your Ashland sales representative. [7]

5.3 Hot-melt Extrusion for Controlled-release Applications

At drug loads of 75% or more, drug mechanical properties of highly soluble drugs may dominate the release profiles in attempted controlled-release formulations. When using typical polymer amounts of 25–30% w/w, polymer chemistry has little impact on modulation of release profiles for these drugs. Such high amounts of drug and polymer create challenges with inadequate tablet compaction properties and inadequate control of drug-release kinetics. High amounts of drug and polymer also can take the size of a tablet to the outer limits of what patients are willing to consume orally.

Twin-screw extrusion combined with new hydrophilic matrix formulation approaches is a possible means to address controlled delivery of highly soluble drugs. Conventional pharmaceutical unit processes can be combined into a single operation within the extruder, enabling continuous processing. Screw configurations and die designs offer large flexibility, and temperature profiles or shear rates are customizable.

Thermoplastic polymers can be extruded at temperatures that do not affect the stability of volatile or heat-sensitive drugs. Klucel™ HPC has a low glass transition temperature, which makes it pliable and easy to extrude. Higher molecular weight grades, such as Klucel HF HPC and Klucel MF HPC, are typically recommended for controlled-release applications.

Ashland scientists[5,6] have investigated the use of hot-melt extrusion to produce highly soluble metformin formulations at high loads (75% w/w drug load). Klucel™ HF HPC and Klucel MF HPC were used as hydrophilic controlled-release polymers. The tablets made by extrusion granulation were less porous when compared with analogous tablets made by wet granulation or direct compression, as a result of intimate mixing of the drug with polymer in the molten state and the substantial elimination of air in the extrudate. Lower porosity not only allows stronger tablets and smaller size tablets but also modulates the release profile, allowing greater drug release retardation with the same formulation. Extrusion also improved compactability and reduced elastic recovery. [8]

5.4 Continuous Granulation

Continuous granulation using twin-screw extrusion also shows benefits as an alternative to high-shear wet granulation and fluid-bed granulation for immediate-release dosage forms. Process benefits include the capability of making stronger yet fast-dissolving tablets, the scalability of manufacturing, and the ability of performing continuous manufacturing with relatively small equipment and with modest capital investments. Various formulation factors for continuous granulation were explored using a GEA Niro ConsiGma-1 extrusion granulator, in a Design of Experiments (DoE) approach. The effects of varying the binder type and use level on granule and tablet physical properties and tablet dissolution profiles were evaluated. Additionally, process variables including screw speed, feed rate, process temperature, and equipment types were evaluated on an optimized formulation.

The thermal and mechanical properties of Klucel HPC make it pliable and easy to extrude. Klucel HPC has a low glass transition temperature, Tg, of approximately −4.5°C, which provides for a low melt viscosity and fast melt-flow properties, depending upon the molecular weight of the polymer used. Low molecular weight grades of HPC are often used as carriers to attain solid dispersions of poorly soluble drugs[9] and typically do not require plasticizers to be extruded. The hydroxyl groups of the cellulose backbone and the incorporated substituent hydroxypropoxyl groups are capable of donating hydrogen bonds to active pharmaceutical ingredients (APIs) with hydrogen-bond accepting groups. Klucel HPC is particularly suitable for extrusion with APIs with hydrogen bond accepting groups. One limitation of HPC for use as solid-dispersion carrier stems from its low Tg. A high Tg helps improve the physical stability of the solid dispersions by preventing recrystallization.

Hot-melt extrusion (HME) can produce tablets with higher compactability and lower friability compared with equivalent formulations made by conventional processes. The process can result in smaller tablets for high-dose drugs and combination products, relative to conventional approaches, by decreasing the need for relatively large amounts of excipients.[5,6]

5.5 Film Coatings

The characteristics of Klucel HPC make it extremely useful for pharmaceutical film coatings, either for application from aqueous (often preferred today) or organic solvent based coating formulations. The inherent compatibility with other commonly used polymers (such as HPMC) makes Klucel HPC a useful formulation modifier to enhance the properties of the final coating formulation. Klucel HPC can also be a suspension stabilizer for pigment dispersions that are used in colored coating formulations.

Film-coating formulations based on Klucel HPC share these general characteristics:

- Outstanding film flexibility
- Good film adhesion (to substrate)
- Relatively low moisture vapor transmission rates (typically 0.60 g 100 cm-2 24 h-1, compared with 1.59 g 100 cm-2 24 h-1 for HPMC)
- Low glass transition temperatures (note: while the true Tg of Klucel HPC is around 150°C, a beta transition at close to 0°C, due to side chain behavior, provides a better explanation for the increased plasticity/flexibility of Klucel HPC coatings).
- Greater degrees of tackiness (compared with coatings based on other commonly used polymers such as HPMC).
- Greater resistance to microbial growth (in aqueous solutions) when compared with coating formulations based solely on HPMC.

The inherent tackiness of Klucel HPC coatings, while not precluding use as the primary polymer in film coating formulations (especially when suitable anti-tack agents are used) often means that combination with other polymers (such as HPMC) is a more suitable option.

Because solution viscosity is mainly a limiting factor with pharmaceutical film-coating formulations (especially when water is used as the solvent), the low molecular weight grades of Klucel HPC (especially EF and ELF) are the preferred choices in these coating formulations.

6. Packaging, Regulatory Status Toxicology, Safety

6.1 Packaging and Shipping

Our hydroxypropylcellulose products are packaged in 100-lb and 10-lb polyethylene-lined, fiber Kraft drums. Drums are sealed with tamper-evident, wire and plastic or cable locking seals. HPC is not packaged in bags because it is a thermo-plastic and will severely cake and/or liquify if enough pressure is applied. If packaged in bags and stacked on pallets, the pressure from the stacked bags/pallets would result in heat formation. This heat would be capable of converting the HPC free-flowing granular powder into a hard cake or lump.

6.2 Regulatory

Information concerning the regulatory status of Klucel is provided in its Product Regulatory Datasheet which will be provided upon request.

6.3 Toxicology

Toxicology summary for Klucel HPC is available upon request.

6.4 Product Safety

Klucel HPC is a flammable dust when finely divided and suspended in air. An explosion can occur if the suspended dust is ignited. Proper design and operation of facilities and good housekeeping practices can minimize this hazard. Floors subject to spills or dusting with Klucel HPC can become slippery when wetted with water. Follow good housekeeping practices and clean up spills promptly.

Read and understand the Safety Data Sheet (SDS) before using this product.

7. References

1. A.M. Railkar and J.B. Schwartz, Use of a moist granulation technique (MGT) to develop controlled-release dosage forms of acetaminophen. Drug. Dev. Ind. Pharm., 27, 337–343, 2001.

2. US Patent 4,704,285, granted 11/3/87, expires 11/18/05 (contact Dow Chemical for further info).

3. US Patent 6,103,263, granted 8/15/00, expires 11/17/14.

4. T. Dürig, W.W. Harcum and R.A. Salzstein, Hydroxypropylcellulose polymer molecular weight, Ashland Pharmaceutical Technology Report, PTR-032, 2006.

5. E. Pinto, H. Yang, A. Pittman, D. Tewari and T. Dürig, Advantages of hot-melt extrusion for the controlled release of high doses of highly soluble actives, Ashland Pharmaceutical Technology Report, PTR-079, 2010.

6. E. Pinto, A. Pittman, C.E. Hood, C.R. Usher, S. Bradley, D. Tewari and T. Dürig, Hot-melt extrusion with Klucel™ hydroxypropylcellulose (HPC) for the controlled release of high doses of highly soluble actives, Ashland Pharmaceutical Technology Report, PTR-081, 2010.

7. T. Dürig, W.W. Harcum, and R.A. Salzstein, Hydroxypropylcellulose polymer molecular weight: Influence on erodible modified release matrix systems. Ashland Pharmaceutical Technology Report, PTR-032, 2005.

8. Deng, W., Majumdar, S., Singh, A., Shah, S., Naqvi Mohammed, N., Jo, S., Pinto, E., Tewari, D., Dürig, T., Repka, M.A., Stabilization of fenofibrate in low molecular weight hydroxypropylcellulose matrices produced by hot-melt extrusion. Drug Dev. Ind. Pharm., 39, 290–298, 2013.

Appendix: Methods

All types of Klucel™ HPC meet certain specifications for moisture, viscosity, and ash content. Detailed descriptions are given of Ashland methods for determining these values.

Moisture

Weigh duplicate samples of 5 g, to the nearest 0.001 g, into previously dried and weighed moisture cans with covers. Place the samples in a gravity convection oven maintained at 105° ± 0.5°C. Heat for 3 hrs. Cool in a desiccator and weigh. Return the sample to the oven for 45 min. Cool and weigh as before. If the second dried weight is not within 0.005 g of the first dried weight, repeat the 45-min oven periods until two subsequent weighings are in agreement. Then, using the lowest dried weight obtained, calculate percent moisture as follows:

$$\frac{\text{Original sample weight} - \text{dry sample weight} \times 100}{\textit{Original sample weight}} = \text{Percent moisture}$$

Ash content

The ash components of Klucel HPC are sodium salts. Determination of these is complicated by the presence of certain anticaking agents, which contribute to the total ash. The ash method is referenced in the *National Formulary,* current edition.

Dispersion and Dissolution

Method 2

Add powdered Klucel HPC to the vortex of well-agitated water at room temperature. The rate of addition must be slow enough to permit particles to separate in the water. Addition of the powder should be completed, however, before any appreciable viscosity buildup is obtained in the solution. The rate of agitation then may be reduced, but continued until a gel-free solution is obtained. Throughout the mixing period, solution temperature should be maintained below 35°C.

Method 3

Dry-blend Klucel HPC with any inert or nonpolymeric soluble material that will be used in the formulation. Blending aids separation of particles of Klucel HPC at first wetting and reduces the tendency to lump. For best results, Klucel HPC should be less than 20% of the total dry blend. This blend is then handled as described in Method 2.

Viscosity in water

As explained on page 10, the apparent viscosity of a solution of Klucel HPC depends on a number of factors. If reproducible results are to be obtained, a closely standardized method of solution preparation and viscosity determination must be followed. Preparation of the solution is critical in that Klucel HPC must be completely dissolved in order to obtain a significant measurement. In weighing out the proper amount of Klucel HPC for a viscosity determination, care must be taken to include a moisture correction. This correction compensates for the moisture in Klucel HPC and places the viscosity measurement of Klucel HPC on a dry basis. The viscosity measurement test must be rigidly standardized because the viscosity reading obtained is dependent on the rate of shear during dissolution, the amount of agitation prior to measurement, the temperature, and the elapsed time between agitation and measurement. The method used in Ashland laboratories is therefore given here in detail.

Solution preparation

Immediately after taking portions of the Klucel HPC polymer sample for moisture determination, portions of the same undried Klucel HPC should be taken for viscosity solution preparation. Weighings of moisture and solution samples should be carried out concurrently to ensure that the moisture content of the respective portions is the same at the time of the weighings.

The standardized Ashland method for determining the viscosity of solutions of Klucel HPC specifies use of the Brookfield viscometer, Model LVF (Brookfield Engineering Labs, Stoughton, Massachusetts; 4 spindles, 4 speeds covering the range 0 to 100,000 mPa·s). The solution volumes specified under item 4 should not be less than outlined or there may not be sufficient solution to cover the appropriate Brookfield spindle.

1. Weigh the specified amounts to ± 0.005 g, as obtained from Table A1, page 23, quickly into clean, ground-glass stoppered weighing bottles. Stopper immediately to eliminate gain or loss of moisture content.
2. From the determined percent moisture, calculate the water to be added for the respective viscosity solutions, as follows:

a. For a 1% viscosity solution:

$$(\text{Weight of Klucel HPC, g}) \times (99 - \%\ \text{moisture}) = \text{Weight of water, g}$$

b. For a 2% viscosity solution:

$$\frac{(\text{Weight of Klucel HPC, g}) \times (98 - \%\ \text{moisture})}{2} = \text{Weight of water, g}$$

c. For a 5% viscosity solution:

$$\frac{(\text{Weight of Klucel HPC, g}) \times (95 - \%\ \text{moisture})}{5} = \text{Weight of water, g}$$

d. For a 10% viscosity solution:

$$\frac{(\text{Weight of Klucel HPC, g}) \times (90 - \%\ \text{moisture})}{10} = \text{Weight of water, g}$$

3. Add the calculated amount of distilled water to a 16-oz bottle.
4. Stir the water with a mechanical agitator to create a vortex, and slowly sift the Klucel HPC into the vortex over a 15 to 30-sec period to ensure good dispersion. An anchor-shaped stirrer turned by a compressed-air or electric motor has been found to be satisfactory. After the solution appears to be complete, stir it for an additional 10 to 15 min at high speed. Be careful to avoid loss of solution.
5. When the solution is complete, cover the mouth of the bottle with cellophane and screw the cap on securely. Place it in a constant-temperature bath (25° ± 0.2°C) for 30 min, or for as long as necessary to adjust the solution temperature to 25° ± 0.2°C.
6. While the solution is in the constant-temperature bath, select from Table A1 the Brookfield spindle-speed combination corresponding to the viscosity type of Klucel HPC being tested. Determine the viscosity of the Klucel HPC within 2 hrs after removing it from the stirrer. If the solution stands longer than 2 hrs, return it to the stirrer for 10 min, place it in a bath for 30 min, and then determine viscosity.
7. Remove the bottle from the constant-temperature bath and stir the solution by hand for 10 sec, using a stirring rod. Avoid shaking or vigorous stirring, as this will increase air bubbles, which interfere with viscosity measurement.
8. Immediately insert the appropriate Brookfield viscometer spindle into the solution and start the spindle rotating. Allow it to rotate for 3 min before taking the reading.
9. Stop the instrument and read the dial. Multiply the dial reading by the factor corresponding to the speed and spindle used. The result is the viscosity of the solution in centipoise.

Table A1. Viscosity Measurement Parameters

Viscosity Type	Concentration, %	Sample weight g	RPM	Brookfield settings Spindle No.
EL	10	25	60	2
E	10	25	30	2
L	5	11	30	1
J	5	11	60	2
G	2	5.2	60	2
M	2	5.2	60	4
H	1	2.3	30	3

Viscosity in ethanol

The viscosity of ethanol solutions of Klucel HPC is determined in the same manner as for aqueous solutions, but with the following modification: To minimize evaporation of the ethanol, the bottle may be capped and mechanically shaken to accomplish solution of the Klucel HPC instead of stirring the solution by hand. Repeat steps 5, 6, 7, 8, and 9 as described in the Viscosity in Water procedures.

Effect of pH on Polymer Hydration

Polymer hydration/viscosity development time was measured using Haake Visco Tester 501 equipped with FL 10 spindle. This instrument measures the amount of torques (force) needed to maintain the rotation of the spindle in the solution at the set speed (300 rpm), as polymer hydrates and thickening occurs.

90% hydration time is the time in minutes required to achieve 90% of the final viscosity. The final viscosity is the average of the last ten (10) readings. Glycerin was used as a wetting agent.

These samples were tested in 0.1N HCl (pH 1.2) and phosphate buffer (pH 6.8) to study the effect of pH on polymer hydration.

Effect of pH on Cloud Point

Method: Cloud point measurement was carried out on Mettler Toledo FP 900 Processor and FP81C Measuring cell. The transmittance data was collected for full temperature range of analysis.

Samples were run at 1% solids in a buffer with different pH, 0.1N HCL (pH1.2) and phosphate buffer (pH 6.8) at a temperature program of 30-60°C to study the effect of pH on cloud point.

Effect of Ionic Strength on Polymer Hydration

Polymer hydration/viscosity development time was measured using Haake Visco Tester 501 equipped with FL 10 spindle. This instrument measures the amount of torques (force) needed to maintain the rotation of the spindle in the solution at the set speed (300 rpm), as polymer hydrates and thickening occurs.

90% hydration time is the time in minutes required to achieve 90% of the final viscosity. The final viscosity is the average of the last ten (10) readings. Glycerin was used as a wetting agent.

These samples were tested in a buffer with different ionic strengths (0.075M, 0.09M & 0.15M) to study the effect of ionic strength on polymer hydration.

Melt Rheology

The rheology measurements were carried out on a TA Instruments AR-G2 stress-controlled rheometer equipped with an Environmental Test Chamber (ETC) oven. A 25mm parallel plate geometry with a cross-hatched top and cross-hatched step-bottom plates was used.

Two types of measurements were performed: 1) frequency sweep at a fixed temperature of 150°C and 2) temperature ramp at a fixed frequency of 6.283 rad/s. For both types of measurements, the strain was set to 0.2%, which was measured to be in the linear viscoelastic region for the polymers. The frequency sweeps were obtained by starting at a frequency of 600 rad/s and ending at a frequency of 0.1 rad/s with 5 data points per decade on the logarithmic scale. The temperature ramps were carried out from 100°C to 200°C at a ramp rate of 2°C/min.

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