J. Pharm. Pharmacol. 1996, 48: 1116–1121
Received June 21, 1995
Accepted March 25, 1996

The Influence of Moisture Content on the Consolidation Properties of Hydroxypropylmethylcellulose K4M (HPMC 2208)

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Abstract

The effect of moisture content, compression speed and compression force on the compaction properties of HPMC K4M has been evaluated.

As the moisture content increased from 0 to 14·9% w/w, the thickness of HPMC K4M compacts increased at constant compression force and speed. This increase in moisture content also resulted in a marked increase in the tensile strength of the tablets. At a speed of 15 mm s^{-1} and force of 10 kN, as the moisture content increased from 0 to 14·9% w/w, the tensile strengths increased from 1·34 to 8·54 Mpa. Equivalent tensile strengths could be obtained with less compression force as the moisture content in the polymer was increased. Increasing the compression speed generally decreased the tensile strength of HPMC K4M tablets.

The dependence of tablet porosity and tensile strength on compression speeds showed that HPMC K4M is consolidated by plastic deformation. At all compression speeds, an increase in moisture content reduced the percentage elastic recovery of HPMC compacts due to greater tablet consolidation. The lowest elastic recovery (1·18%) was found for tablets made at 15 mm s^{-1} and 5 kN, containing 14·9% w/w moisture content.

Hydroxypropylmethylcellulose (HPMC) is a cellulose ether that is widely employed in controlled release matrices. Such polymers take up and retain large amounts of water in their amorphous portions when exposed to water vapour. This absorbed water can influence the physical properties of the polymer. It is therefore important to understand the effect of moisture on the compaction properties of HPMC whose matrices should remain indivisible in the gastrointestinal tract and must be mechanically strong. Since a major component of a matrix is the polymer, it is important to characterize the response of such polymers to compression.

Kawashima et al (1993) investigated the effects of particle size, degree of hydroxypropyl substitution and moisture content of a low-substituted hydroxypropylcellulose on its compactibility with paracetamol. The crushing strengths of the tablets increased on decreasing the particle size of hydroxypropylcellulose and its degree of hydroxypropyl substitution. The crushing strength of tablets containing paracetamol and hydroxypropoxylcellulose reached a maximum at moisture levels of between 9 and 14%.

Water sorbed to starches and cellulose exists in at least 3 states: tightly bound to anhydroglucose units; less tightly bound; and bulk water (Zografi et al 1984). Studying the effect of particle size and sorbed moisture on the compression behaviour of HPMCs, Malamataris et al (1994) showed that HPMC K100M of particle size < 120 μm, had the greatest tendency to take up moisture in comparison with other grades and that the corresponding size fraction of HPMC F4M showed the lowest uptake. Nokhodchi et al (1995, 1996) investigated the effects of particle size and viscosity grade of the K series of HPMC on its compaction properties in the absence of moisture. They showed that particle size of HPMC, viscosity grade, compression force and compression speed significantly affected the compaction properties of HPMCs. HPMC K100 was more plastic than the other viscosity grades of HPMC and the mean yield pressures were independent of particle size, with the exception of HPMC K100M.

Tensile strengths provide basic information on the compaction properties of compressed powders. Such data have been used widely, e.g. in the optimization of formulation, the evaluation of direct compression of powders and the characterization of deformation, bonding and capping behaviour of single components or binary mixtures.

Although some studies have examined the effect of moisture content on the compaction properties of HPMC, the data are incomplete and there are no reports on the effect of moisture content on the compaction properties of HPMC at different compression speeds and different compression forces in the presence of moisture. This study examines whether changes in moisture content of HPMC K4M have any effects on its compaction properties and the tensile strengths of its resulting tablets.

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Materials and Methods

Materials

Hydroxypropylmethylcellulose K4M (HPMC K4M) (Dow Chemicals, USA) was used. The 45–125-μm particle size fraction was obtained by sieving the material through test sieves (Endecott, UK) on a mechanical vibrator (Pascal Engineering, UK) and dried in a vacuum oven at 70°C for 5 days before use.

Determination of true density

The true density of HPMC K4M was determined using a Beckman air pycnometer (Model 930, Fullerton, USA) and was calculated from the mean of five determinations.

Moisture sorption by HPMC K4M

Dried samples of HPMC K4M were placed in tared, 5-cm diameter Petri dishes and exposed to different relative humidities using desiccators which had been pre-equilibrated and stored at 22 ± 3°C. Saturated salt solutions of potassium acetate, magnesium chloride, potassium carbonate, sodium bromide or sodium chloride were used to give relative humidities of 22, 33, 43, 58 or 75% respectively. The Petri dishes containing HPMC were taken out of the desiccators (12, 18, 24, 48, 96, 120 and 168 h) and accurately weighed to ensure that equilibrium water uptake had occurred. Moisture contents were determined on a dry weight basis of HPMC K4M. The equilibrium moisture contents of samples which were subjected to compression analysis were 0, 2·2, 3·8, 5·9, 9·6 and 14·9% w/w.

Compression

Compression was carried out using a high speed compaction simulator (ESH Testing Ltd Brierley Hill,West Midlands,UK), as modified at the Liverpool School of Pharmacy, using 12·5-mm flat-faced punches. The details of the compaction simulator have been described elsewhere (Nokhodchi et al 1995). A sawtooth time-displacement profile was used to control both upper and lower punches. Dwell times were not used. Four tablets were produced at each compression speed (15, 140, 280 or 500 mm s^{-1}) for the different moisture contents of HPMC, to a compression force of 10 kN. Four tablets were produced for each moisture content at compression forces of 5, 10, 15 or 20 kN at a compression speed of 15 mm s^{-1}. Constant weight (400 mg) was maintained for each sample. The die wall was cleaned with acetone and prelubricated with 4% w/w magnesium stearate in acetone before each compression. During compression, upper punch load and punch separation were monitored to an accuracy of ±0·05 kN and ±12 μm, respectively.

Determination of elastic recovery (ER)

The percentage elastic recovery of tablets, made with different moisture contents at different compression speeds, was determined using equation 1 (Armstrong & Haines-Nutt 1972):

$$ER(\%) = [(H_t - H_m)/H_m] \times 100 \quad (1)$$

where H_m is the height of the tablet at maximum compression force and H_t is the tablet height 24 h after ejection when thickness and diameter of the tablets were measured to ±10 μm using a micrometer (Mitutoyo, Japan). The mean elastic recovery of four tablets was determined for each experimental condition.

Determination of minimum porosity of tablet under compression

The minimum percentage porosities of tablets in the die under compression were calculated from force and displacement data, where the compression forces reached their maxima.

Tensile strength

Tablet crushing strengths were determined from the force required to fracture tablets by diametral compression on a motorised tablet hardness tester (Model 2E, Schleuniger, Switzerland). The corresponding tensile strengths were calculated according to equation 2 (Fell & Newton 1970):

$$T = 2P/\pi DH \quad (2)$$

where T is the tensile strength (MPa), P is the applied load (MPa), D and H are tablet diameter and thickness respectively. The results are the mean of four determinations.

Scanning electron microscopy (SEM)

The tablet faces of HPMC K4M containing different moisture contents were examined by scanning electron microscopy (Jeol Model JSM T200, Tokyo, Japan).

Statistical interpretation of data

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

Results and Discussion

The effect of moisture content on the thicknesses of HPMC tablets made at different compression forces and a compression speed of 15 mm s^{-1} is illustrated in Fig. 1. At each compression force, an increase in moisture content resulted in a reduction in the thickness of the tablets. Two-way analysis of variance showed that both moisture content and compression force had significant effect on the thickness of the HPMC tablets. Tukey's test showed that at each relative humidity the thickness of tablets made at different compression forces could be clearly differentiated from each other, but there were generally no significant differences between the thicknesses of the tablets made at 10 and 15 kN. At high moisture content (14·9%

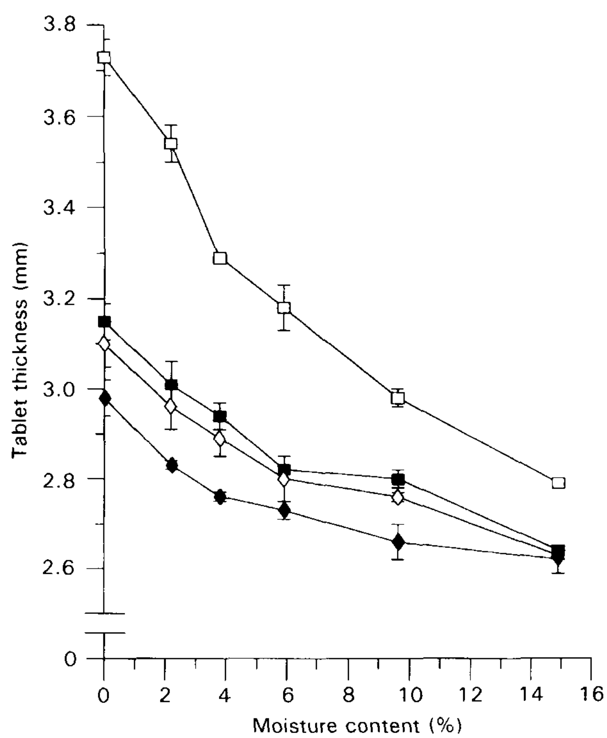

FIG. 1. The effect of moisture content on tablet thickness of 400 mg of HPMC K4M tablets compressed at 5 (□), 10 (■), 15 (◇) and 20 (◆) kN at a compression speed of 15 mm s^{-1}.

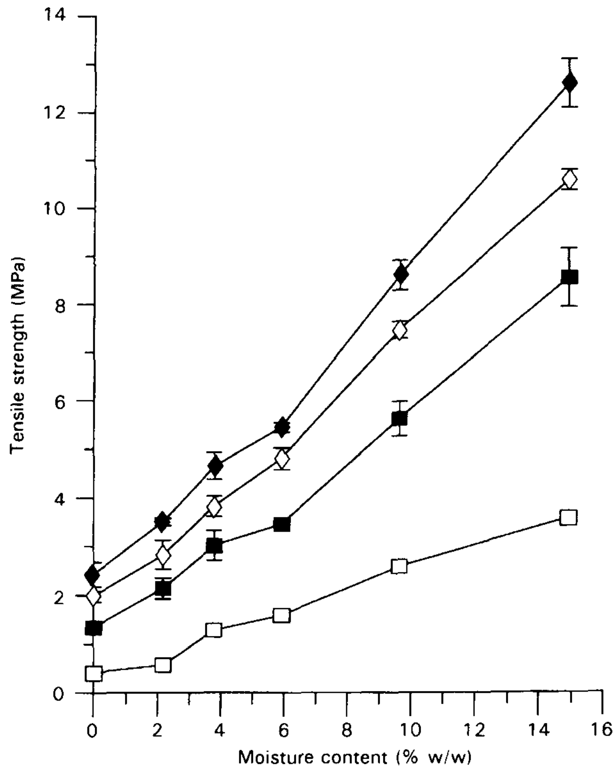

FIG. 2. The effect of moisture content on the tensile strength of HPMC K4M tablets compressed at 5 (□), 10 (■), 15 (◇) and 20 (◆) kN at a compression speed of 15 mm s^{-1}.

w/w) there was no significant difference between the thickness of the tablets made at 10, 15 or 20 kN.

The tensile strength of tablets is mainly determined by the range and magnitude of the van der Waals' forces between the particles and the development of additional bonds formed by plastic deformation, melting of the powder particles or the binder films developed during granulation (Malamataris & Pilpel 1983). Fig. 2 shows the effect of moisture content and compression force on the tensile strengths of the HPMC tablets. Malamataris & Karidas (1994) reported that the tensile strengths of HPMC K4M tablets initially increased with increasing moisture content, reached a maximum at about 10% moisture content and then decreased as the moisture content was further increased from 10 to about 20%. The initial increase in tensile strength from 0 to about 10% was attributed either to an increase in the number and area of interparticle bonds (due to an increase in packing fraction) or to an increase in the strength of the interparticle bonds. The subsequent decrease in tensile strengths with moisture content above 10% was attributed to a weakening of the interparticle bonds between the molecules of the polymers constituting the particles, especially at their surface due to disruption of the forces. However, the present study shows that when the moisture content of HPMC K4M was increased from 10 to about 15% w/w, the tensile strength of HPMC tablets increased from 5·6 to 8·5 MPa at a compression force of 10 kN. Increases in moisture content resulted in increased tensile strengths at each compression force.

It is probable that differences in tablet strength were due to the presence of water which influenced the bonding within the tablet matrix. At low moisture content, there would be little water available while as the water load increased, bonding between the points of contact would be facilitated. Since the thicknesses of HPMC tablets also decreased with moisture (Fig. 1), at least part of the increased tablet tensile strengths can be presumed to be due to increased contact between the particle surfaces. Additionally, the water could facilitate the formation of interparticle hydrogen bonding and/or increase the van der Waals' forces. The tensile strengths of the HPMC K4M tablets were significantly affected by changing the compression force and moisture content. As more water molecules adhere to the surface, they are subjected to both surface binding and diffusional forces, the latter tending to cause moisture transfer into the material. Then the water diffusing and penetrating the micropore structure may cause softening of the particles and under high pressure the area of contact between the particles will increase with plastic deformation, and more solid bonds may be formed.

Fig. 2 also shows that the force required to achieve a specific tablet tensile strength decreased as the moisture content of the polymer was increased.

The effect of compression speed on the tensile strengths of HPMC K4M tablets of different moisture contents is shown in Fig. 3. Generally, at all moisture contents an increase in compression speed resulted in a reduction in the tensile strengths of the tablets. This was probably due to there being less time available for the plastic deformation of the HPMC

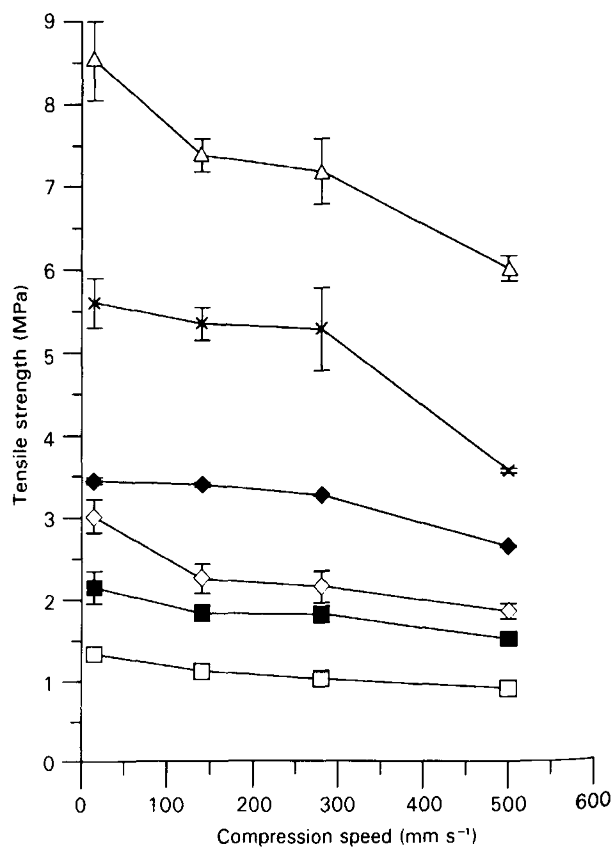

FIG. 3. The effect of compression speed on the tensile strength of HPMC K4M tablets containing 0 (□), 2.2 (■), 3.8 (◇), 5.9 (◆), 9.6 (X) or 14.9 (△) % w/w compressed at 10 kN.

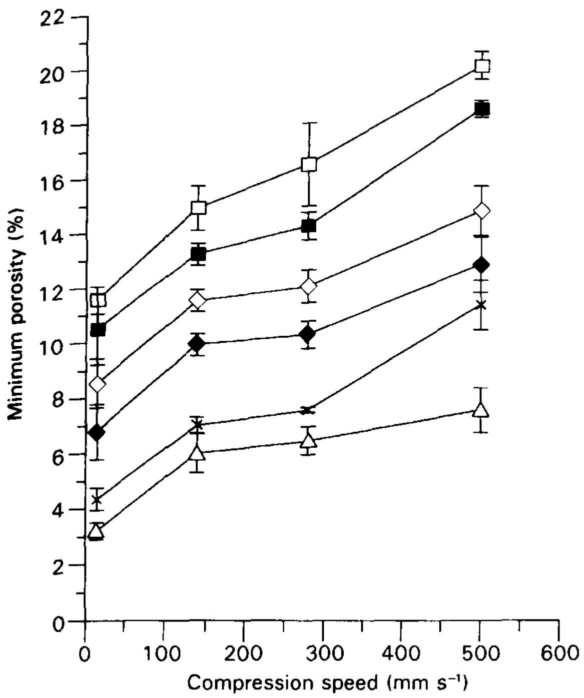

FIG. 4. The effect of compression speed on minimum porosity of HPMC K4M tablets in the die under compression containing 0 (□), 2.2 (■), 3.8 (◇), 5.9 (◆), 9.6 (X) or 14.9 (△) % w/w compressed at 10 kN.

powder at the higher speeds and hence for the formation of bonds, resulting in weaker tablets. A reduction in the tensile strengths of HPMC tablets with increasing compression speed in the absence of moisture has been reported by Nokhodchi et al (1996). Two-way analysis of variance showed that the tensile strengths were significantly affected by compression speed and moisture content. The tensile strengths of the tablets made with different moisture contents were significantly different from each other at each compression speed.

The effect of compression speed and moisture content on the minimum porosity of the tablets in the die under compression was also investigated (Fig. 4). The porosities of the HPMC compacts increased with increasing speed of compaction.

Tablets made at the lower speed showed much lower porosities, as the more extensive time-dependent deformation results in denser tablets. Examination of Figs 3 and 4 shows that changes in porosity which result from compression at different speeds may be correlated with the changes in tablet tensile strength. An increase in porosity is generally associated with a reduction in tensile strength, and vice-versa. This is probably because an increase in porosity is likely to be associated with less extensive contact and therefore bonding between particles and a greater incidence of flaws within the tablets. The pores within the tablet could act as stress concentrators reducing the stress required to propagate a crack through the tablet. An increase in the porosity is therefore likely to result in a decrease in tablet tensile strength.

Armstrong & Palfrey (1989) showed that the reduction in porosity of a powder bed on compression could be a function of the velocity of the punch of the press. Substances which consolidated principally by fragmentation (such as lactose or Emcompress) showed relatively little velocity dependence, whereas microcrystalline cellulose and starch 1500, which primarily deformed by plastic deformation, showed stronger velocity dependence. Since the porosities of HPMC K4M tablets were relatively more velocity-dependent, this again confirms that the HPMC powder was consolidated by plastic deformation; as the compression speed was increased from 15 to 500 mm s^{-1} the porosities of HPMC tablets increased from 11·5, 8·5 and 4·3% to 19·9, 14·7 and 11·3% for moisture contents of 0, 3·9 and 9·6% w/w respectively. The increase in the porosity of tablets in the die with compression speed was significant, and at moisture contents of 0, 2·2, 3·8, 5·6 or 9·6% w/w, the porosities of tablets in the die could be differentianted from each other. At the highest moisture content (14·9% w/w) there was no significant difference between the porosities of tablets made at 140, 280 or 500 mm s^{-1}. Therefore, the porosities of HPMC compacts at high moisture content are not greatly changed by compression speeds above 140 mm s^{-1}.

At any compression speed, an increase in moisture content resulted in a decrease in the porosity of tablets (Fig. 4), indicating that water probably acts as a plasticizer promoting the deformation of the particles and bringing them closer to each other, resulting in greater particle-particle interaction and ultimately producing stronger tablets (Fig. 3).

Scanning electron microscopy (SEM) was used to examine the faces of tablets (Fig. 5). Each photograph shows the face of the tablet which was in contact with the upper punch. There were marked changes in the surface texture of the tablet as the moisture content increased. A high surface porosity was observed at 0% w/w moisture content. But at the high moisture content (14·9% w/w) a substantial reduction in tablet porosity occurred. Fig. 5d shows that compression of HPMC K4M of high moisture content produced a smooth tablet surface with less pores. Increase in moisture content clearly improved the consolidation at the tablet faces. Therefore, the SEM studies showed that moisture content improved tablet consolidation, due to a combination of increased particle plasticity and decrease porosity.

Nokhodchi et al (1996) showed that the porosities of HPMC tablets in the absence of moisture were very sensitive to compression force. They reported that there was a straight-line relationship between the logarithm of the tensile strength (δ_x) and the porosity (ε) of tablets in absence of moisture. Attempts were therefore made to fit the data in this study to equation 3:

$$\mathrm{Ln}(\delta_x) = B - A\epsilon \tag{3}$$

where A represents the slope of the resultant straight line and B is the intercept which is the tensile strength at zero porosity. The regression constants and regression coefficients for this relationship for HPMC K4M at each moisture content are listed in Table 1. For moisture contents of 5·9, 9·6 and 14·9% w/w, the correlation coefficients slightly decreased. The values of B generally increased as the moisture content increased. This indicates that at zero porosity, the tensile strength of the tablets would increase as the moisture content increased and this confirms that the presence of moisture improved the mechanical properties of HPMC K4M tablets.

Fig. 6. illustrates the effect of moisture content on the percentage elastic recoveries obtained at various compression speeds. At each speed, an increase in moisture content resulted in a reduction in the elastic recovery of the HPMC compacts.

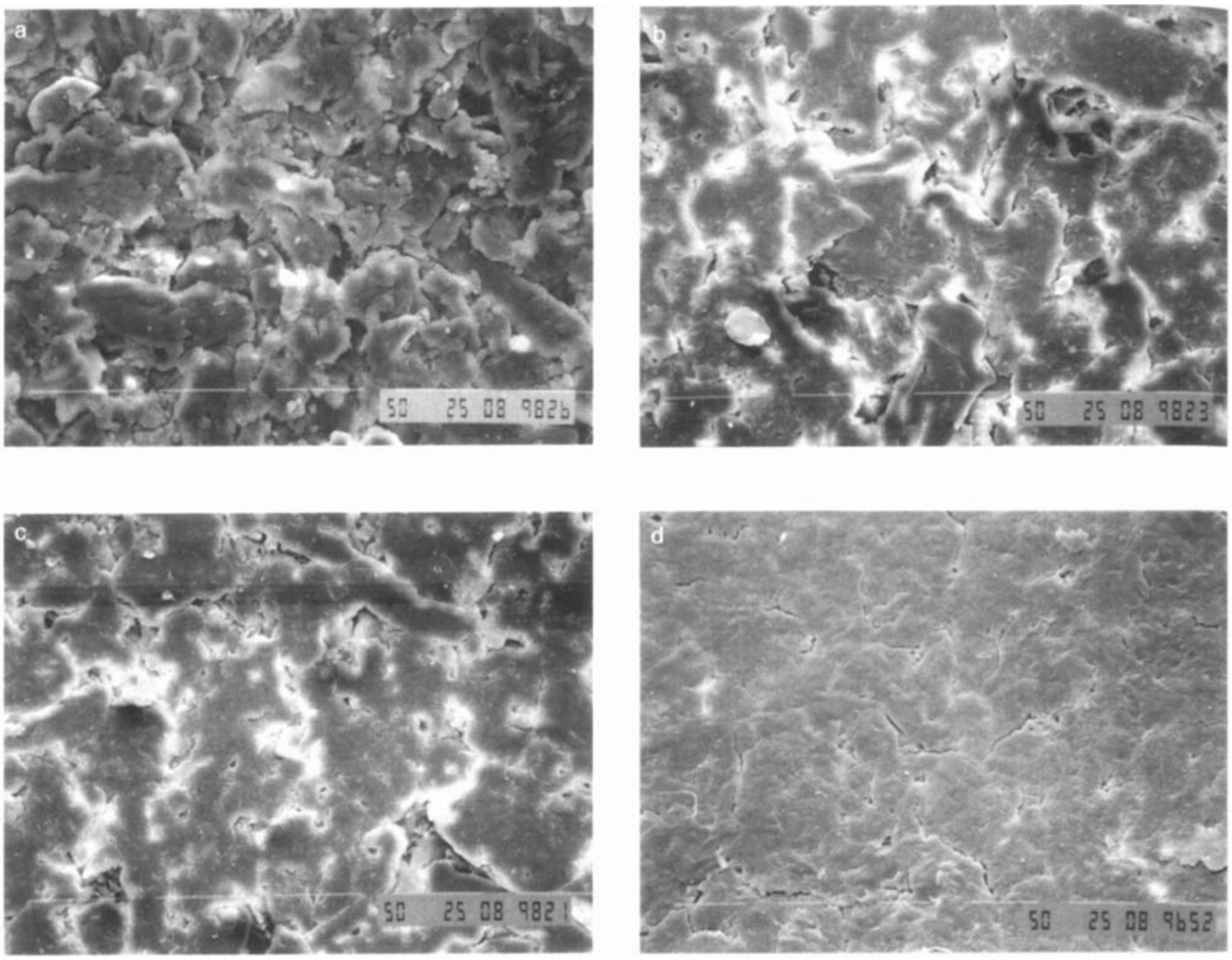

FIG. 5. SEM (× 300) of faces of HPMC K4M tablets containing different moisture content; a. 0, b. 5·9, c. 9·6 and d. 14·95% w/w.

Table 1. The effect of moisture content of HPMC K4M on the constants A and B of equation 3 for compression forces between 5 and 20 kN and correlation coefficients between porosity and logarithm of tensile strength.

Moisture content (%)	Constants		Correlation coefficient (r)
	A (MPa)	B (MPa)	
0	0·090	2·59	0·992
2·2	0·103	2·85	0·994
3·8	0·090	2·73	0·993
5·9	0·100	2·93	0·979
9·6	0·112	3·30	0·977
14·9	0·204	4·27	0·968

One explanation is that the moisture within the pores acts as an internal lubricant and facilitates slippage and flow of the individual particles. After plastic deformation the particles of HPMC are so close that hydrogen bonding can occur and moisture will prevent elastic recovery by forming bonds through hydrogen bond bridges. This is shown by the reduced thickness of tablets with increasing water content. A similar explanation has been proposed for microcrystalline cellulose for which, at lower tablet porosities and in the presence of an optimum amount of water, hydrogen bonding purportedly prevented elastic recovery upon decompression by formation of bonds through hydrogen bond bridges (Khan et al 1981). A similar situation probably applies to HPMC where elastic recovery is not prevented but is reduced and that reduction in elastic recovery occurs over the range of 0 to 14·9% w/w. At compression speeds of 500 mm s^{-1} there were no significant differences between the elastic recoveries of tablets containing 9·6 and 14·9% w/w moisture indicating that the elastic recoveries of HPMC tablets at high compression speed were not greatly modified by moisture contents between 9·6 and 14·9% w/w.

At the lower moisture content (2·2% w/w) tablet consolidation is smaller (Fig. 4) for a given compression force than at the higher moisture contents such as 14·9% w/w when the tablet porosity under compression was much lower.

Fig. 7 shows the effect of moisture content on the percentage elastic recoveries at various compression forces. At each compression force an increase in moisture content resulted

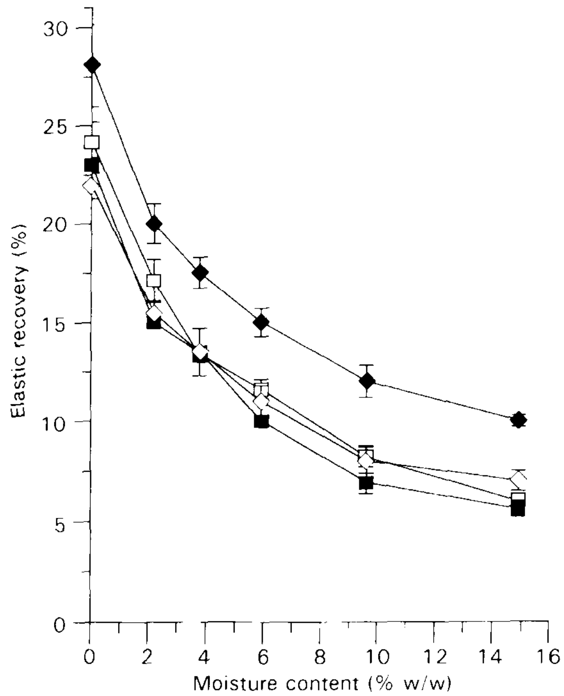

FIG. 6. The effect of moisture content on the elastic recoveries (%) of HPMC K4M tablets made at compression speeds of 15 (□), 140 (■), 280 (◇) or 500 (◆) mm s^{-1} to a compression force of 10 kN.

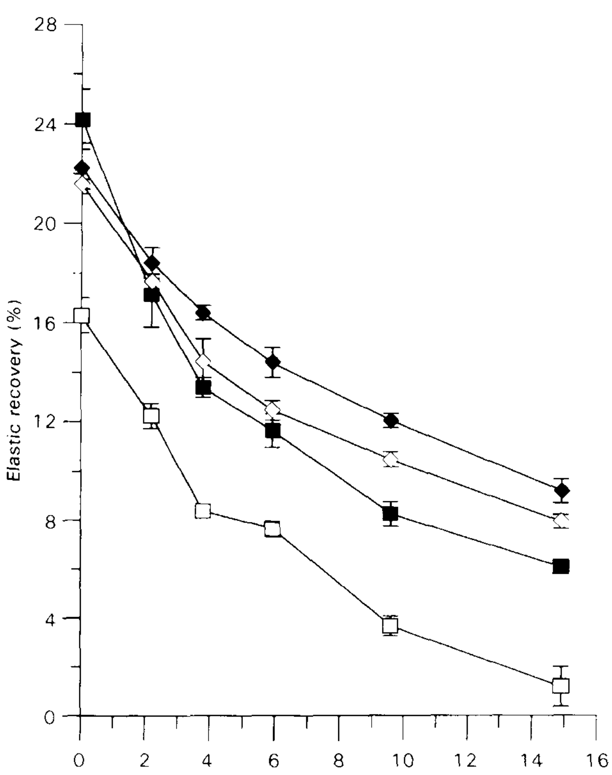

FIG. 7. The effect of moisture content on the elastic recoveries (%) of HPMC K4M tablets made at compression forces of 5 (□), 10 (■), 15 (◇) or 20 (◆) kN at a compression speed of 15 mm s^{-1}.

in a reduction in the elastic recovery of the HPMC tablets. Fig. 6 also shows that at a moisture content between 3·8 and 14·9% w/w, as the compression force increased, the elastic recoveries of the tablets increased. The compression force had a significant effect on the elastic recoveries of the tablets at various moisture contents.

In conclusion, moisture significantly affects the consolidation properties of HPMC K4M powder and must be carefully controlled. The extent of consolidation and the bonding of particles depended not solely on moisture content but also on the speed of compression and compression force. By careful control of these parameters tablet quality can be optimised. As the content of moisture increased, the tensile strength of HPMC, the packing and binding of HPMC particles become stronger. The tensile strengths of HPMC compacts were also affected by compression speed. Moisture content had a significant effect on the tablet porosity at different compression speeds. An increase in moisture content resulted in a reduction in the elastic recovery of HPMC compacts probably by forming hydrogen bonding between HPMC molecules.

Acknowledgements

The authors are very greateful to Colorcon Ltd for the supply of the Methocel and to the Ministry of Health and Medical Education of Tehran, Iran for financial support.

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