Physical Mechanical and Tablet Formation Properties of Hydroxypropylcellulose: In Pure Form and in Mixtures

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ABSTRACT

The aim of the study was to analyze hydroxypropylcellulose (HPC) in pure form and in excipient mixtures and to relate its physical and chemical properties to tablet binder functionality. The materials used were Klucel hydroxypropylcellulose grades ranging from low to high molecular weight (80-1000 kDa) of regular particle size (250 μm mean size) and fine particle size (80 μm mean size). These were compared with microcrystalline cellulose, spray-dried lactose, and dicalcium phosphate dihydrate. Thermal behavior of HPC was analyzed by modulated temperature differential scanning calorimetry (MTDSC). Tablets of the pure materials and of dry blends with 4% low viscosity, fine particle HPC and 30% high viscosity, fine particle HPC were produced on an instrumented eccentric tableting machine at 3 relative humidities. The 3-dimensional (3-D) model with the parameters time plasticity d, pressure plasticity e, and the twisting angle ω, the inverse of fast elastic decompression was compared with the Heckel method for characterization of compaction. Elastic recovery and compactibility were also studied. The results show that HPC tablet formation is characterized by high plastic deformation. The d, e, and ω values were markedly higher as compared with the reference materials. Plasticity was highest for the fine particle size HPC types. Maximum compactibility was observed for low molecular weight, fine particle size HPC. Tableting of the mixtures showed deformation, which was strongly influenced by HPC. Plasticity and crushing force of formed tablets was increased. In conclusion, HPC is characterized by strong plastic deformation properties, which are molecular weight and particle size dependent.

KEYWORDS: Tableting, hydroxypropylcellulose, DSC, 3-D modeling, mixtures, elastic recovery, plastic deformation.

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INTRODUCTION

Hydroxypropylcellulose (HPC) is a well-known solid dosage form excipient. Frequently, low molecular weight HPC is used as an immediate-release tablet binder at levels of 2% to 8% in combination with other materials. At higher polymer levels of 20% to 30%, HPC grades of varying molecular weight function as hydrophilic matrix formers. Binders are necessary to improve the unfavorable compression properties of most drugs and to obtain tablets with adequate strength and friability. Good drug-binder adhesion is important and correlates with tablet strength.[1] Binders should also show substantial plastic deformation.[2] Solution binders can be used in dissolved form for wet granulation, while pressure binders are employed in dry granulation and direct compression. It is often demonstrated that with addition of binder, tablet strength increases.[3-5] Fine particle size grades of HPC are most suited as pressure binders, while regular particle size grades are more readily water dispersible, making them useful as solution binders.

Selmeczi[6] and Alvarez-Lorenzo et al[7] highlighted the favorable binder performance of HPC in which tablets had a short disintegration time and high mechanical strength. Later investigations evaluated HPC as a binder for roller compaction.[8,9] Increased HPC levels greatly reduced capping tendencies of problematic formulations. HPC also improved tablet strength and friability of wet granulated formulations.[10]

Binder functionality depends on the physicochemical properties of a material, especially the thermal properties. Up to now, examinations of thermal properties of HPC were mostly performed with films. Suto et al[11] used films from solutions and from hot compression. Using differential mechanical analysis (DMA), 2 second-order transitions at 25°C and 110°C, however, were observed. No primary glass transition could be detected. In concentrated aqueous solutions, HPC formed a liquid crystalline phase. Rials and Glaser[12] analyzed HPC films (Klucel HPC L) by DSC. Melting of the crystalline material was detected between 165°C and 210°C. A secondary transition occurred at 20°C. Corresponding relaxations were found by DMTA. Kararli et al[13] analyzed HPC films (Klucel HPC EF) by thermomechanical analysis (TMA) and DMA. A primary transition could not be found. By DMA, 2 secondary transitions between −60°C and −100°C

and between 0°C and 40°C were detected. In summary, the thermal properties of HPC appear complex and require further clarification.

There have been few detailed and mechanistic studies documenting the fundamental compaction and tableting behavior of various HPC grades. An understanding of the tableting behavior of the pure materials is important for the prediction of the underlying basic properties of tablet formulations.

To characterize the tableting behavior of new excipients, it is useful to apply the new 3-dimensional (3-D) modeling technique using porosity, pressure, and time.[14,15] Three-dimensional modeling uniquely characterizes the 3 important variables during the tableting process (normalized time, pressure, and density) simultaneously. The fitting parameters of the model, *d*, *e*, and ω, can be used to describe the tableting process.

$$\begin{aligned} z &= \ln\left(1/(1 - D_{rel})\right) \\ &= ((t - t_{max}) \cdot (d + \omega \cdot p_{max} - p)) + (e \cdot p) \\ &\quad + (f + d \cdot t_{max}) \end{aligned} \tag{1}$$

where D_{rel} indicates relative density; t, time; t_{max}, time at maximum pressure; p, pressure; p_{max}, maximum pressure; *d*, time plasticity; *e*, pressure plasticity; *f*, intersection; and ω, angle of torsion.

Time plasticity (*d*) describes the plastic deformation of the excipient according to time and thus how fast the substance is deformed. It can be influenced by tableting speed. With increasing time plasticity, the powder is deformed faster during tableting. This means, for example, that with increasing mass of powder, time plasticity increases. Pressure plasticity (*e*) describes the relationship between density and pressure. It considers only plastic deformation due to pressure. With increasing pressure plasticity, the pressure, which is necessary for deformation, decreases. The angle of torsion (ω) is a measure for the elasticity of the material. With increasing angle of torsion (ω), elasticity decreases. It can be interpreted as the ratio between compression and decompression and thus describes, indirectly, instantaneous elastic decompression during decompression.

The aim of the study is first to analyze the compaction and consolidation behavior of different molecular weight and particle size grades of HPC using the well-known tableting excipients dicalcium phosphate dihydrate (brittle fracturing), lactose (brittle-plastic deformation), and microcrystalline cellulose (plastic deformation) as reference materials. Second, the effect of moisture is evaluated at 30%, 45%, and 60% relative humidity (RH). In addition, the compaction behavior of binary mixtures of fine particle size HPC and microcrystalline cellulose (plastic model compound) or dicalcium phosphate dihydrate (brittle fracturing model compound) was studied. Last, an attempt was made to correlate the mechanical properties with the glass transition temperature of HPC.

MATERIALS

The following HPC types were studied: the coarsely milled Klucel® Pharm Hydroxypropylcellulose (HPC) grades EF, MF, and HF (D50 typically 300-500 μm with a molecular weight of 80, 850, and 1150 kDa respectively) and the extra fine particle sized Klucel® Pharm Hydroxypropylcellulose (HPC) grades EXF and HXF (D50 typically 60-100 μm with a molecular weight of 80 and 1150 kDa) (Aqualon, Hercules Inc, Wilmington, DE). Additional tableting materials were Avicel® PH 102 microcrystalline cellulose (MCC) NF (FMC Corporation, Philadelphia, PA); Prosolv™ HD90 silicified microcrystalline cellulose, NF (JRS Pharma, HolzmÃ¼hle, Germany); Fast Flo® spray-dried lactose NF, (Foremost Farms, Rothschild, WI); and DiTab® dicalcium phosphate dihydrate USP (Rhodia, Cranbury, NJ).

METHODS

Test Conditions

All materials and tablets were equilibrated, produced, and stored at 23°C ± 0.5°C and RH of 45% ± 2%. Additionally, HPC EXF and HPC HXF were also tested at 30% and 60% ± 2% RH.

Powder Properties

Particle Form and Size

Particle size measurements were made by laser light diffractometry using a dry feeder (Malvern PS 2600c, Malvern Instruments, Malvern, UK) equipped with software capable of calculating the median particle size (D50) and particle size distribution for 10% (D10) and 90% (D90) as well as the specific surface area of the powder. Powder and tablet morphology were studied by scanning electron microscopy (SEM) (JSM 6400, JEOL Ltd, Tokyo, Japan).

Densities

The apparent particle density of the powders was determined by helium gas pycnometry (Accupyc 1330, Micrometrics Instrument Corp, Norcross, GA) in triplicate. Bulk density and tapped were calculated by the quotient of the powder weight filling a 100-mL cylinder and the volume of this powder or the constant tapped volume (Stampfvolumter SVM, ERWEKA Apparatebau, Heussenstamm, Germany).

Flowability

The Carr Index, which represents the compressibility, is the difference between tapped and bulk density based on the tapped density.[16] In addition, the flow rate of the powder was determined according to the European Pharmacopoeia 1997, 2.9.16, using steel funnels of sizes 10-, 15-, and 25-mm diameter.

Water Content and Sorption Behavior

The water content of the powders equilibrated at 45% RH was determined by thermogravimetry (TG 209 with a TASC 414/3 controller, Netzsch Gerätebau GmbH, Selb, Germany) in triplicate. Moisture sorption and desorption were further studied gravimetrically. Three samples of 1 g each were placed in controlled humidity chambers over saturated salt solutions: 0%, 11%, 22%, 33%, 43%, 53%, 58%, 69%, 75%, 80%, and 90% RH. Sorption started at 32% RH and followed up to 90% RH, then desorption was analyzed downwards up to 0% RH. The results were calculated on the basis of the weight of the dry powder at 0% RH.

Thermal Analysis and Powder X-ray Diffraction

Thermal behavior was studied by modulated temperature differential scanning calorimetry (MTDSC, DSC 2920, TA Instruments Inc, New Castle, DE). Approximately 10-mg quantities were hermetically sealed in aluminum pans and equilibrated at −65°C then heated at a rate of 2°C/min, a modulated temperature amplitude of 0.4°C and a period of 60 seconds under a helium purge of 25 cc/min up to a maximum temperature of 260°C. With MTDSC, the nonreversible moisture desorption endotherms typically found in these binders can be separated from reversible events such as glass transition temperature (T_g) and crystallization. The T_g was determined by calculating the temperature of the half step height during the first heating. To verify the results, the first derivative was determined. Moisture content was determined thermogravimetrically (TGA 2950, TA Instruments Inc) using sealed pans with a pinhole (0.3429 mm) in the lid at a scan rate of 2°C/min under a nitrogen purge of 100 cc/min. HPC samples were further analyzed at 40 kV and 35mA with an x-ray diffractometer XRD-6000 (Kratos Analytical, Shimadzu, Kyoto, Japan). Data were collected between 4° and 45° of 2θ at a rate of 2° per minute. The Kratos software was further used to estimate by crystallinity smoothing, background subtraction, removal of the k α 2 contribution, and the detected peak positions.

Mixtures

The mixtures consisting of either dicalcium phosphate dihydrate or MCC and 4% HPC EXF or 30% HPC HXF were produced by mixing for 15 minutes at level 6 in a cubic mixer (ERWEKA).

Tableting Behavior

Tablets were produced on an instrumented eccentric tableting machine (Korsch EK0/DMS, No 1.0083.92, Korsch Maschinenfabrik, Berlin, Germany) equipped with an inductive transducer (W 20 TK, Hottinger Baldwin Meßtechnik, Darmstadt, Germany) with 11-mm flat-faced punches (Ritter Pharma GmbH, Hamburg, Germany). Elastic deformation of the punches and of the machine was corrected. Data acquisition was performed by a DMC-plus system (Hottinger Baldwin Meßtechnik, Darmstadt, Germany). Data were stored by BEAM-Software (AMS-Flöha, Germany). The mass for each tablet was calculated using the maximum relative density ($\rho_{rel,\ max}$) and manually weighed on a laboratory balance (Mettler-Toledo, Gießen, Germany). The powder for each tablet was manually filled into the die, and the tablets were produced at 0.75, 0.80, 0.85, 0.90, and 0.95 $\rho_{rel,\ max}$ with an accuracy of ±0.001. At each condition 15 tablets were produced.

Porosity-Pressure-Time-Profile: 3-D Model

Three-dimensional modeling was used for analysis as described in the Introduction.[14] The parameters of the fitted plane, d, e, and ω, of the 5 compaction cycles at each tableting condition (material at a given $\rho_{rel,\ max}$) were averaged. Means and standard deviations were calculated. The parameters were exhibited in the 3-D parameter plot. The mean standard deviation for d was 0.01; for e, 0.0001; and for ω, 0.0002.

Porosity-Pressure-Profile According to Heckel

Heckel[17,18] describes the decrease of porosity with pressure by first-order kinetics. The slope of the Heckel equation gives information on the plastic deformation of the powder.

$$-\ln \varepsilon + \ln(1/(1 - D_{rel})) = K \cdot p + A \qquad (2)$$

where ε, indicates porosity; D_{rel}, relative density; K, slope of the Heckel equation; p, pressure; and A, point of intersection with the Y-axis.

Tablet Properties

Elastic Recovery

Axial recovery was determined by a micrometer screw (Mitutoyo, Tokyo, Japan) at 0, 1, 3, 6 hours and 1 and 10 days after

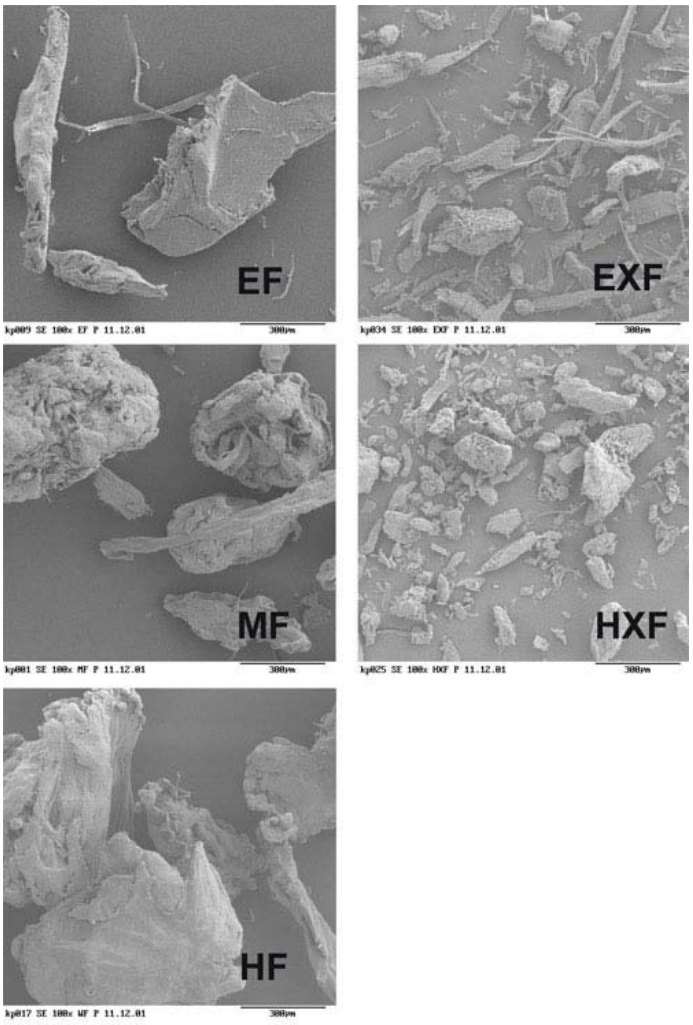

Figure 1. Scanning electron photomicrographs of the various Klucel Hydroxypropylcellulose grades at original magnification ×100.

tableting for 15 tablets. Axial recovery was additionally determined by thermomechanical analysis (TMA 202 coupled with a TASC 414/3 controller, Netzsch). This method was only used for tablets made of the different HPC types at a $\rho_{rel,max}$ of 0.90.

Crushing Force

The crushing force was determined by a radial crushing force tester TBH 30 (ERWEKA) for 5 tablets 1 and 10 days after tableting.

Results and Discussion

Hydroxypropylcellulose Particle Characteristics

Figure 1 shows examples for the morphology of particles of the different products. The different coarse types HPC EF, MF and HF show particles with different structures. After analyzing several particles, HPC EF appears to consist predominantly of agglomerated elongated particles; HPC MF particles show a more fluffy structure; and most particles of HPC HF seem to consist of rounded particles with flaws. For the fine particle HPC grades, low molecular weight (MW) HPC EXF has more elongated structure, while high MW HPC HXF has spherical structure.

Particle size, density, flow, and moisture content data are summarized in Table 1. The D90 for coarse HPC grades as measured by light scattering is typically smaller than 1400 μm. For fine particle HPC, EXF and HXF D90 is typically below 350 μm, with D50 ranging from 60 to 100 μm.

Similar to other derivatized cellulosic excipients, bulk, tapped, and true densities for HPC were lower or similar to MCC, lactose and dicalcium phosphate showed higher values (Table 1). Low density can affect flowability; however, the Carr Index and flow rate experiments show generally acceptable flow characteristics as defined by Carr.[16] At RH generally used in tableting (30%-50%) the water content of HPC was lower than for MCC; however, at RH higher than 60%, the slope of the moisture sorption isotherms for HPC increased more steeply (Figure 2).

Thermal Characterization

A typical MTDSC curve for HPC is shown in Figure 3a. The study investigations show that HPC is a semicrystalline polymer with a glass transition temperature (T_g) in the range of −25°C to 0°C as moisture varies from ~10% to 1%. Water is therefore an effective plasticizer for the amorphous domains, resulting in a decline in T_g with increasing moisture content (Figure 3b). Table 2 shows that the crystalline domains undergo a melting transition in the range of 180°C to 220°C as nominal MW increases from 80 to 1000 kDa (HPC EXF and HXF, respectively). Based on powder XRD, total crystallinity for the various grades was consistently estimated between 7% and 9%. Table 2 also shows a 4 degree shift in T_g, but this is attributable to the higher equilibrium moisture content of high MW polymer. At equivalent water contents, low and high MW HPC EF and HF have similar T_g (Figure 3b). The nonlinear relationship can be described by the Gordon-Taylor equation as described by Hancock and Zografi.[19] The relatively low T_g of HPC and the high degree of amorphous content suggest a high degree of molecular mobility and consequently a high degree of plasticity.

Tableting Behavior and Tablet Properties

Characterization of Various HPC Grades

Tablets comprising pure HPC of varying MW and particle size were analyzed by 3-D modeling (Figure 4). The e-values and the ω-values for HPC were generally higher than for MCC, lactose, and dicalcium phosphate, indicating that HPC

Table 1. Powder Characteristics for the Various Excipients Examined in this Study*

Material	Particle Size D_{50} (μm)	Particle Size D_{10} (μm)	Particle Size D_{90} (μm)	Bulk Density (g cm^{-3})	Tap Density (g cm^{-3})	True Density (g cm^{-3})	Carr Index (%)	Flow Rate (g s^{-1})	% Water Content at 45% RH
Klucel EF	337.97 ± 82.02	193.25 ± 3.87	1376.66 ± 22.38	0.331 ± 0.006	0.453 ± 0.006	1.214 ± 0.001	26.69	0.117 ± 0.003	2.81 ± 0.17
Klucel EXF	98.75 ± 1.27	16.60 ± 5.06	341.76 ± 31.73	0.294 ± 0.006	0.368 ± 0.010	1.209 ± 0.001	19.98	0.150 ± 0.044	2.75 ± 0.23
Klucel MF	916.00 ± 82.02	193.25 ± 104.04	1376.66 ± 22.38	0.433 ± 0.003	0.537 ± 0.006	1.201 ± 0.001	19.32	0.060 ± 0.000	3.20 ± 0.21
Klucel HF	520.63 ± 9.66	148.13 ± 92.45	1282.64 ± 45.75	0.404 ± 0.003	0.508 ± 0.003	1.204 ± 0.001	20.53	0.070 ± 0.000	3.25 ± 0.15
Klucel HXF	66.57 ± 0.80	15.45 ± 0.42	195.51 ± 16.70	0.408 ± 0.008	0.488 ± 0.011	1.222 ± 0.005	16.53	0.067 ± 0.006	3.28 ± 0.10
DiTab†	169.77 ± 20.84	90.35 ± 4.88	235.17 ± 3.96	0.849 ± 0.005	1.014 ± 0.014	2.370 ± 0.002	16.23	0.150 ± 0.000	0.64 ± 0.03
Fast Flo lactose	116.37 ± 0.11	54.74 ± 1.50	181.03 ± 8.04	0.594 ± 0.006	0.711 ± 0.019	1.550 ± 0.000	16.47	0.173 ± 0.006	0.83 ± 0.17
Avicel PH 102‡	109.23 ± 0.82	35.19 ± 0.40	195.52 ± 1.14	0.345 ± 0.006	0.432 ± 0.008	1.582 ± 0.001	20.03	0.154 ± 0.013	4.58 ± 0.09
Prosolv HD90§	144.87 ± 2.52	54.49 ± 4.17	217.57 ± 4.13	0.472 ± 0.005	0.562 ± 0.008	1.580 ± 0.002	16.06	0.225 ± 0.013	4.29 ± 0.13

*RH indicates relative humidity. All values are mean ± standard deviation.
†Dicalcium phosphate dihydrate.
‡Microcrystalline cellulose.
§Silicified microcrystalline cellulose.

is highly plastic during tableting (Figure 4a). A sharp decrease in ω-values with increasing d-values indicates brittle behavior as described by Picker and Hoag.[20] Comparing the HPC grades in Figure 4b, increased brittle behavior can be seen for the coarsely milled, larger particle grades. At the same time, there is an increase in elasticity with increasing maximum relative density. A clear dependence on MW and on particle size is therefore evident, with HPC EXF followed by HPC HXF showing highest plasticity and lowest brittleness. In addition, HPC EXF and HPC HXF are better deformable, since their plots are flatter.

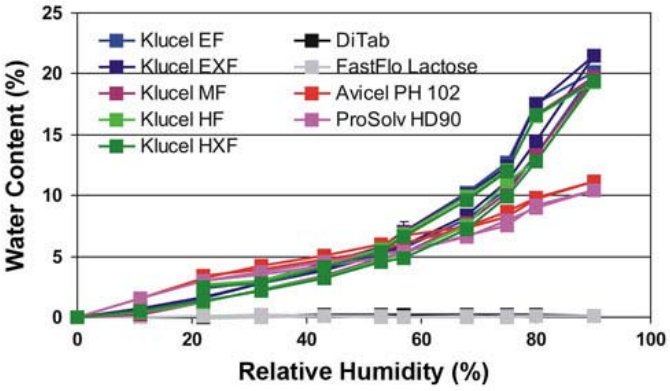

Figure 2. Water sorption isotherms of the tableting materials used.

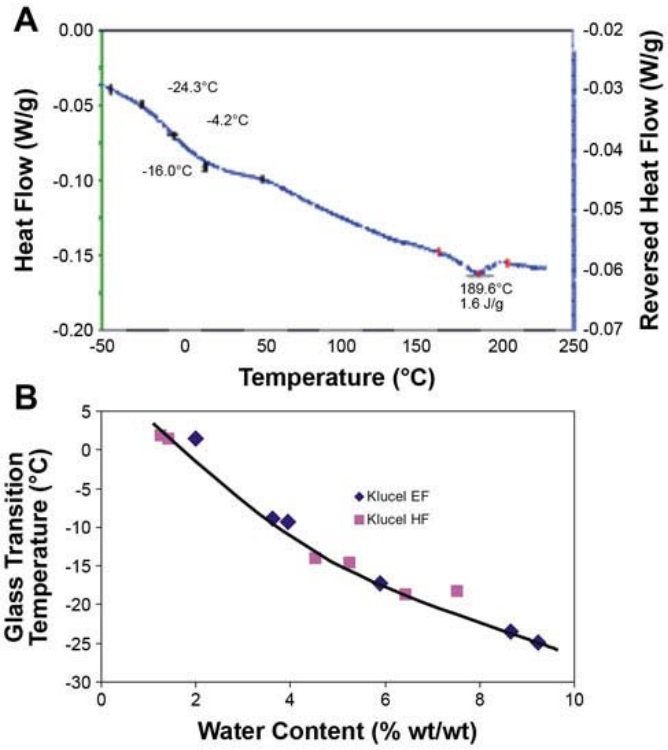

Figure 3. Typical modulated temperature differential scanning calorimetry curve for Klucel Hydroxypropylcellulose (HPC) EF (a) and (b) variation in glass transition temperature with change in water content for Klucel HPC EF and HF.

Table 2. Glass Transition and Melting Temperatures for Various Grades of HPC*

Grade	Nominal MW (kDa)	Moisture Content (%)†	T_g Half Height (°C)	Melting Peak Temperature (°C)
Klucel EF	80	2.14	−4.2	189.6
Klucel HF lot A	1000	3.87	−7.9	211.9
Klucel HF lot B	1000	3.68	−7.0	211.0

*HPC indicates hydroxypropylcellulose; MW, molecular weight; T_g, glass transition temperature.
†Moisture content "as received."

Analysis of compaction behavior with the Heckel method (Figure 5a) further supports the observation that the HPC grades are highly deformable compared with MCC, lactose, and dicalcium phosphate. Heckel analysis also shows that HPC EXF has significantly lower yield pressures (higher slope of the Heckel function) followed by HPC HXF. However, the MW dependency is not seen for the coarser HPC grades.

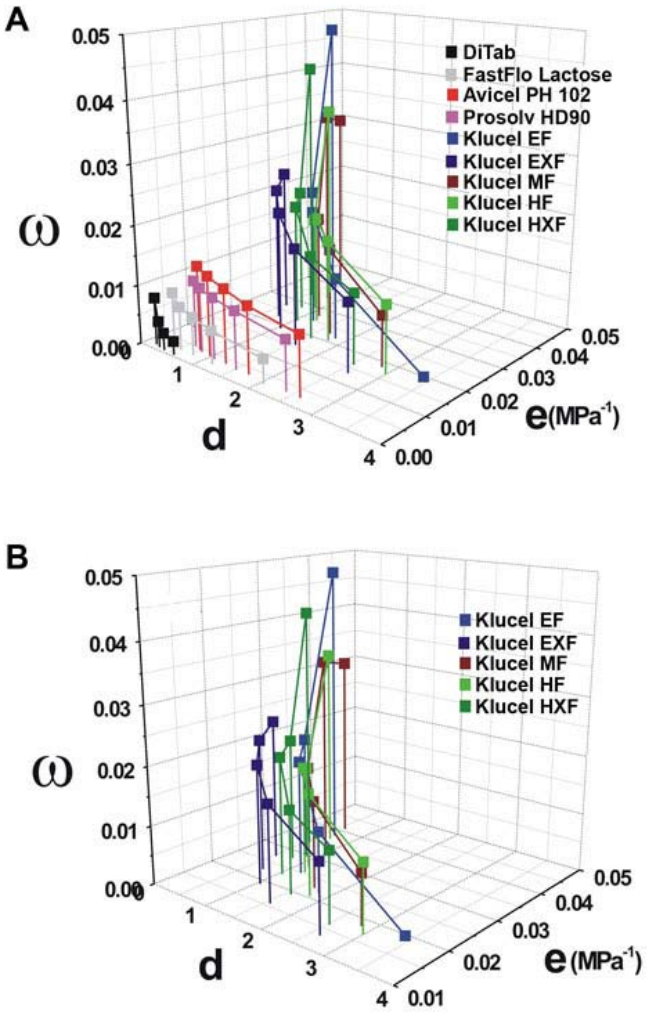

Figure 4. Three-dimensional parameter plot of the different Klucel Hydroxypropylcellulose products (a) in comparison to other tableting excipients and (b) in detail. ω indicates the angle of torsion; d, time plasticity; e, pressure plasticity.

Figure 5b shows that the postejection elastic recovery of tablets is greater for HPC as compared with the less viscoelastic reference materials. Comparing the various HPC grades, a clear dependence on MW and on particle size is visible, with lower elastic recoveries for smaller particle size and lower MW.

Compactibility is alternately defined as the relationship between tablet crushing force and applied pressure or the relationship between tablet strength and maximum "in-die" relative density. The focus in this study is on the relationship between tablet strength and applied pressure. Figure 6 shows that coherent HPC compacts of substantial strength are formed at applied pressures significantly lower than those required for MCC, lactose, or dicalcium phosphate. HPC compactibility increases with smaller particle size (increased bonding area) and lower MW, with highest compactibility for HPC

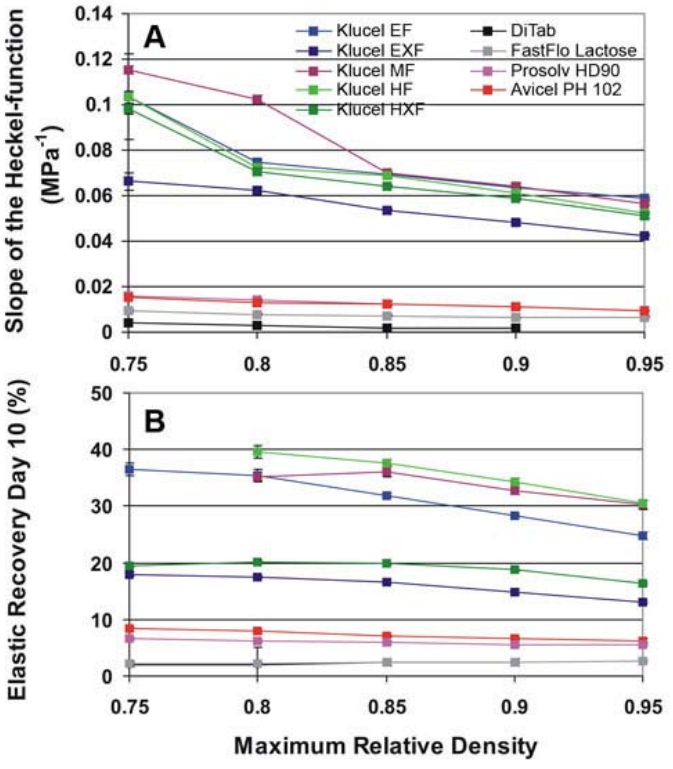

Figure 5. (a) Slope of the Heckel-function and (b) elastic recovery after 10 days.

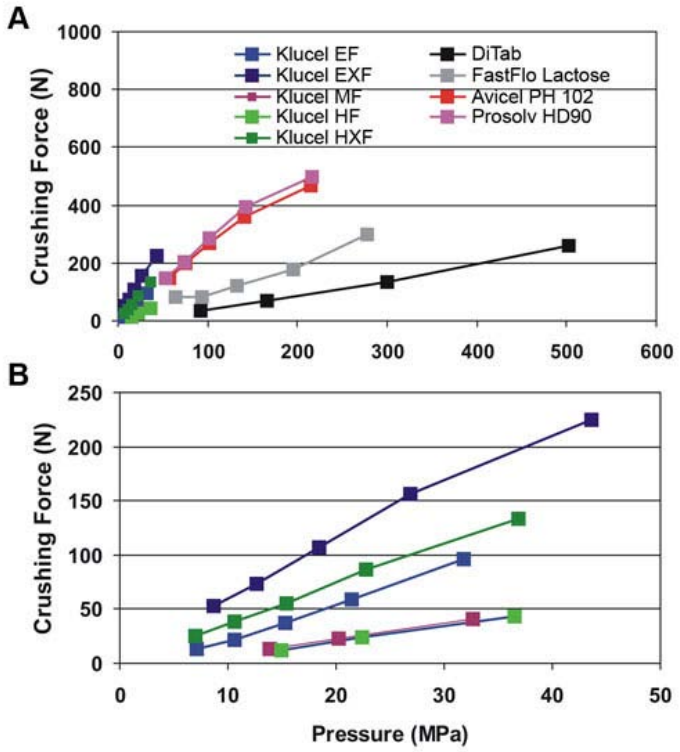

Figure 6. Compactibility plot of the different Klucel Hydroxypropylcellulose grades (a) in comparison to other tableting excipients and (b) in detail.

EXF (crushing strength ~200 N at 45 MPa applied pressure). The general relationship between polymer MW and mechanical properties is well known.[21] Typically, longer polymer chains exhibit greater flexibility and elasticity. Plasticity and molecular mobility depend on concentration of chain ends, thus increase with lower MW. For compressed specimens like tablets, lower MW therefore results in less postejection elastic recovery and greater permanent deformation. In summary, the results show that HPC is a visco-elastic polymer. The high plasticity as compared with filler-binders such as MCC, lactose, and dicalcium phosphate results in a material that is highly suited as a binder, as high compactibility is achieved at low compaction pressures.

Tableting Behavior of HPC at Different Relative Humidities

According to Figure 7, compaction behavior is relatively unchanged for HPC stored at 30% and 45% RH prior to compaction. In contrast, there is a marked increase in ω- and e-values, indicating increased plasticity if HPC is tableted after storage at 60% RH. The increase in plasticity is most pronounced for high MW HPC HXF as opposed to low MW HPC EXF. Increased deformability after exposure to high humidity is also seen in the marked increase in the slope of Heckel function (Figure 8a). Here too the moisture effect is strongest for high MW HPC HXF. In addition, axial elastic recovery is slightly reduced at the higher humidity levels of 45% and 60% RH (Figure 8b). The increase in RH from 30% to 45% (corresponding to moisture contents of ~3% and 4%, respectively) had only minimal influence on compactibility (data not shown); however, at 60% RH (corresponding to 6%-7% equilibrium moisture content) plasticity and toughness increased to the extent that it was no longer possible to accurately determine crushing force as the tablets continued to deform during the hardness test without any clear failure point.

Water is well known for its ability to plasticize polymeric and amorphous systems in general. The above observations of increasingly plastic deformation behavior and increased toughness with increased moisture levels coincide well with the earlier observed decrease in the T_g and resultant increased molecular mobility due to the plasticization effect of water. For formulations with high HPC levels (eg, sustained release matrix systems with 30% polymer), high HPC moisture levels are best avoided; however, the high plasticity at 6% to 7% moisture levels induced by exposure to 60% RH may be advantageous for typical immediate-release binder systems, where the polymer component does not exceed the 2% to 6% range.

Tableting Behavior of Binary Mixtures Containing HPC

The deformation behavior of binary blends of MCC or dicalcium phosphate dihydrate with 4% HPC EXF or 30% HPC HXF lies between the behaviors of the pure substances. Addition of HPC increases the plasticity as evidenced by increases in the ω- and e-values (Figure 9). The addition of HPC increases the plasticity of brittle-fracturing dicalcium

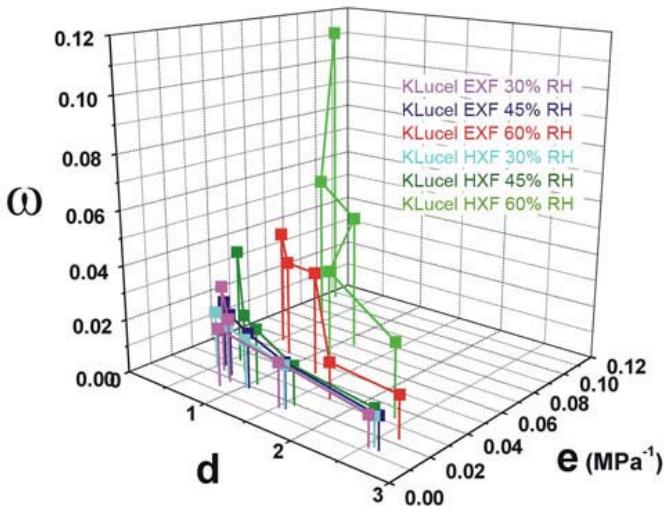

Figure 7. Three-dimensional parameter plot of Klucel Hydroxypropylcellulose EXF and HXF at different RH. ω indicates the angle of torsion; d, time plasticity; e, pressure plasticity; RH, relative humidity.

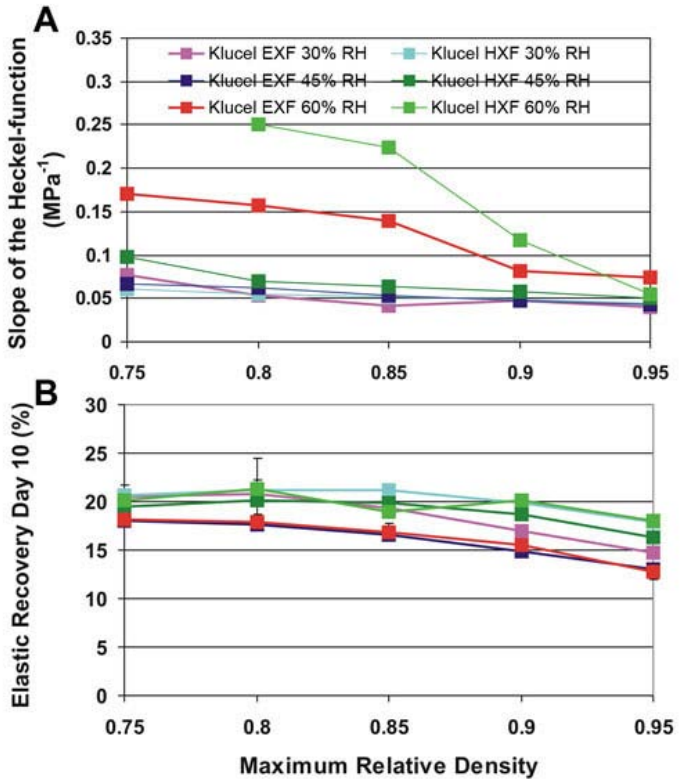

Figure 8. (a) Slope of the Heckel-function and (b) elastic recovery after 10 days at different RH. RH indicates relative humidity.

phosphate to a greater extent than MCC. The Heckel analysis confirms 3-D modeling results. The plasticity in the mixtures is increased, more for the brittle dicalcium phosphate dihydrate (Figure 10a). However, elasticity after tableting is increased as well. In this case, the influence clearly depends on the material percentage (Figure 10b).

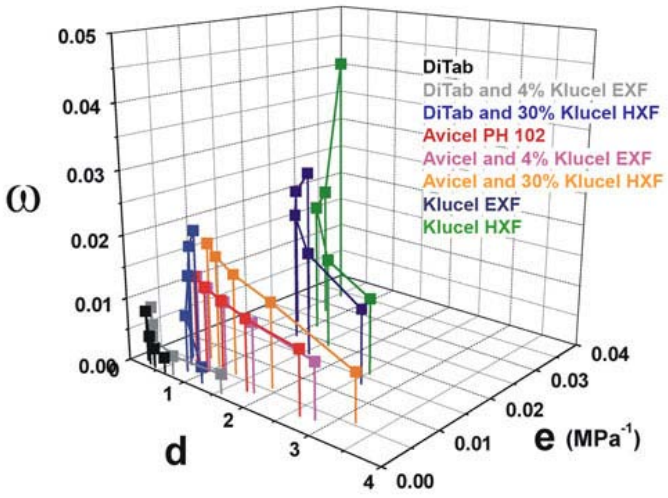

Figure 9. Three-dimensional parameter plot of mixtures with Klucel Hydroxypropylcellulose EXF and HXF. ω indicates the angle of torsion; d, time plasticity; e, pressure plasticity.

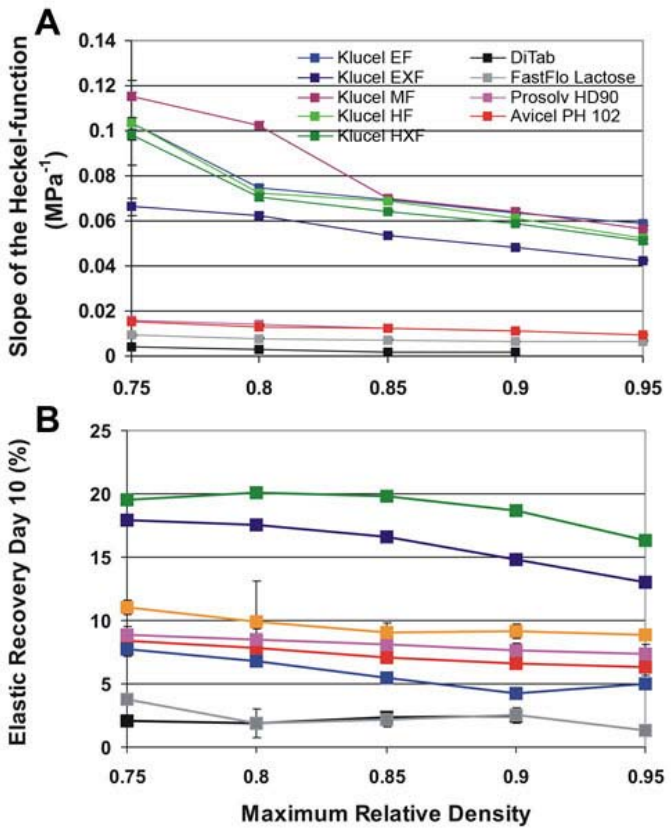

Figure 10. (a) Slope of the Heckel-function and (b) elastic recovery after 10 days of mixtures with Klucel Hydroxypropylcellulose EXF and HXF.

Addition of 30% HPC HXF increases compactibility markedly for dicalcium phosphate, while compactibility of MCC is significantly reduced. In contrast, addition of 4% HPC EXF did not markedly enhance crushing strength of dicalcium phosphate, while compactibility of MCC was improved (Figure 11).

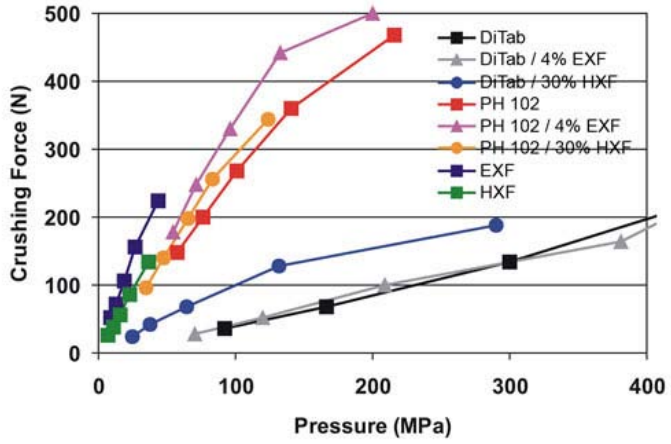

Figure 11. Compactibility plot of mixtures with Klucel Hydroxypropylcellulose EXF and HXF.

CONCLUSIONS

In comparison to the traditional filler-binders such as MCC, lactose, and dicalcium phosphate, HPC behavior is dominated by high levels of plastic deformation and high axial recovery (ie, HPC is a visco-elastic material). Compactibility and plasticity increase with lower molecular weight and particle size. Conversely, elastic deformation is more pronounced as molecular weight and particle size increase. Plasticity is also increased as moisture content increases; this can be related to the marked reduction in the T_g as moisture increases.

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