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Compressibility and compactibility properties of ethylcellulose

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Abstract

Compaction characteristics of various viscosity grades of ethylcellulose were examined using an instrumented tablet press. Four different data analysis techniques were employed to characterize the compactibility and compressibility data: tablet hardness-compression force profiles, ejected tablet Heckel analysis, work calculations from force-displacement data and force-time profile analysis. The calculated parameters derived from these approaches included the following: mean yield pressure from the Heckel analysis, net work and elastic work from the force-displacement data and the area to height (A/H) ratio from force-time data. Lower viscosity grades of ethylcellulose were found to be more compactible as described by tablet hardness-compression force profiles. Lower viscosity grades also exhibited a lower mean yield pressure from the Heckel analysis, indicating greater compressibility. Higher viscosity grades exhibited a decrease in net work and an increase in elastic work. Higher viscosity grades also exhibited greater values for the A/H ratio derived from force-time analysis, indicating lower compressibility. Higher viscosity grades of ethylcellulose showed increases in true density, melting point, and heat of fusion. The variation in compactibility and compressibility properties of different viscosity grades of ethylcellulose can be attributed to changes in the polymer's degree of order.

Keywords: Keywords: Ethylcellulose; Viscosity grade; Compressibility; Compactibility; Heckel plot; Net work; Elastic work

1. Introduction

Ethylcellulose is an inert, hydrophobic polymer which has been extensively used as a tableting excipient. It has been used as a binder (Muti and Othman, 1988), a controlled release coating (Goodhart et al., 1984), a controlled release solid dispersion matrix (Shaikh et al., 1987) and recently as a controlled release matrix in direct compression (Upadrashta et al., 1993). Only limited compression data exist in the literature to support the use of ethylcellulose in direct compression applications (Nesic, 1986). The purpose of this investigation was to characterize the com-

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pression properties of various viscosity grades of ethylcellulose to support its utility in direct compression.

No single technique is universally accepted to characterize the compression behavior of powders. Considerable debate has appeared in the literature as to the usefulness and limitations of various methods for analysis of compression data. For this reason, a range of data analysis techniques were employed to better characterize the compression properties of ethylcellulose. These techniques included tablet hardness-compression force profiles, ejected tablet Heckel analysis, work calculations from force-displacement data, and force-time profile analysis.

The use of tablet hardness-compression force profiles is a relatively simple, yet useful, method of characterizing compactibility (Higuchi, 1953; Carstensen, 1993). The radial tensile strength may be calculated from the tablet hardness (breaking force) to compare tablets of varying dimensions (Fell and Newton, 1968). A limitation of this method is that at high compression forces the radial tensile strength may not reflect the axial tensile strength and that capping/lamination is more likely to be related to the axial strength than the radial strength (Jarosz and Parrott, 1982).

A large number of compressibility models have been proposed to relate the ability of a powder to undergo volume reduction under compression stress (MacLeod, 1983). These models are empirical or semi-empirical and the physical significance of the constants describing the various models is not straightforward. Heckel analysis is one of the more commonly used models to treat compressibility data. Heckel models can be classified as tablet-in-die and ejected tablet methods based on whether the tablet dimension measurements are performed within the die or after ejection. While the in-die method is influenced by both reversible and irreversible deformation mechanisms, the ejected tablet method is primarily influenced by the irreversible deformation mechanisms. The extent of particle rearrangement during compression, the consolidation mechanism, and the mean yield pressure may be obtained from Heckel analysis (Heckel, 1961a,b). The mean yield pressure derived from Heckel analysis is an indicator of the ease with which deformation occurs and is related to the true yield strength of the material.

The determination of the mechanical energy expended during tableting has also been proposed as a useful technique to characterize the compression properties of differing materials (De Blaey et al., 1971; Krycer et al., 1982). Analysis of the force and displacement data in the compression and decompression phases of the tableting cycle allows determination of the gross mechanical energy, die-wall frictional energy, elastic energy in decompression, and the net mechanical energy expended.

The slope of a plot of the area under the force-time profile vs the maximum compression force (A/H ratio) has been proposed as a means to assess the compressibility of tablet formulations (Chilamkurti et al., 1983). The A/H ratio was suggested to be a measure of the time required to transmit energy to the compressed material and is inversely related to the compressibility. The A/H ratio is dependent on both the material being compressed and the tablet press used (Hoblitzell and Rhodes, 1986, 1989). In a study of three direct compression formulations, the A/H ratio was found to be no better than the maximum compression force in predicting tablet properties (Martinez-Pacheco et al., 1990).

2. Materials and methods

Four viscosity grades (10, 20, 45 and 100 cp) of ethylcellulose, NF (standard grade) were gifts from Dow Chemical Co. (Midland, MI) and have an ethoxy content of 48.0 to 49.5%. A 420–840 μm particle size sieve fraction was obtained from each viscosity grade to control particle size effects.

An instrumented single punch tablet press (Korsch EK-0, Korsch Tableting Inc., Somerville, NJ) was used for tableting. The compression conditions were: 200 mg tablet weight, 5/16 inch standard concave tooling and a press speed of 20 tablets per min. The compression force was varied between 2 and 12 kN in 2 kN increments. A Schleuniger hardness tester (Model 2E Vector

Corp., Marion, IA) was used for measuring tablet hardness and samples of 10 tablets were analyzed for each condition studied. A helium pycnometer (Quantachrome Multipycnometer, Quantachrome Corp., Syosset, NY) was used for true density determinations in triplicate. A DuPont DSC 2000 differential scanning calorimeter (E.I. duPont de Nemours, Inc., Wilmington, DE) was used to measure the enthalpies of fusion and the melting point range. The heating rate was 10°C/min. The X-ray powder diffraction patterns were obtained with a Scintag XDS diffractometer equipped with CuKα radiation source and a scintillation counter detector.

The maximum compression force, ejected tablet dimensions, and porosity data were analyzed using the Heckel compressibility model (Heckel, 1961a,b). One form of the Heckel equation is:

$$\ln(1/(1-D)) = KP + A$$

where D is the relative density, $(1-D)$ denotes the pore fraction, P is the applied pressure, and K and A are constants. A plot of $\ln(1/(1-D))$ vs P is referred to as a Heckel plot. The constants K and A are the slope and intercept, respectively, calculated from the linear region of the Heckel plot. While the plot is curved at lower pressures, typically a linear region results at higher pressures. The reciprocal of the slope of the linear region is referred to as the mean yield pressure of the powder. The intercept is related to the initial packing density of the powder. The initial curved region of the Heckel plot is due to particle rearrangement and the extent of particle rearrangement can be quantitated from the following relationship:

$$D_b = D_a - D_o$$

where D_b is the increase in the relative density due to particle rearrangement, $D_a = 1 - e^{-A}$ represents the extrapolated relative density from the intercept (A) of the linear portion of the Heckel plot and D_o is the initial relative density.

Force-displacement data were analyzed by the software system supplied by the press manufacturer and this system's output included the total work, elastic work, and net work. Total work is the sum of the net work and elastic work. The elastic work is the elastic energy delivered by the compact back to the punch during the decompression phase of tableting and the net work is the work permanently imparted to the tableted material. Deformation of the tablet press components, which arises from the resistance of the powder bed to densification and the elastic recovery of the material, was considered. The elastic work was expressed as a percentage of the total work. The percentage of elastic work was calculated to obtain a relative measure of the elastic nature of the materials studied.

Force-time profiles were analyzed by the press manufacturer's software system. Five profiles were analyzed and averaged at each compression force studied. A plot of the area under the force-time profile vs the upper punch force was constructed and the slope of this line yielded the A/H ratio (Chilamkurti et al., 1982).

3. Results and discussion

Table 1 presents the true density, melting point temperature range, and heat of fusion data for the various viscosity grades of ethylcellulose. The higher viscosity grades had an increase in the molecular weight of the ethylcellulose polymer chain. As the viscosity grade and molecular weight increase, the true density increases and the approximate melting point increases. The X-ray powder diffraction studies revealed that all four viscosity grades were amorphous and no significant differences were found between the grades. The melting point of the 100 cp viscosity grade

Table 1
Density, melting point range and heat of fusion of different viscosity grades of ethylcellulose

Viscosity grade (cp)	True density (g/cm^3)	Melting range [a] (°C)	Heat of fusion (cal/g)
10	1.228	165.8–177.7	1.170
20	1.244	171.1–182.4	1.448
45	1.286	174.8–184.6	1.493
100	1.310	177.2–186.4	1.577

[a] Melting range is from the initial melting point to the peak melting point temperature.

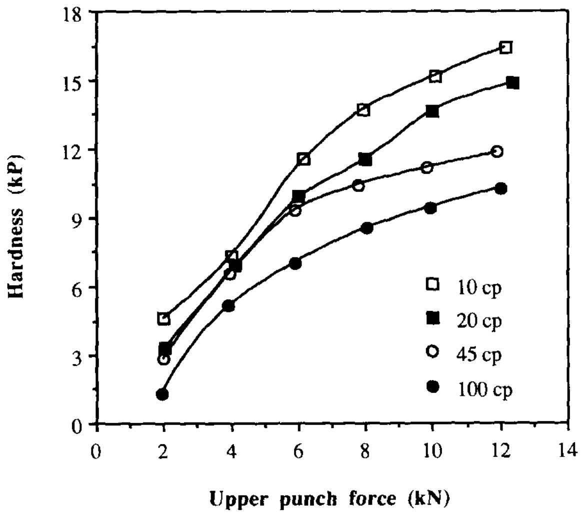

Fig. 1. Influence of compressional force on tablet hardness.

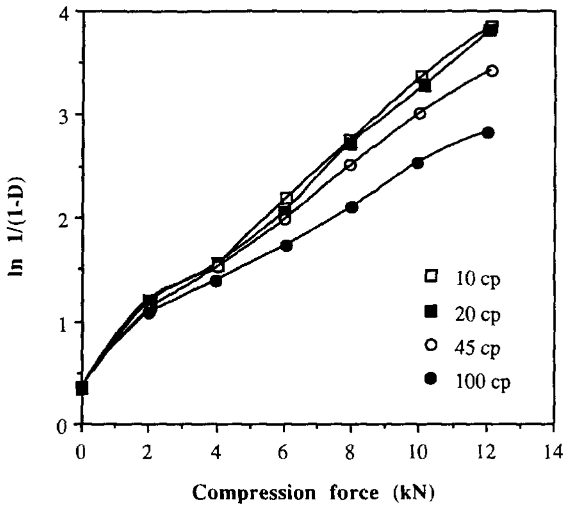

Fig. 2. Heckel plots of different viscosity grades of ethylcellulose.

was approx. 10°C higher than that of the 10 cp grade. A well defined melting point is not observed with ethylcellulose and melting occurs over an approx. 10°C temperature range for all grades. Increases in density and heat of fusion indicate an increase in polymer crystallinity (Suryanarayanan and Mitchell, 1985; Gedde, 1990). Thus, the higher molecular weight grades were inherently more ordered than the lower molecular weight grades.

Fig. 1 shows the tablet hardness-compression force profiles for the four viscosity grades. In all cases, the tablet hardness increased with an increase in compression force over the entire range of forces studied. Based on this analysis, the rank order of the compactibility was 10 cp > 20 cp > 45 cp > 100 cp. The increase in compactibility with a decrease in viscosity grade may be due to the decrease in order of the polymer at the lower molecular weights. This finding is consistent with data reported for various crystalline forms of lactose (Morits et al., 1984; Vromans et al., 1987). These two groups of authors found that decreasing the crystalline content of lactose resulted in tablets with greater hardness.

Fig. 2 shows typical ejected tablet Heckel plots. The compressibility of the materials is clearly related to the viscosity grade of ethylcellulose. In all cases, the linear region of the Heckel plots was in the compression force range of 4-12 kN. Table 2 presents the parameters derived from the Heckel analysis. The initial relative density was consistent in all cases. This is because particle size effects were controlled by using a specific sieve cut. The extent of rearrangement (D_b) increased slightly as the viscosity grade decreased. The mean yield pressure increased with increasing molecular weight across all viscosity grades studied. Compressibility is inversely related to the mean yield pressure and the rank order of the compressibility was 10 cp > 20 cp > 45 cp > 100 cp. This suggests that the lower viscosity grades are more easily deformed than the higher viscosity grades. A similar relationship was reported for polyethylene glycol (Al-Angari et al., 1985).

Table 2
Constants obtained from density measurements and the Heckel equation

Viscosity grade (cp)	D_a	D_o	D_b	Yield pressure (MPa)	r^2
10	0.541	0.298	0.243	66.2	0.987
20	0.535	0.293	0.242	66.8	0.981
45	0.520	0.301	0.219	80.7	0.996
100	0.499	0.302	0.197	104.8	0.992

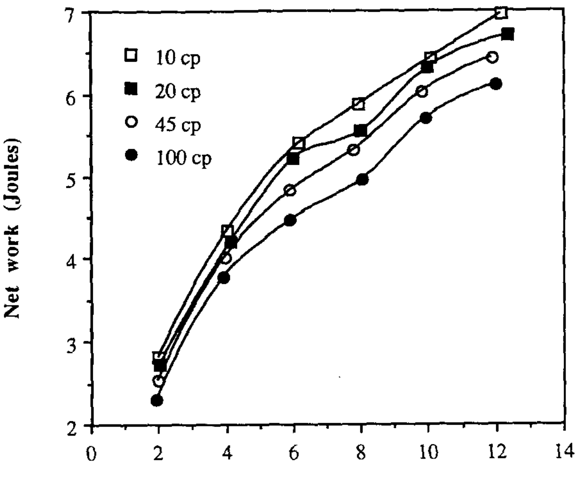

Fig. 3. Influence of upper punch force on the net work during compression.

Fig. 3 and 4 show plots of the net work and elastic work, respectively, vs the upper punch compression force for the four viscosity grades of ethylcellulose. As expected, the net work and elastic work increased with increasing compression force for all grades. The absolute magnitudes of the net work and elastic work are significantly influenced by the viscosity grade. Table 3

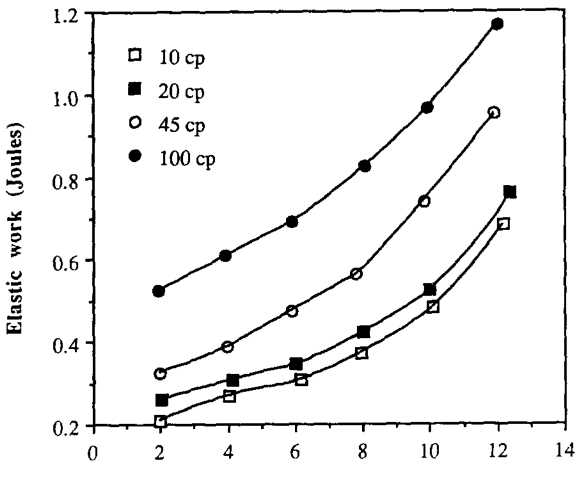

Fig. 4. Influence of upper punch force on the elastic work during compression.

Table 3
Effect of viscosity grade on the energy analysis of ethylcellulose tablets at a compaction force of 10 kN

Viscosity grade (cp)	Net work (J)	Elastic work (J)	Percentage of elastic work (%)
10	6.43	0.48	6.95
20	6.31	0.52	7.61
45	6.02	0.74	10.95
100	5.69	0.97	14.56

lists the net work, elastic work, and percentage of elastic work. With an increase in the viscosity grade, the net work decreased and the elastic work increased. The combined effect of this is that an even more significant increase occurs in the percentage of elastic work compared to the absolute magnitude of the elastic work. The percentage of elastic work approximately doubled from the 10 cp to 100 cp viscosity grades. The elastic nature of the material is important as it influences the survival of the interparticulate bonds formed during compression. The greater the elastic nature, the less permanent are the interparticulate bonds formed during the tableting cycle, and the compactibility will be diminished.

Table 4 presents the slopes and intercepts obtained from linear fits of the area under the force-time peaks vs the maximum compression force data (Chilamkurti et al., 1983). These authors have proposed that the A/H ratio, obtained from the analysis of the force-time profiles, is inversely related to the compressibility. The A/H ratios of ethylcellulose (10 cp) were 141.7 and 56.6 ms at press speeds of 20 and 50

Table 4
Area/height ratio and intercept values for different viscosity grades of ethylcellulose

Viscosity grade (cp)	Area/height	
	Ratio (ms)	Intercept (N s)
10	141.7	119.1
20	144.7	102.8
45	145.1	107.0
100	147.3	102.0

tablets per min, respectively. This demonstrates a significant influence of the compression conditions on the A/H ratio values. The A/H ratio was determined at the 50 tablets per min press speed as a system validation check, allowing a more direct comparison with literature values on other excipients at a similar press speed (Hoblitzell and Rhodes, 1986). Based on the values for the A/H ratios in Table 4, the rank order of compressibility for the four viscosity grades of ethylcellulose was 10 cp > 20 cp > 45 cp > 100 cp. The intercept value is positive for all viscosity grades but tends to decrease as the viscosity grade increases. However, the significance of the sign and magnitude of the intercept is not fully understood (Hoblitzell and Rhodes, 1989).

4. Conclusions

The rank orders of compressibility for the four viscosity grades of ethylcellulose obtained from the Heckel analysis and the force-time profile analysis are in agreement. The rank order of the compactibility as determined by tablet hardness-compression force profiles is in agreement with that for the compressibility. In addition, the rank order for the elastic nature of the four viscosity grades is 100 cp > 45 cp > 20 cp > 10 cp. The inverse relationship between the compactibility and the elastic nature is consistent with the notion that the greater the elastic component of the work done, the less permanent interparticulate bonding will be. In the case of ethylcellulose, compressibility and compactibility are positively correlated. The dependence of the compressibility and compactibility on molecular weight and viscosity grade is expected to be due to the increase in polymer order as a result of increased molecular weight.

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