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International Journal of Pharmaceutics 104 (1994) 115–123

international
journal of
pharmaceutics

# Effect of particle size and sorbed moisture on the tensile strength of some tableted hydroxypropyl methylcellulose (HPMC) polymers

S. Malamataris *, T. Karidas

*Laboratory of Pharmaceutical Technology, Department of Pharmacy, University of Thessaloniki, Thessaloniki 54006, Greece*

(Received 1 July 1993; Accepted 14 September 1993)

## Abstract

The tensile strengths of compacts produced from powdered HPMC polymers with different particle size, methoxy/hydropropoxy substitution ratio, molecular size and moisture content achieved by equilibration at different relative humidities have been determined either immediately after their compression or after storage. It has been found that the tensile strength of tablets compressed at certain pressure level increases with moisture content, reaches a maximum at about 10 wt% moisture and then decreases while the tensile strength of tablets at fixed packing fraction exhibits an initial plateau up to 6 wt% moisture content and then decreases. The changes in tensile strength are related with the changes in the compressional characteristics and the moisture distribution effects mainly due to alterations in the particle size and in the methoxy/hydropropoxy substitution ratio while no dependence on the molecular size is evident. The profiles of particle packing vs moisture content were found to be sigmoidal, possibly due to the lubrication effect of tightly bound moisture up to 6 wt%, and the tensile strength maxima are attributed to the combined effect of closer packing of particles and softening of interparticle bonds. Our previous finding that tensile strength begins to decrease when the moisture content is about double that corresponding to tightly bound or 'monomolecular' water has been confirmed.

*Key words:* Hydroxypropyl methylcellulose; Sorbed moisture content; Particle size; Methoxy/hydropropoxy substitution; Molecular size; Compression; Tensile strength

## 1. Introduction

The effects that the particle size and the molecular characteristics of cellulose ethers (HPMC) have on moisture sorption and distribution when they are stored at different environmental relative humidity and furthermore on the compressional characteristics when they are tableted were reported previously (Malamataris et al., 1994). It was shown that particle packing and deformation of HPMC powders during their tableting are related with the moisture distribution changes due to the particle size and methoxy/hydropropoxy substitution ratio while no effect was observed due to molecular size alterations.

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* Corresponding author.

*SSDI* 0378-5173(93)E0279-Y

In practice, packing and binding of HPMC particles in contolled release tablet matrices may account for differences in availability, especially for the relatively insoluble or hydrophobic and non-swelling drugs, because of the internal stresses that can occur during hydration and swelling of HPMC polymers (Methocel Information Handbook; Malamataris and Ganderton, 1991). It was therefore considered appropriate to determine whether changes produced in moisture distribution by particle size, methoxy/hydropropoxy substitution ratio and environmental relative humidity in the HPMC powders would have a significant and predictable effect on their binding during compression and the resulting tensile strength of tablets.

## 2. Materials and methods

The same grades and particle size fractions of HPMC powders as used in the previous work (Malamataris et al., 1994) were tableted after storage at different relative humidities and the tensile strength of the resulting tablets was measured by diametral loading until breaking either immediately after compression or after storage.

For each size fraction of HPMC, samples of known moisture content corresponding to 500 mg of dry polymer were weight in small glass vials, stored in the same relative humidity for more than 3 days and then were compressed using 13 mm diameter flat faced punches and a die which were lubricated with a suspension of magnesium stearate in chloroform. Tablets were prepared by applying compression pressure from 10 to 125 MPa in a hydraulic press. The pressure was applied to the upper punch by lowering the hydraulic ram at a rate of 1.5 mm $s^{-1}$. After ejection from the die the tablets were weighed to the nearest 0.1 mg and their thickness and diameter were measured to the nearest 0.01 mm. The packing fraction ($p_f$ = bulk density/true density)

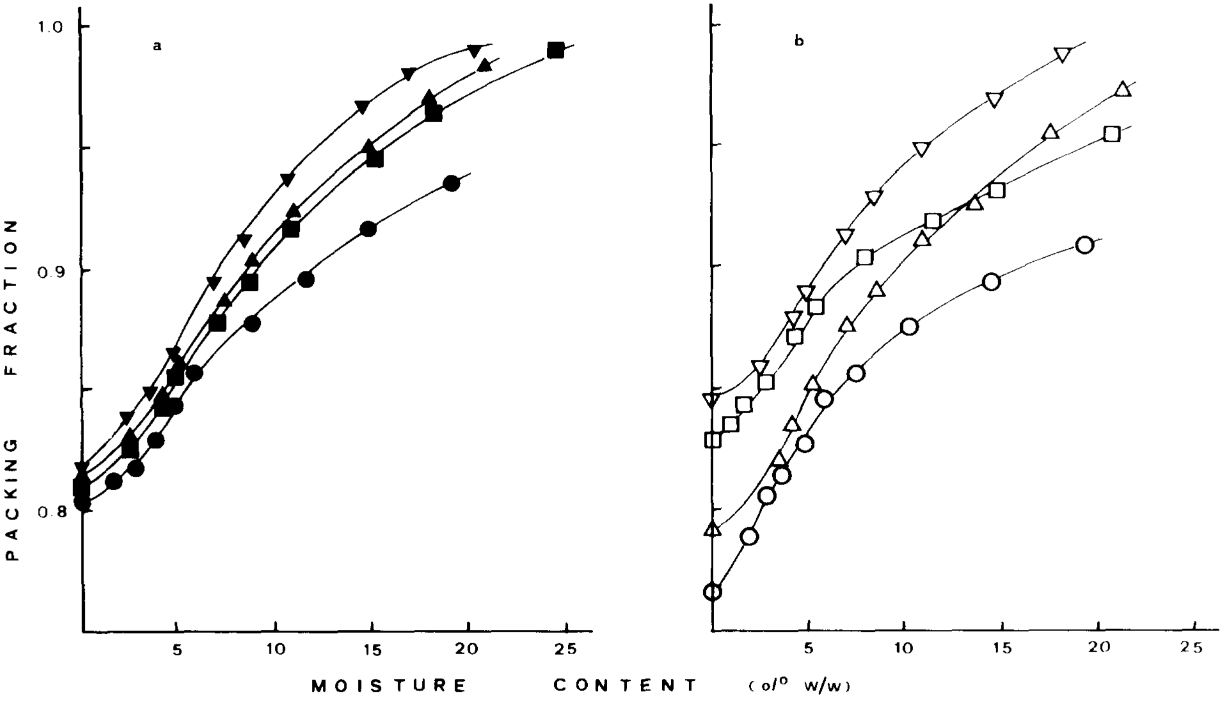

Fig. 1. Plots of packing fraction vs moisture content for powdered HPMC polymers: (a) of different type [K100M (■), K15M (▼), K4M (▲) and F4M (●) of size 120–320 μm] and (b) of different particle size [K4M < 120 μm (▽), K4M > 320 μm (△), F4M < 120 μm (□) and F4M > 320 μm (○)], compressed at 75 MPa after equilibration at different relative humidities and tested immediately after compression.

of each tablet was calculated and the diametral breaking strength was determined immediately after compression and converted to tensile strength. The tensile strength ($T$) at a fixed packing fraction was calculated by applying linear regression analysis between log $T$ and $p_f$.

Equilibrated HPMC powders were also tableted at a certain compression level, 75 MPa, and tested in diametral breaking after 15 days storage at the same relative humidity as that of equilibration. More tablets were prepared from samples equilibrated at 0% relative humidity (over phosphorus pentoxide) and were stored at different increasing relative humidities, 11–93%, before the diametral breaking. The weight, thickness and diameter of all the tablets were measured both before and after storage.

The diametral breaking strength was determined by using a JJ T30K material testing machine (JJ Lloyd Instruments Ltd, Southampton, U.K.) operated at a cross-head speed of 50 mm min$^{-1}$. The results were converted to tensile strength according to the relationship used by Fell and Newton (1970).

## 3. Results and discussion

Representative packing fraction results for different types of HPMC polymers and for different size fractions compressed at a certain pressure level (75 MPa) after equilibration at different relative humidities are plotted vs the moisture content in Fig. 1a and b.

It is seen from Fig. 1a and b that HPMC of type K exhibits greater packing ability than type F4M and small differences in packing fraction due to molecular size changes are observed. The packing ability for all the HPMC polymers under investigation increases with decreasing particle size (Fig. 1b) and seems to be related with the moisture distribution and its presence as externally adsorbed or tightly bound form.

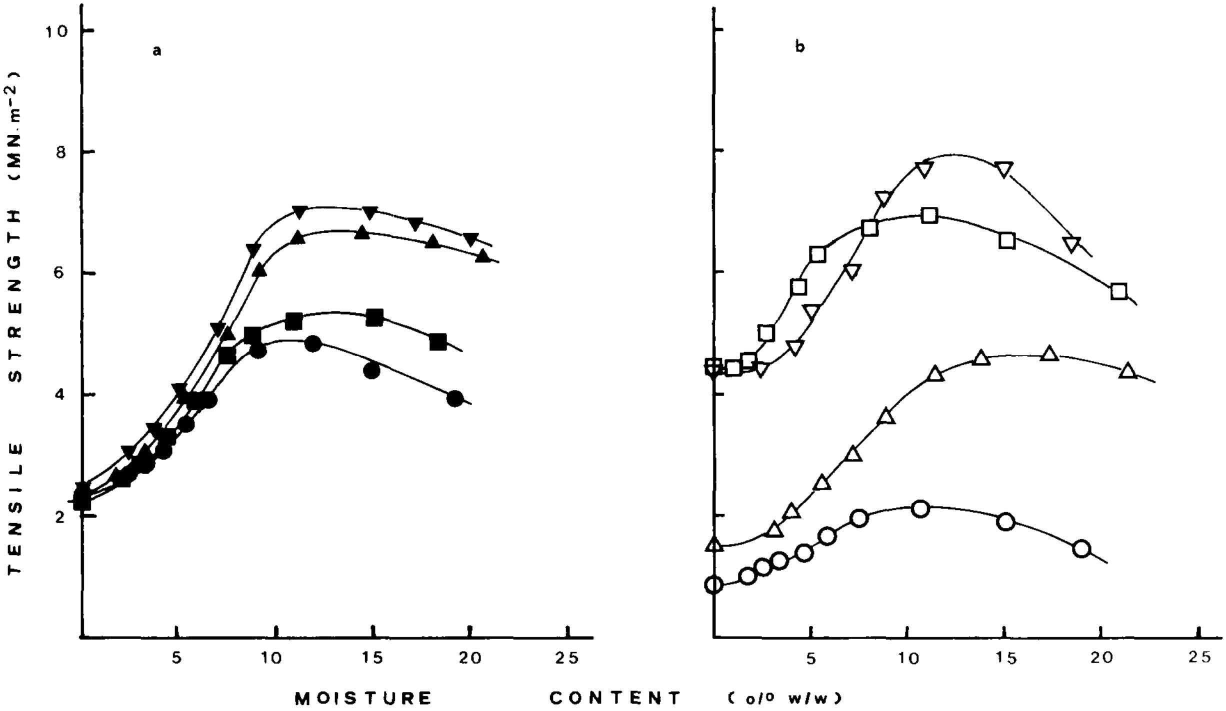

Fig. 2. Plots of tensile strength vs moisture content for powdered HPMC polymers: (a) of different type and (b) of different particle size, compressed at 75 MPa after equilibration at different relative humidities and tested immediately after compression (symbols as in Fig. 1).

The packing fraction plots in Fig. 1a and b are sigmoidal and show two phases of packing fraction increase due to moisture content, the initial one up to about 6 wt% moisture (with increased rate of packing fraction change) and a final phase for higher moisture content (with decreased rate of packing fraction change). The increased rate of packing fraction change up to 6 wt% moisture content can be attributed to easier packing of HPMC particles and may be related to the distribution and binding of moisture. There is experimental evidence in the literature to suggest that the first approx. 6 wt% moisture is strongly bound by hydrogen bonds to the hydroxyl groups in the cellulose structure rather than being present as an adsorbed mono- or multilayer on the surface of the particles (Sadeghejad et al., 1986; Zografi and Kontny, 1986; Khan and Pilpel, 1987). Therefore, water in this physical state appears to act as a lubricant despite its binding within the particles rather than on their external surface.

Tensile strength results for tablets compressed at 75 MPa from different types and size fractions of HPMC polymers equilibrated at different relative humidities and tested immediately after compression are plotted vs moisture content in Fig. 2a and b.

From Fig. 2a and b, it is seen that the tensile strength initially increases, reaches a maximum and then decreases. Although the plots in Fig. 2a and b show similarity in shape, the values of the tensile strength differ significantly, as expected, due to changes in the particle size and in the molecular characteristics, particularly in the range of moisture content above 10 wt%.

The initial increase in tensile strength evident in Fig. 2a and b may be attributed either to an increase in the number and area of interparticle bonds, due to an increase in packing fraction (Fig. 1a and b), or to an increase in the strength of interparticle bonds. The subsequent decrease in tensile strength with moisture content should

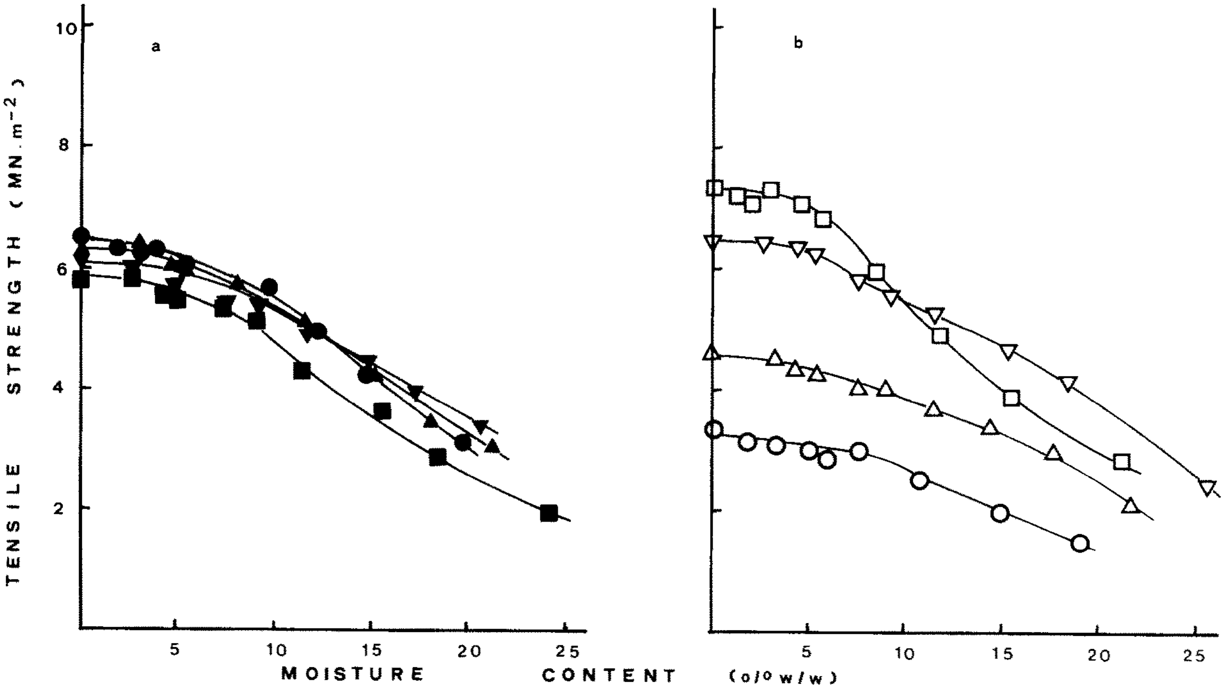

Fig. 3. Plots of tensile strength at $p_f$ 0.9 vs moisture content for powdered HPMC polymers: (a) of different type and (b) of different particle size, compressed after equilibration at different relative humidities and tested immediately after compression (symbols as in Fig. 1).

Table 1
Moisture distribution, tensile strength at $p_f$ 0.9 and compressional parameters (yield pressure and elastic recovery) for powdered HPMC polymers of different type and particle size at mean environmental relative humidity (52%)

| HPMC product | Particle size (μm) | Moisture distribution (wt%) | | | Tensile strength (MN $m^{-2}$) | Yield pressure (MPa) | | Elastic recovery (%) |
|---|---|---|---|---|---|---|---|---|
| | | $A \cdot \theta$ | $A \cdot (\theta + \beta)$ | $B \cdot \psi$ | | In-die | Ejected | |
| K100M | 120–320 | 3.6 | 6.8 | 1.3 | 5.3 | 43 | 118 | 8.6 |
| K15M | 120–320 | 3.8 | 6.7 | 1.6 | 5.4 | 42 | 120 | 7.7 |
| K4M | < 120 | 4.5 | 8.0 | 0.9 | 5.8 | 48 | 85 | 4.9 |
| | 120–320 | 3.9 | 6.9 | 1.7 | 5.5 | 52 | 123 | 7.6 |
| | > 320 | 3.6 | 6.4 | 1.9 | 4.1 | 56 | 172 | 9.4 |
| E4M | < 120 | 2.7 | 4.9 | 1.4 | 5.7 | 67 | 124 | 6.9 |
| | 120–320 | 2.4 | 4.4 | 1.6 | 4.4 | 76 | 149 | 8.2 |
| | > 320 | 1.9 | 3.4 | 2.4 | 2.1 | 73 | 155 | 9.1 |
| F4M | < 120 | 2.9 | 5.2 | 1.4 | 6.8 | 77 | 112 | 7.5 |
| | 120–320 | 2.1 | 3.8 | 1.8 | 5.6 | 78 | 161 | 8.1 |
| | > 320 | 1.7 | 3.0 | 2.3 | 2.7 | 83 | 193 | 9.0 |

be attributed to weakening of the interparticle bonds due to disruption of the forces between the molecules of the materials constituting the particles, especialy in their surface. The tensile strength maxima occurred at moisture content around 10 wt%, which is almost double the mean of the corresponding values of externally adsorbed or tightly bound 'monomolecular' water

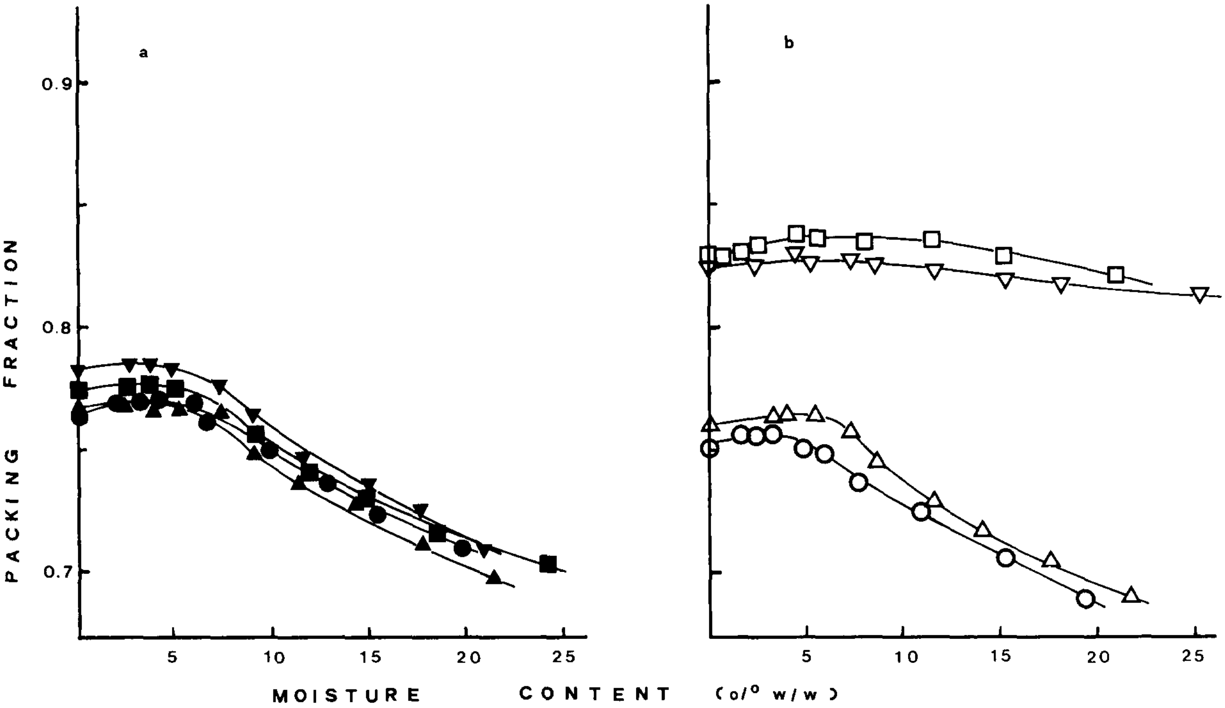

Fig. 4. Plots of packing fraction vs moisture content for powdered HPMC polymers: (a) of different type and (b) of different particle size, compressed at 75 MPa after equilibration at 0% RH and stored before testing at increasing relative humidity (symbols as in Fig. 1).

($W_m$% and $A \cdot \theta$%; Malamataris et al., 1994). The occurrence of tensile strength maxima at this level of moisture content may constitute evidence that the increase in tensile strength is caused by the externally adsorbed monomolecular or tightly bound water. This tightly bound water can be regarded as a part of the surface molecular structure of the particles, which facilitates the formation of interparticle hydrogen bonding (Zografi and Kontny, 1986; Khan and Pilpel, 1987) or increases the van der Waals' forces, smoothing out the surface microirregularities, facilitating packing of particles and reducing the interparticle separation (Eaves and Jones, 1972).

In order to eliminate the effect of particle packing on the tensile strength and evaluate the influence of bonding strength, the overall interparticle bonding force was determined as tensile strength at a fixed packing fraction (0.9) by applying linear regression analysis between log $T$ and $p_f$ of tablets compressed at increasing pressure, from 10 to 100 MPa. The results for different types and particle size HPMC polymers are plotted against the moisture content in Fig. 3a and b.

The tensile strength results in Fig. 3a do not show significant differences as a result of changes in the type of HPMC, however, they differ significantly due to the size and chemical substitution in Fig. 3b. Also, from Fig. 3a and b it is seen that the tensile strength exhibits an initial plateau up to 6 wt% moisture content and then decreases as the moisture content increases. Similar observations have been reported previously for microcrystalline cellulose (Khan et al., 1988; Malamataris et al., 1991, 1992). The initial plateau and the subsequent tensile strength decrease may be related to the way that moisture is taken up by cellulose derivatives. In other words, the attachment of water molecules by strong and weak hydrogen bonding to the cellulose chain exerts an effect on these parameters. The end of the tensile strength plateau at about 6 wt% moisture corre-

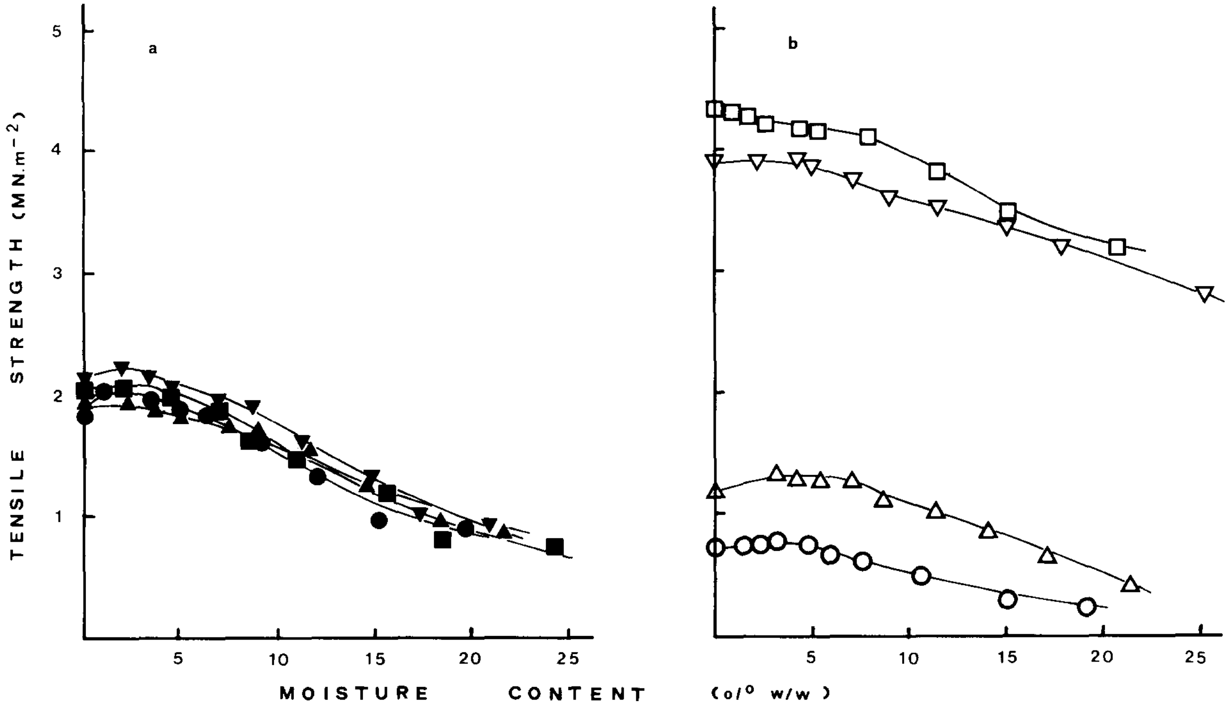

Fig. 5. Plots of tensile strength vs moisture content for powdered HPMC polymers: (a) of different type and (b) of different particle size, compressed at 75 MPa after equilibration at 0% RH and stored before testing at increasing relative humidity (symbols as in Fig. 1).

sponds to the level at which it has been suggested that water molecules probably attach to already strongly attached ones but by dipole attraction known as weak hydrogen bonding (Khan and Pilpel, 1987). This weakly bonded water shows similarity to water in bulk, which is described as internally absorbed water according to the model for moisture sorption of Young and Nelson (1967) and should be responsible for the final tensile strength decrease already attributed to plasticizing of the particles and weakening of the interparticle bonds.

In order to correlate the changes in overall interparticle bonding strength due to changes in the molecular characteristics of the HPMC polymers, representative tensile strength results are given in Table 1 together with the compressional characteristics quantified as yield pressure and elastic recovery derived from Heckel plots for the mean environmental relative humidity of 52% (Malamataris et al., 1994).

From Table 1 it is seen that the tensile strength results are mainly affected by alterations in the particle size and in the methoxy/hydropropoxy substitution ratio while no dependence on the molecular size is evident. Also, the changes in the tensile strength results in Table 1 appear to be related with those in the compressional parameters and moisture distribution. In general, the overall interparticle bonding strength decreases with increase in the yield pressure, elastic recovery and internally absorbed moisture, $B \cdot \psi$.

For examination of the effect of moisture uptake on the strength of existing (preformed) bonds between particles of tableted HPMC polymers, the packing fraction and tensile strength results for tablets compressed, at 75 MPa, from powders after equilibration at 0% RH and then stored at increasing relative humidity, are plotted against moisture content in Fig. 4a and b and Fig. 5a and b, respectively.

From Fig. 4 a and b it is seen that the packing

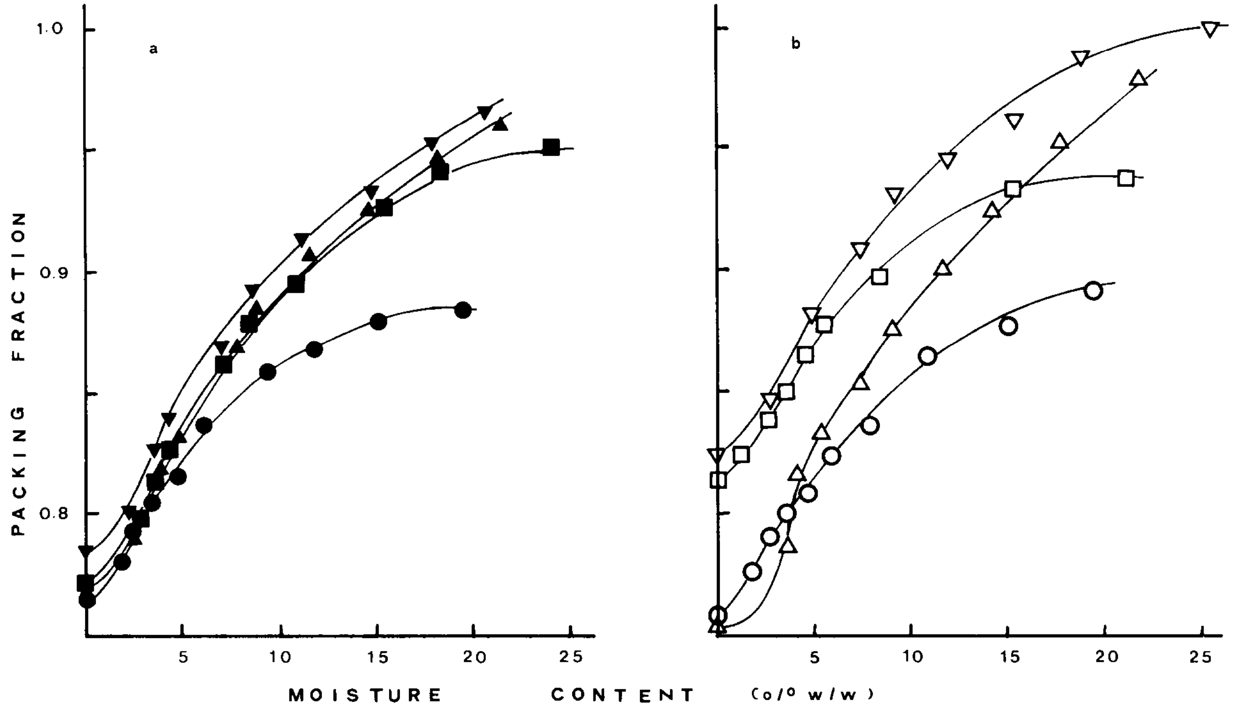

Fig. 6. Plots of packing fraction vs moisture content for powdered HPMC polymers: (a) of different type and (b) of different particle size, compressed at 75 MPa after equilibration at different relative humidities and stored before testing in the same environment (symbols as in Fig. 1).

fraction increases slightly with moisture content and then decreases except for the case of the smaller particle size fraction, < 120 μm (Fig. 4b). These changes are probably caused by changes in the bulk density of tablets (weight and dimensions) due to moisture uptake and elastic relaxation of tablets. The exception for the smaller size may be related to the smaller extent of elastic recovery observed with both the reduction in particle size and the increase in relative humidity, as reported previously (Malamataris et al., 1994). The corresponding tensile strength results in Fig. 5(a–b) show an initial plateau and then a decrease which should be related to weakening of the interparticle bonds due to softening of the HPMC polymers as has been mentioned above.

The packing fraction and tensile strength results for tablets compressed at 75 MPa from powders equilibrated at different relative humidity and then stored in the same environment as that of equilibration are given in Fig. 6a and b and Fig. 7a and b, respectively.

The packing fraction results are similar to those in Fig. 1a and b and the tensile stength data are consistent with those in Fig. 2a and b corresponding to tablets tested immediately after compression without storage. The occurrence of the tensile strength maxima at moisture content around 10 wt% (Fig. 7a,b and 2a,b), in combination with the end of the plateau in the tensile strength plots (Fig. 3a,b and 5a,b), and the alteration of the packing mechanism (Fig. 1a,b, 4a,b and 6a,b), at about 6 wt% moisture content suggest that: (a) the tensile strength increase with moisture can be regarded as being the result of the closer packing of the HPMC particles without simultaneous weakening of the interparticle bonds due to softening of particles; and (b) the tensile strength

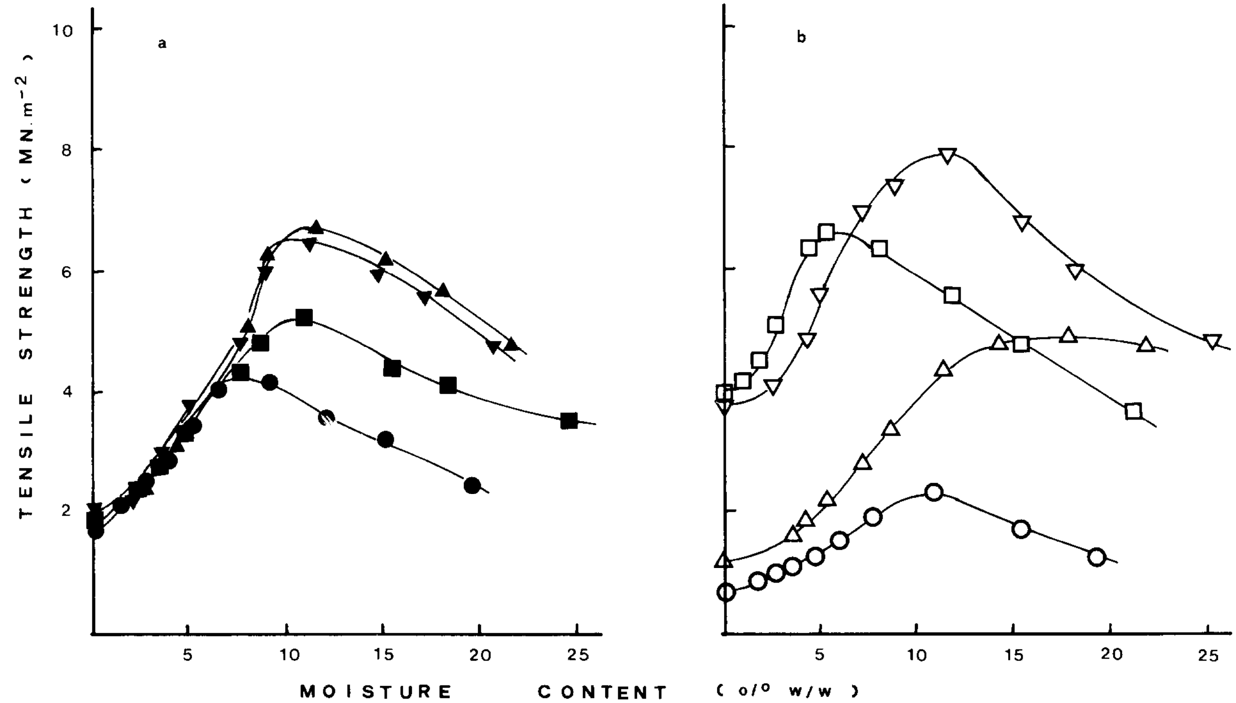

Fig. 7. Plots of tensile strength vs moisture content for powdered HPMC polymers: (a) of different type and (b) of different particle size, compressed at 75 MPa after equilibration at different relative humidities and stored before testing in the same environment (symbols as in Fig. 1).

maxima are the combined effect of closer particle packing and less weakening of interparticle bonds due to particle softening.

From the above-mentioned observations, it may be concluded that the changes in the interparticle bonding of HPMC polymers due to storage at different relative humidities are related with the changes in their compressional characteristics and the moisture distribution effects mainly due to alterations in the particle size and in the methoxy/hydropropoxy substitution ratio while a dependence on the molecular size is not evident.

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