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The Effect of Moisture on the Heckel and Energy Analysis of Hydroxypropylmethylcellulose 2208 (HPMC K4M)

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Abstract

The influence of moisture content on the Heckel analysis, energy analysis and strain-rate sensivity of hydroxypropropylmethylcellulose 2208 (HPMC K4M) has been evaluated.

An increase in moisture content from 0 to 14·9% w/w decreased the mean yield pressure, probably due to a plasticizing effect of moisture which reduced the resistance of particles to deformation. For each moisture content (0, 2·2, 3·8, 5·9, 9·6 and 14·9% w/w), the initial relative density and the extrapolated density from the linear portion of the Heckel plot, tended to decrease with increasing compression speed. Minor changes were observed in the initial relative density due to changes in the moisture content. The strain-rate sensitivity increased from 21·6 to 50·7% as the moisture content increased from 0 to 14·9% w/w, indicating that the plasticity of HPMC increased with increase in moisture content, whereas increase in moisture content from 0 to 14·9% w/w decreased the plastic energy.

Increase in compression force or speed of compaction increased both the plastic and elastic energies. An increase in moisture content from 0 to 5·9% w/w slightly reduced the elastic energy but above 5·9% moisture content the elastic energy was unaffected by the moisture content.

The presence of moisture in a pharmaceutical powder can play a significant role in influencing its consolidation properties. The mean yield pressure, relative density, tablet-crushing strength and capping pressure of paracetamol are significantly affected by its moisture content. The compaction properties of ibuprofen, which is a poorly compressible material, can be improved by the presence of up to about 2·5% w/w moisture (Nokhodchi et al 1995a).

Energy is needed for the compaction of materials and the formation of strong tablets. It seems logical to correlate the properties of tablets with the energy input rather than compression pressure.

This study investigates the effect of moisture content on the compression properties of hydroxypropylmethylcellulose 2208 (HPMC K4M).

Materials and Methods

Materials

HPMC K4M (Dow Chemicals, USA) was used. The 45–125-μm fraction was obtained by sieving and dried, and HPMC K4M containing different moisture contents was produced as described previously (Nokhodchi et al 1996).

Compression

Compression was carried out using a High Speed Compaction Simulator (ESH Testing Ltd, Brierley Hill, West Midlands, UK), as modified at Liverpool School of Pharmacy and fitted with 12·5-mm flat-faced punches. The details of the compaction simulator have been discussed elsewhere (Nokhodchi et al 1995a,b).

Determination of true density

The true density of HPMC K4M was determined using a Beckman air pycnometer (model 930) and was calculated from a mean of five determinations.

Measurement of net work of compaction (plastic energy) and expansion work (elastic energy)

The manipulation of compression data was explained previously (Nokhodchi et al 1995c). For a system where both punches are mobile, the punch separation may be plotted against upper punch force. The area under this curve will be the work done or energy. The plastic (net work of compaction) and elastic energies of compaction of HPMC at varying speeds (15, 140, 280 or 500 mm s^{-1}) were measured using energy analysis on the force-punch separation plots. Elastic energy is the energy delivered by the compact back to the punch during the decompression phase. Net work of compaction (plastic energy) is energy permenantly imparted to the tableted material. The elastic deformation of the punches was evaluated to allow the true displacement to be determined.

Heckel Analysis

The deformation mechanisms were investigated using the Heckel equation (Heckel 1961a,b), equation 1:

$$\mathrm{Ln}[1/(1-D)] = KP + A \qquad (1)$$

where D is the relative density of the tablet in the die at pressure P, (1 − D) denotes the pore fraction or porosity, and K denotes a material constant which is the slope of the straight line portion of the plot, the reciprocal of which is the mean yield pressure. A is the value of the intercept of the straight line and is a function of the initial bulk volume. A plot of ln[1/(1 − D)] vs P is referred to as a Heckel plot. While the plot was curved at lower pressures, a linear region typically existed at higher pressures (Heckel 1961a,b). Regression

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analysis were carried out on the Heckel plots between 20 to 75 MPa and the mean yield pressures from four compressions were determined. All data are thus the means of four determinations.

The initial curved region of the Heckel plot is attributed to particle rearrangement and its extent can be quantified using the relationship (Heckel 1961b):

$$D_b = D_a - D_0 \qquad (2)$$

where D_b is the increase in relative density due to particle rearrangement. The relative density (D_a), is the extrapolated relative density from the intercept (A) of the linear portion of the Heckel plot and was calculated from equation 3 (Heckel 1961b); D_0 is the initial relative density.

$$D_a = 1 - e^{-A} \qquad (3)$$

Statistical analysis

All data were statistically analysed by two-way analysis of variance and Tukey's multiple comparison tests. Results are quoted as significant where $P < 0.05$.

Results and Discussion

Fig. 1 shows typical Heckel plots for HPMC K4M of different moisture contents. Increase in the moisture content resulted in increases in the relative densities for a given applied pressure and indicates that powder consolidation was facilitated under compression and that a reduced resistance to particle deformation occurred with an increase in moisture content.

The effect of compression speed on the Heckel plots was also investigated. Fig. 2 shows the plots for HPMC containing 0% of moisture at four compression speeds. The slopes of all the Heckel plots decreased as the compression speed was increased and the curves progressively moved down the y axis indicating a decrease in densification. A similar trend was obtained for all moisture contents (Fig. 3). The effects of compression speeds and moisture contents on the mean yield pressures are shown in Fig. 4. The increase in the mean yield pressures with increasing compression speed equates to a reduction in the amount of plastic deformation, due to the time-dependent nature of plastic flow, and thus to an increase in bond formation and or an increase in brittle behaviour (Roberts & Rowe 1985). These results suggest ductile behaviour (plastic behaviour) for HPMC K4M. At each moisture content, the rank order of the mean yield pressures of HPMC K4M tablets at different compression speeds was 500 > 280 = 140 > 15 mm s^{-1}. Increasing the compression speed from 15 to 500 at moisture contents of 0, 2·2, 3·8, 5·9, 9·6 or 14·9% w/w, caused increases of 28, 38, 40, 54, 72 or 100% in the mean yield pressures respectively.

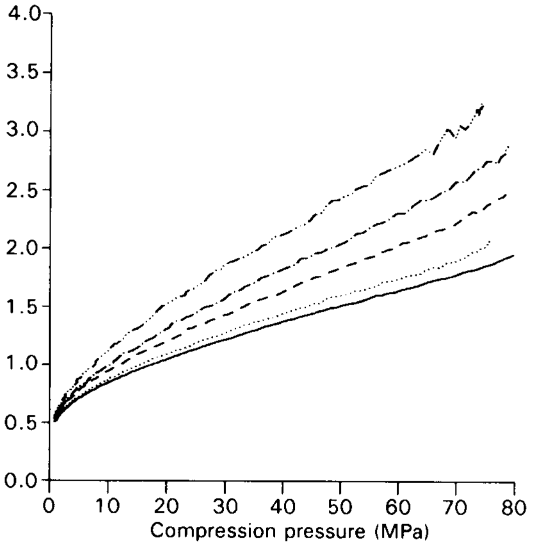

FIG. 1. The effect of moisture content on the Heckel plots of HPMC K4M at a compression speed of 15 mm s^{-1}. (—) 0% w/w, (···) 2·2 % w/w, (— —) 5·9 % w/w, (– ·) 9·6 % w/w, (– ···) 14.9 % w/w.

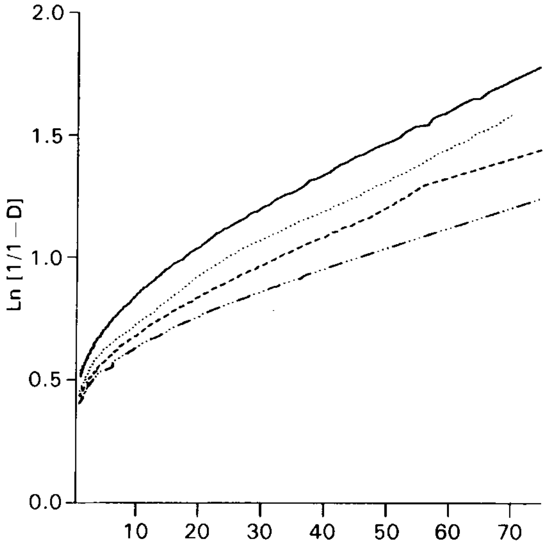

FIG. 2. The effect of compression speed on the Heckel plots of HPMC K4M (moisture content 0%). (—) 15 mm s^{-1}, (···) 140 mm s^{-1}, (— — —) 280 mm s^{-1}, (– ···) 500 mm s^{-1}.

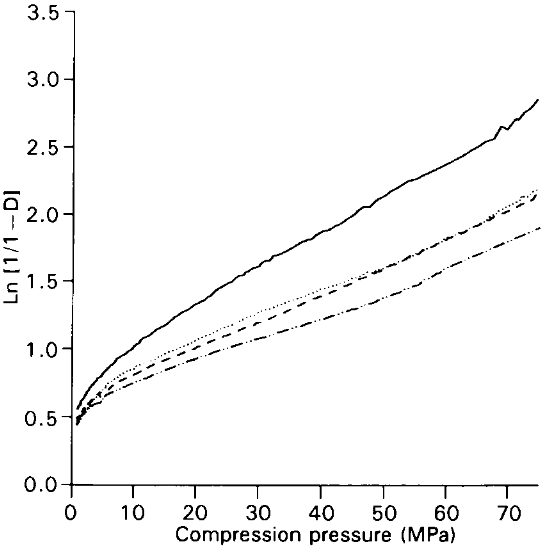

FIG. 3. The effect of compression speed on the Heckel plots of HPMC K4M (moisture content 9·6% w/w). (—) 15 mm s^{-1}, (···) 140 mm s^{-1}, (— —) 280 mm s^{-1}, (– ···) 500 mm s^{-1}.

Fig. 4 also shows that an increase in moisture content from 0 to 14·9% w/w resulted in marked reductions in the mean yield

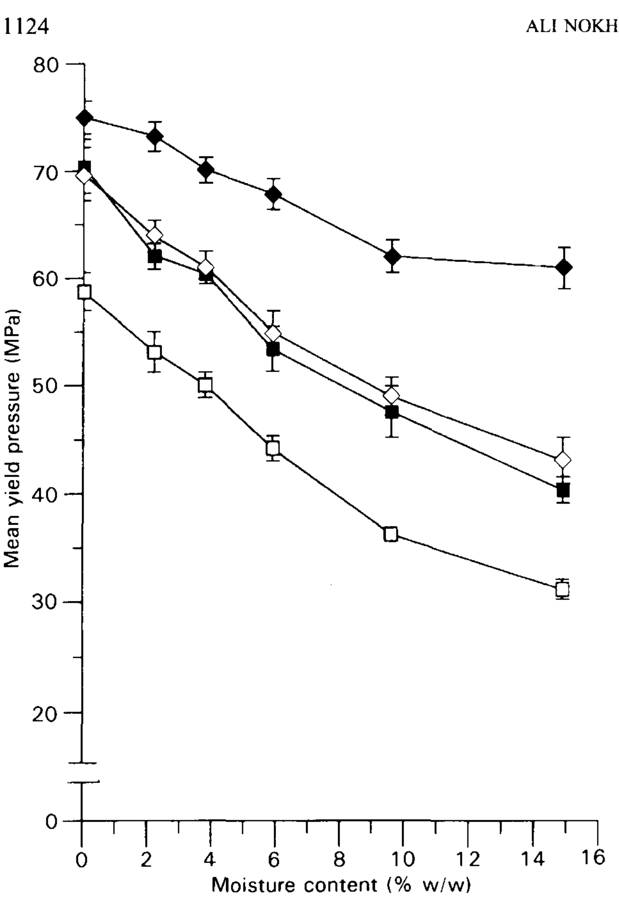

FIG. 4. *The effect of moisture content on the mean yield pressures of* HPMC K4M tablets made at compression speeds of 15 (□), 140 (■), 280 (◇) or 500 (◆) mm s^{-1} to a compression force of 10 kN. Results are the means and standard deviations of four determinations.

Table 1. Values of the correlation coefficients, obtained from the early compression phase (3–40 MPa) and values of strain rate sensitivity (SRS) of HPMC K4M at various moisture contents.

Moisture content (%)	Correlation coefficient (r)	SRS (%)
0·0	0·982 ± 0·000	21·60 ± 2·14
2·2	0·987 ± 0·001	27·38 ± 2·54
3·8	0·989 ± 0·001	28·54 ± 1·76
5·9	0·989 ± 0·002	34·92 ± 1·98
9·6	0·991 ± 0·001	41·81 ± 2·43
14·9	0·995 ± 0·000	50·67 ± 2·57

Results are the means and standard deviations of four determinations.

pressures from 58·8 to 31·1 MPa at a compression speed of 15 mm s^{-1}. This indicates that the presence of up to 14·9% *w/w moisture enhanced the plastic deformation of the powder* under compression by acting as an internal lubricant. Increasing the moisture content from 0 to 14·9% w/w caused 47, 43, 40 or 15% decreases in the mean yield pressures at compression speeds of 15, 140, 280 or 500 mm s^{-1}, respectively. Thus, the densification of the polymer became easier as the moisture content increased. The values of mean yield pressure for HPMC containing 0 and 14·9% w/w moisture at a compression speed of 15 mm s^{-1} were 58·8 and 31·1 MPa, respectively. Thus HPMC without moisture is hard, less plastic and needs higher pressure to deform, whereas at high moisture content, the HPMC is soft, more plastic, and easily compressible at lower pressures. Both moisture content and compression speed had significant effects on the mean yield pressures of HPMC K4M. Generally, the mean yield pressures of different moisture contents could be clearly differentiated from each other at different compression speeds. However, at 500 mm s^{-1} there were no significant differences between the mean yield pressures of HPMC K4M containing 0 or 2·2, 3·8 or 5·9 or 9·6 or 14·9% w/w moisture content.

In Table 1, the correlation coefficients of the early compression phases of the Heckel plots are shown at various moisture contents obtained in the pressure range of 3–30 MPa. When the applied pressure is relatively low, the porosity reduction should be strongly enhanced by particle fragmentation (Duberg & Nystrom 1986). The curvature of the plot could be evaluated as the deviation from a straight line and expressed as the correlation coefficient which reflected the degree of fragmentation during the early compression phase. The small decreases in correlation coefficient observed for HPMC with decreasing moisture content might, therefore, indicate slight increases in the degree of fragmentation. The deviation from linearity during the early compression phase has also been attributed to particle slippage and rearrangement in the die (York 1978). The slight change in correlation coefficient can therefore also be due to changes in the ability of the particles to rearrange in the die during the volume reduction. The results indicate, however, that there are changes in behaviour of the volume reduction of HPMC in the early compression phase, due to the sorbed moisture.

Table 2 lists the initial relative densities (D_0), the extrapolated densities from the linear portions of the Heckel plots (D_a), and the changes in the relative densities attributed to particle rearrangement (D_b) for different moisture contents at

Table 2. Values of D_0, D_a and D_b at at low (15 mm s^{-1}) or high (500 mm s^{-1}) compression speeds at various moisture contents.

	Compression speed (mm s^{-1})					
	15			500		
Moisture content (%)	D_0	D_a	D_b	D_0	D_a	D_b
0·0	0·401 ± 0·002	0·542 ± 0·002	0·141 ± 0·004	0·321 ± 0·002	0·401 ± 0·003	0·080 ± 0·006
2·2	0·407 ± 0·003	0·552 ± 0·012	0·145 ± 0·007	0·331 ± 0·005	0·416 ± 0·006	0·085 ± 0·004
3·8	0·410 ± 0·006	0·547 ± 0·009	0·137 ± 0·006	0·333 ± 0·005	0·421 ± 0·003	0·088 ± 0·001
5·9	0·414 ± 0·003	0·551 ± 0·009	0·137 ± 0·012	0·345 ± 0·004	0·435 ± 0·007	0·090 ± 0·011
9·6	0·421 ± 0·005	0·567 ± 0·002	0·146 ± 0·006	0·363 ± 0·004	0·463 ± 0·006	0·100 ± 0·004
14·9	0·425 ± 0·003	0·616 ± 0·008	0·191 ± 0·005	0·384 ± 0·008	0·514 ± 0·004	0·130 ± 0·007

Results are the means and standard deviations of four determinations.

two compression speeds (15 and 500 mm s^{-1}). For each moisture content, D_0, D_a and D_b decreased with an increase in compression speed. It has been shown that a decrease of D_0 with increasing compression speed is due to a decrease in the rearrangement and particle slippage phase of the densification of a powder bed. This may be due to an increase in the friction and adhesive forces between particles opposing the rearrangement process (Roberts & Rowe, 1985). Minor changes were observed in the initial relative density (D_0) due to changing the moisture content (Table 2).

The values of D_b became lower with increasing compression speed (Table 2). D_b gives an indication of the extent of particle rearrangement and slippage. Its reduction could be due to an increase in the frictional and adhesive forces between the particles opposing the rearrangement. Additionally, as this process involves movement of particles, it will be time-dependent. Consequently, at higher compression speeds, less time is available for rearrangement, so the values of D_b are reduced. The values of intercepts of the Heckel plots (D_a) increased with increasing moisture content (Table 2).

D_a is a parameter relating to densification due to the slippage and rearrangement of particles (Roberts & Rowe 1985). The values indicate that moisture may act as a lubricant smoothing out the surface micro-irregularities, reducing the frictional forces and facilitating particle rearrangement and slippage during the densification phase of compaction.

Equation 4 was used to calculate the strain rate sensitivities (SRS) from the slopes of Heckel plots obtained at 15 mm s^{-1} (low compression speed) and 500 mm s^{-1} (high compression speed).

$$SRS = [(P_{y_2} - P_{y_1})/P_{y_2}] \times 100 \qquad (4)$$

In equation 4, P_{y1} and P_{y2} are the mean yield pressure at 15 and 500 mm s^{-1}, respectively. The results are shown in Table 1. Materials which are more strain-rate sensitive are those materials which plastically deform (Roberts & Rowe 1985). Generally the SRS values increased as the moisture content increased (Table 1), confirming that the plasticity of HPMC concomitantly increased.

Fig. 5 illustrates the effects of moisture content and compression force on the plastic energies (net work of compaction) produced at a compression speed of 15 mm s^{-1}. The plastic energies increased as the compression force increased from 5 to 20 kN at all moisture contents. For any given compression force, an increase in moisture content significantly decreased the plastic energies. Increases in the moisture contents probably affected the net compaction energies (plastic energies) by a combined effect of reducing the resistance of particles and enhancing the particle deformation, reducing the interparticle friction owing to the lubrication effects of the moisture. Two-way analysis of variance showed that both moisture content and compression force affected the plastic energies of HPMC K4M tablets. However, at each moisture content the plastic energies of tablets made at a 15 and 20 kN could not be statistically differentiated from each other.

Fig. 6 shows plastic energy plotted as a function of tablet tensile strength for the different moisture contents. To achieve a specific tablet strength, a higher plastic energy was needed for the dried material. In other words, to achieve a constant tensile strength, a lower plastic energy was needed with increasing moisture content. For example, to obtain tablets with a tensile strength of about 2 MPa, the plastic energies required were 7·65, 4·60 and 2·86 at moisture contents of 0, 5·9 and 14·9% w/w, respectively.

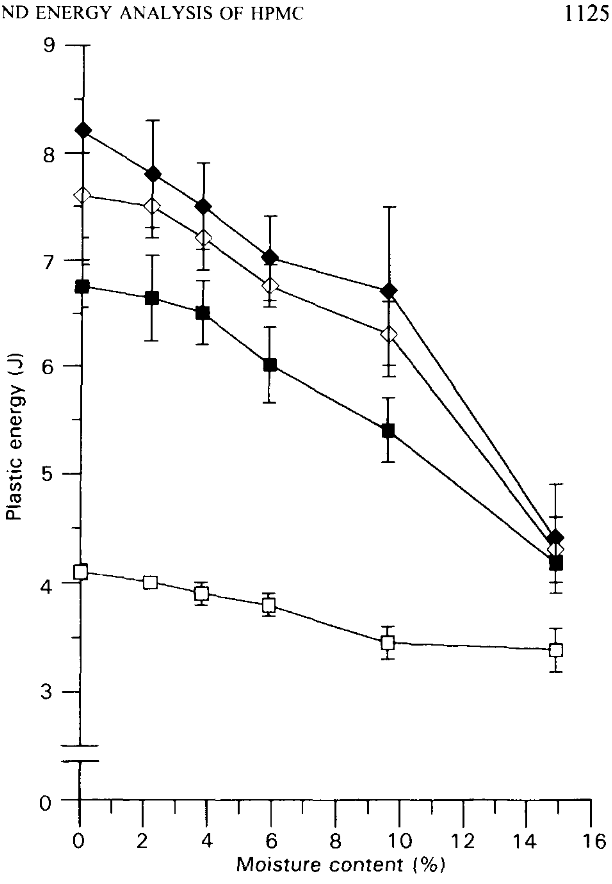

FIG. 5. The effect of moisture content on the plastic energies of HPMC K4M tablets made at compression forces of 5 (□), 10 (■), 15 (◇) or 20 (◆) kN at a compression speed of 15 mm s^{-1}. Results are the means and standard deviations of four determinations.

The effects of compression force and moisture content on the elastic energies are shown in Fig. 7. At all moisture contents an increase in compression force resulted in an increase in the elastic energies. With increasing compression force the amount of elastic deformation contributing to the whole deformation process increased and relatively less of the total energy was used for the formation of bonds between particles. This was because bond formation energies are implicit in the plastic energies whose contribution to the compaction process concomitantly decreased as the contribution by the elastic energy increased. At each moisture content the plastic energy of the tablets made at different compression forces could be clearly differentiated from each other. An increase in moisture content from 0 to 5·9% w/w slightly decreased the elastic energy (Fig. 7), whereas above 5·9% w/w moisture content the elastic energy was not affected by the moisture content with the exception of compacts made at 5 kN.

Table 3 gives the effects of compression speed and moisture content on the plastic energies, elastic energies and percent elastic energies at a compression force of 10 kN. As the compression speed was increased from 15 to 500 mm s^{-1} at varying moisture contents, both plastic energies and elastic energies increased. There is the possibility that part of the net energy might be utilised in particle rearrangement, die wall

Table 3. Effect of moisture content and compression speed on the plastic energy (PE), elastic energy (EE) and percentage of elastic energy (%EE) of HPMC K4M tablets at a compression force of 10 kN.

	Compression speed (mm s^{-1})					
	15			500		
Moisture content (%)	PE (J)	EE (J)	% EE	PE (J)	EE (J)	% EE
0·0	6·73 ± 0·10	1·53 ± 0·09	18·52 ± 1·90	7·61 ± 0·15	5·20 ± 0·08	40·69 ± 4·91
2·2	6·58 ± 0·20	1·45 ± 0·08	18·06 ± 1·18	7·30 ± 0·09	4·97 ± 0·11	40·50 ± 4·50
3·8	6·48 ± 0·18	1·30 ± 0·07	16·70 ± 1·80	7·10 ± 0·11	4·50 ± 0·18	38·79 ± 5·90
5·9	5·89 ± 0·19	1·35 ± 0·11	18·61 ± 1·99	7·01 ± 0·08	4·68 ± 0·21	41·44 ± 3·98
9·6	5·27 ± 0·09	1·34 ± 0·12	20·39 ± 2·06	6·40 ± 0·15	5·01 ± 0·25	44·44 ± 4·12
14·9	4·17 ± 0·21	1·38 ± 0·07	24·87 ± 3·88	5·49 ± 0·19	5·14 ± 0·29	48·16 ± 5·97

Results are the means and standard deviations of four determinations.

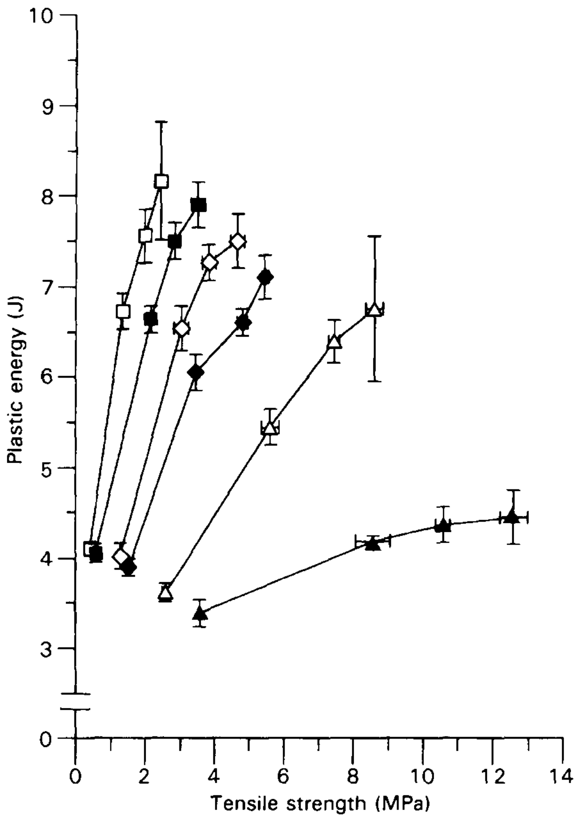

FIG. 6. The relationship between tensile strengths and plastic energies of HPMC tablets containing 0 (□), 2·2 (■), 3·8 (◇), 5·9 (◆), 9·6 (△) or 14·9 (▲) % w/w compressed at 15 mm s^{-1}. Results are the means and standard deviations of four determinations.

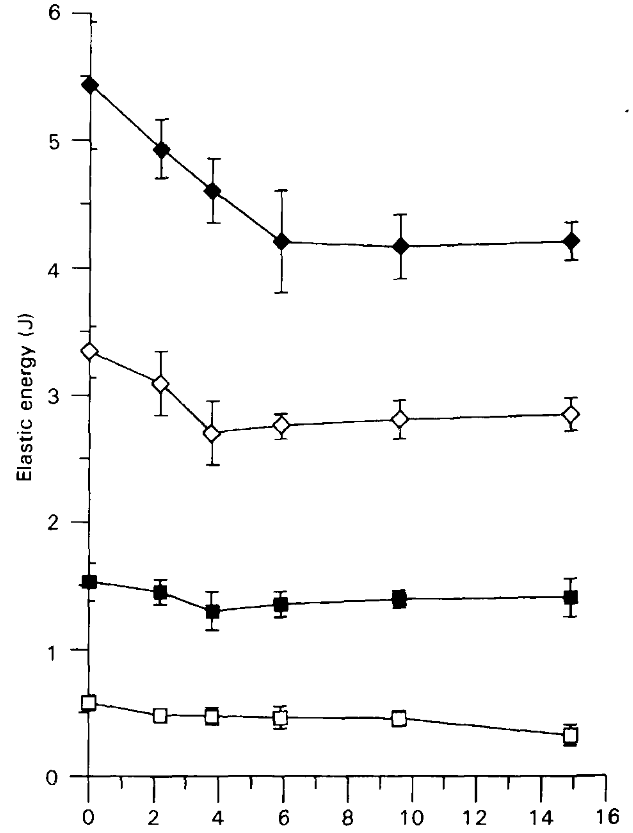

FIG. 7. The effect of moisture content on the elastic energies of HPMC K4M tablets made at 5 (□), 10 (■), 15 (◇) or 20 (◆) kN at a compression speed of 15 mm s^{-1}. Results are the means and standard deviations of four determinations.

friction and increased inter-particulate friction that may occur at higher compression speeds. The sum of the net energy and elastic energy (gross energy) increased as the compression speed increased. The percentage elastic energy showed a more than twofold increase as the compression speed was increased from 15 to 500 mm s^{-1}. At the high compression speed of 500 mm s^{-1}, the elastic energy slightly decreased as the moisture increased from 0 to about 3·8% w/w, whereas above 3·8% w/w moisture content, the elastic energies were unaffected by the moisture content. Comparison of the percentage elastic energies at different moisture contents showed that the moisture content did not affect the percentage elastic energy at 15 and 500 mm s^{-1}.

In conclusion, the mean yield pressures, correlation coefficients of Heckel plots during early compression phase, strain rate sensitivity, tensile strengths and net compaction energies were affected by compression speed and moisture content. The values D_0, D_a and D_b decreased on increasing the compression speed. The percentage elastic energy was unaffected by the changing moisture content, but it was affected by increasing the compression speed.

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