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PII:S0144-8617(96)00009-4

*Carbohydrate Polymers* **29** (1996) 105–109

0144-8617/96 $15.00+.00

# Molar mass and viscometric characterisation of hydroxypropylmethyl cellulose

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(Received 30 August 1995; revised version received 13 December 1995; accepted 15 January 1996)

The weight average molar masses and molar mass distributions of three different preparations (identical in chemical composition, but different in the average degree of polymerization) of hydroxypropylmethyl cellulose have been characterized by SEC/MALLS (size exclusion chromatography coupled to multi-angle laser light scattering). The intrinsic viscosity and the viscosity in the semi-dilute region have also been measured. When the viscosity data is presented in the form of logarithmic plots of the zero shear specific viscosity against the coil overlap parameter ($c[\eta]$), a higher viscosity than would be expected from the usual 'master curve' relationships is found. This was particularly the case for the highest molar mass preparation ($M_w = 2.2 \times 10^6$ g/mol). It is suggested that the high viscosity is a consequence of enhanced intermolecular interactions as a result of solvent quality effects. Although the data is limited, the values of the Mark–Houwink–Kuhn–Sakurada exponent (0.4–0.5) suggested by the $[\eta], M_w$ data set would be consistent with water being a poor solvent for this polysaccharide. A related factor may be interactions induced when the chains are aligned during drying which are not completely disrupted on hydration. Copyright © 1996 Elsevier Science Ltd

## INTRODUCTION

Hydroxypropylmethyl cellulose (HPMC) is a polysaccharide prepared from cellulose. It contains both methyl and hydroxypropyl substitutes (Fig. 1), and in fibre form has an extended linear structure as visualized by X-ray diffraction (Blackwell, 1982). It has a wide range of industrial applications (largely deriving from its excellent coating properties) particularly in the field of health care and opthalmics (see e.g. Grover, 1993; Silver *et al.*, 1994). Within our group we are particularly interested in food and pharmaceutical uses. Several of the food uses are based on the ability of aqueous solutions of the polysaccharide to gel on heating. The objective of the present study is to characterise the molar mass (weight average), molar mass distribution and viscosity behaviour of two samples of very finely milled commercially available material and compare these samples with an experimental high viscosity preparation with the same degree of substitution.

## MATERIALS AND METHODS

### HPMC

The commercial food grade HPMC preparations {K15M, and K8515} and the experimental material {XU40468} were kindly provided by Dow-Chemicals Ltd. The 'experimental material', although chemically identical to the other two preparations (degree of substitution = 1.2–1.5), is so-called because it has received the minimum amount of mechanical processing thus giving the longest possible polymer chains.

### Solutions

A phosphate chloride buffer was used (pH = 6.5, I = 0.10) with the following composition (Green, 1933): 4.595 g $Na_2HPO_4.12H_2O$, 1.561 g $KH_2PO_4$, 2.923 g NaCl per litre of deionised distilled water. Polysaccharide solutions were prepared by adding the samples to buffer or pure deionised distilled water at 80–90°C on a hot-plate with stirring. After cooling to

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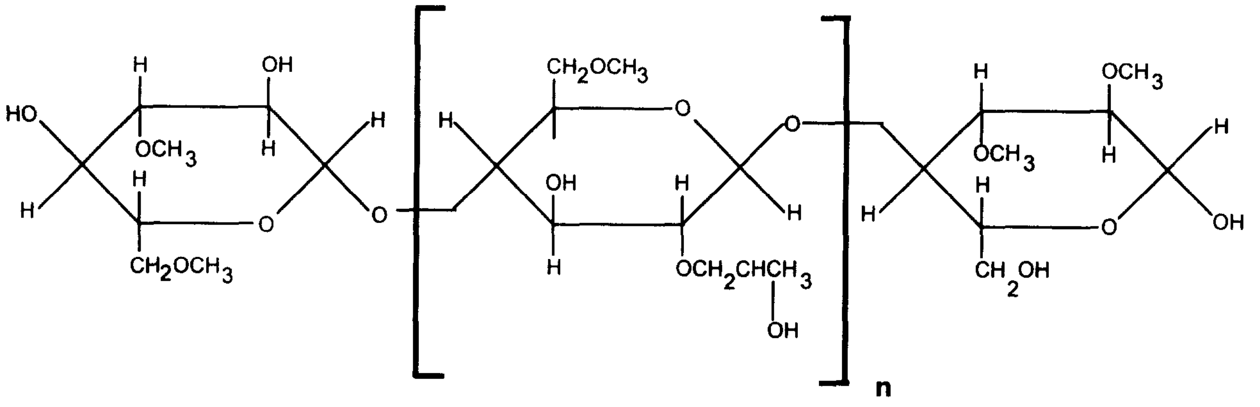

$C_8H_{15}O_6(C_{10}H_{18}O_6)_n\text{-}C_8H_{15}O_5$

**Fig. 1.** Hydroxypropylmethylcellulose.

room temperature, samples were centrifuged on an MSE benchtop centrifuge at a speed of 4000 rev/min for 20 min. For SEC-MALLS measurements the supernatant was filtered through a 0.45 mm filter (Millex MV, Millipore, Watford, UK). Intrinsic viscosity measurements were performed in the buffer and also with pure deionised distilled water as the solvent. Rotational viscosity measurements in the semi-dilute region were made in water.

### Size exclusion chromatography/multi-angle laser light scattering (SEC-MALLS)

SEC-MALLS (Wyatt, 1992) was used to obtain estimates for (i) the purity of the material; (ii) the weight average molar mass $M_w$; and (iii) the molecular weight distribution of each preparation. In our particular system, the eluant for the columns was degassed on-line (Degasys DG-1220, Phenomenex, Macclesfield, UK) and pumped by a Waters (Waters-Millipore, Watford, UK) 590 programmable solvent delivery system at a flow rate of 0.8 ml/min. One hundred microlitres of sample (1 mg/ml) were injected via a Rheodyne (St Louis, USA) Model 7125 injection valve. The column system consisted of TSK G6000PW, G5000PW and G4000PW columns connected in series and protected by a TSK PW guard column. Column effluent was monitored using a DAWN-F (Wyatt Technology, Santa Barbara, USA) MALLS Detector, equipped with a 5 mW He–Ne laser (632.18 nm) capable of collecting the intensity of the scattered light at 15 angles (from diode detectors positioned around the scattering envelope) simultaneously, and an Optilab 901 interferometric refractive index detector (Wyatt Technology), used to obtain (after a volume delay correction) the concentrations passing through the flow cell. A value for the refractive increment (dn/dc) of 0.15 ml/g was used. Data were collected and analysed on a PC using the dedicated ASTRA software (Wyatt Technology). This software generates (i) an elution profile in terms of concentration (refractive index) versus elution volume; (ii) the apparent molar mass $M_{w,app}$ for each elution slice from the Debye relation (Debye, 1947; Zimm, 1948). Because of the low concentrations ($<0.2$ mg/ml) of the sample 'slices' passing through the light scattering flow cell after dilution by the column, no correction for thermodynamic ideality was necessary and to a good approximation $M_w \approx M_{w,app}$.

### Viscometry

Measurements of viscosity were made at 25.0°C using either a 1 ml Schott-Geräte automatic Ostwald glass capillary viscometer or a Bohlin constant stress rotational viscometer equipped with either double gap or Couette (C25) geometry. Measurements using the rotational viscometer were made in the shear rate range 0.5–100 $s^{-1}$, and concentrations up to 20 mg/ml. Where the zero shear viscosity ($\eta_o$) was not clearly defined from the flow curves, it was obtained by fitting the following Cross equation (Cross, 1965) to the data using the software supplied with the rheometer:

$$\eta = \eta_\infty + (\eta_o - \eta_\infty)/\{1 + (\tau\gamma)^n\} \quad (1)$$

where $\eta$ is the viscosity, $\gamma$ the shear rate and $\eta_o$, $\eta_\infty$, $\tau$ and $n$ are constants.

At low concentrations (0.25–1.5 mg/ml), it was found that the flow behaviour measured in the rotational viscometer was Newtonian and therefore it was appropriate to obtain an intrinsic viscosity $[\eta]$ from capillary viscosity measurements made in this concentration range. The Huggins (1942) relationship was employed:

$$\eta_{red} = [\eta](1 + K_\eta[\eta]c) \qquad (2)$$

with $K_\eta$ the Huggins (1942) constant.

## RESULTS AND DISCUSSION

A summary of the 'dilute solution' hydrodynamic properties discovered in this study is given in Table 1.

### Homogeneity

Only single elution peaks were observed from the SEC-MALLS elution profiles (using both the refractive index and the 90° scattering angle detectors) for each HPMC preparation (Fig. 2) supporting the view that these preparations are essentially homogeneous. The peaks were however not symmetric, with a trailing edge on the high elution (low molar mass) side. The small peak in the refractive index trace at high elution volumes is probably due to some residual buffer salts.

### Molar mass averages and molar mass distributions

Weight average molar masses, $M_w$ for each elution slice or volume, $V_e$ were obtained from Debye (1947) plots of $R_{(\theta)}/K_c$ versus $\sin^2(\theta/2)$ according to Wyatt (1992) with the limiting value of $R_{(\theta)}/K_c$ at $\sin^2(\theta/2) = 0$ of $M_w$. (This method of extrapolation usually gives more stable estimates for $M_w$ compared with the $K_c/R_{(\theta)}$ method, although is less useful for radius of gyration and other angular dependence measurements, not used in this study.) These Debye plots showed significant curvature and second-order fits were found appropriate. Since the polysaccharide concentration, $c$ for each $V_e$ was also recorded (from the refractometer) it was possible to evaluate molar mass distributions and these are shown in Fig. 3. Its is seen that the series K15M, K8515 and XU40468 becomes progressively higher in molar mass (with whole distribution weight averages, $M_w$, respectively of $0.77 \times 10^6$, $1.46 \times 10^6$ and $2.20 \times 10^6$ g/mol) and progressively sharper. It is possible to quantify the sharpness of these distributions by the derived whole distribution number and z-averages and the 'polydispersity indices' $P_w$ $(=M_w/M_n)$ and $P_z$ $(=M_z/M_w)$, and these results are summarized in Table 1. Some caution needs to be expressed, however, since the low values obtained may be a reflection of the lack of separation of the high molecular weight species — an unavoidable feature of column chromatography.

### Viscosity parameters

The measured intrinsic viscosities were slightly higher in water compared with the high ionic strength buffer (Table 1) presumably reflecting solvent quality affects. The uncertainty in the quoted values may be estimated as ≈±10% since replicate runs are within this range. Figure 4 displays the logarithmic plot of zero shear viscosity obtained from the rotational viscometer as a function of the coil overlap parameter $c[\eta]$. (Values of $c[\eta]$ are all $< 1.5$ which would suggest Newtonian behaviour.) The two lower molar mass samples superimposed closely, the slope being in the range $(3.94 \pm 0.04)$. The high molar mass sample showed a slightly steeper slope (4.20) and gave higher viscosities at comparable values of $c[\eta]$. Values for the slope ranging from 3.3 to 5.2 have been reported in the literature for a wide range of polysaccharides (Lapasin & Pricl, 1995). Even the lowest molar mass samples (K15M and K8515) have high viscosities compared with the 'master curve' reported by Morris *et al.* (1981). For example, at $\log\{c[\eta]\} = 1$ the value of $\log\{\eta_{spo}\}$ from the master curve is ≈2.3 $\{\eta_{spo}$ is the zero shear specific viscosity$\}$ whereas for the two low molar mass samples it was ≈3.1. For the high molar mass sample it was as high as 3.5. This may reflect a

**Table 1. Dilute solution parameters for HPMC-preparations**

| | HPMC-K15 | MHPMC-K8515 | HPMC-XU40468 |
|---|---|---|---|
| $10^{-6} \times M_w$ (g/mol) $\{\pm 10\%\}$ | 0.77 | 1.46 | 2.20 |
| $10^{-6} \times M_n$ (g/mol) $\{\pm 15\%\}$ | 0.40 | 1.00 | 1.87 |
| $10^{-6} \times M_z$ (g/mol) $\{\pm 15\%\}$ | 2.43 | 2.71 | 2.87 |
| $P_w$ | 1.92 | 1.42 | 1.18 |
| $P_z$ | 3.15 | 1.91 | 1.30 |
| $[\eta]$ (ml/g) | 770 | 960 | 1300 |
| $[\eta]$ (ml/g) $I=0.0$ | 920 | 1200 | 1400 |

Parameters refer to measurements in the $I=0.10$ solvent unless otherwise indicated.

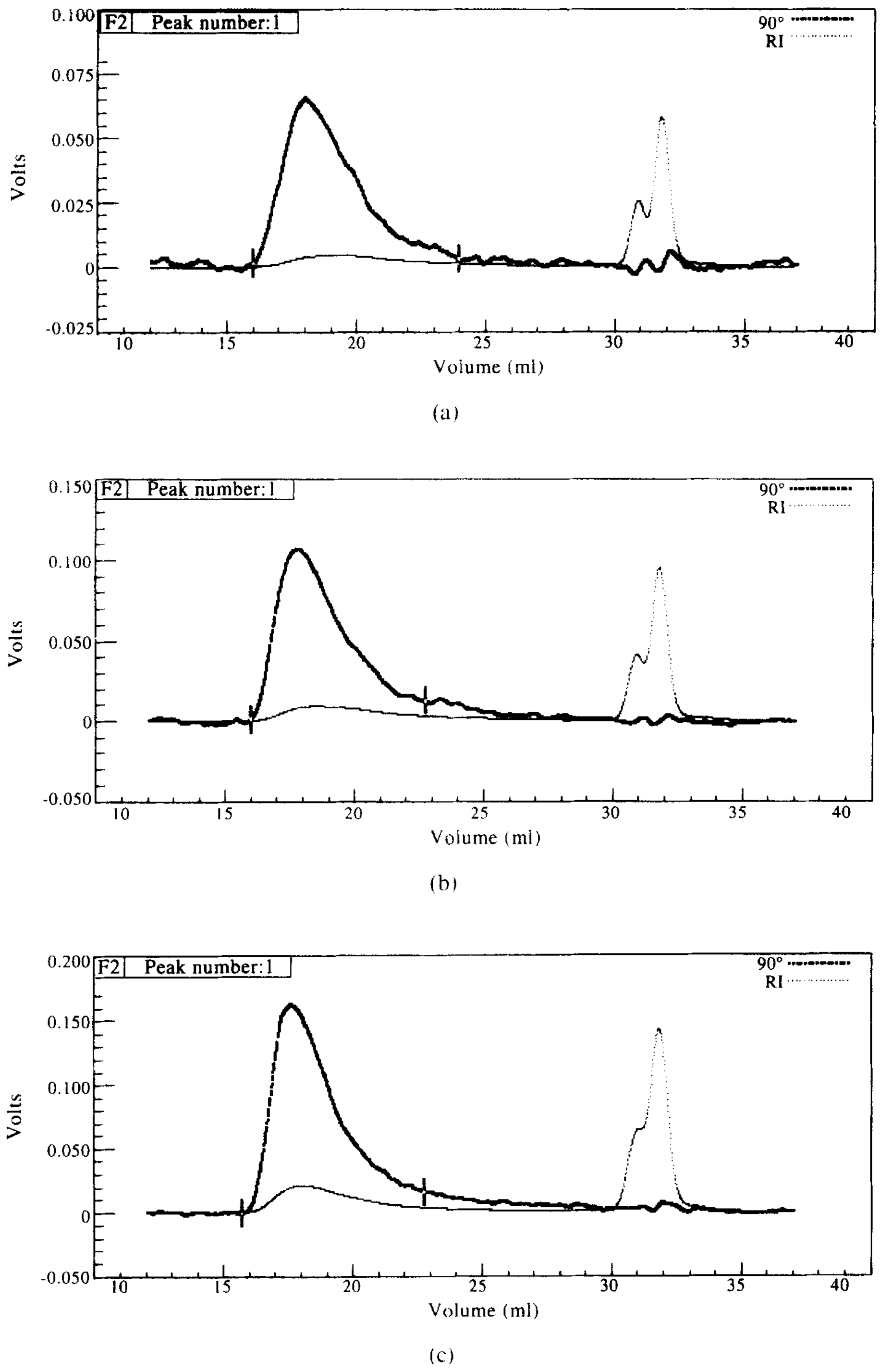

**Fig. 2.** Elution profiles from HPMC samples (a) K15M, (b) K8515, (c) XU40468.

low degree of hydrophobic interaction between the chains which at high temperatures is strong enough to initiate gelation, or it could be associated with some residual association instigated when the chains are forced into a more parallel alignment as a result of having to accommodate water loss during drying. It is interesting that for carboxymethylcellulose a birefringent mesophase has been reported to be maintained on hydrating to quite high water contents (Hatakeyama *et al.* 1989). It does not seem unreasonable that uncharged cellulose derivatives will preserve an element of interchain interaction, which could be the cause of a high viscosity at high concentrations. The probability of interchain associations which will require juxtaposition of regions with particular substitution patterns will be greater for the higher molar mass material.

The values obtained from a double logarithmic plot

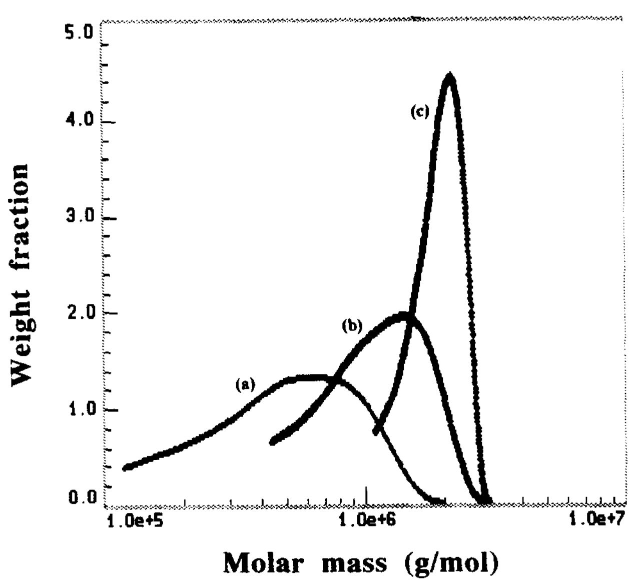

**Fig. 3.** Molecular weight distributions from SEC-MALLS (i) K15M, (ii) K8515 and (iii) XU40468.

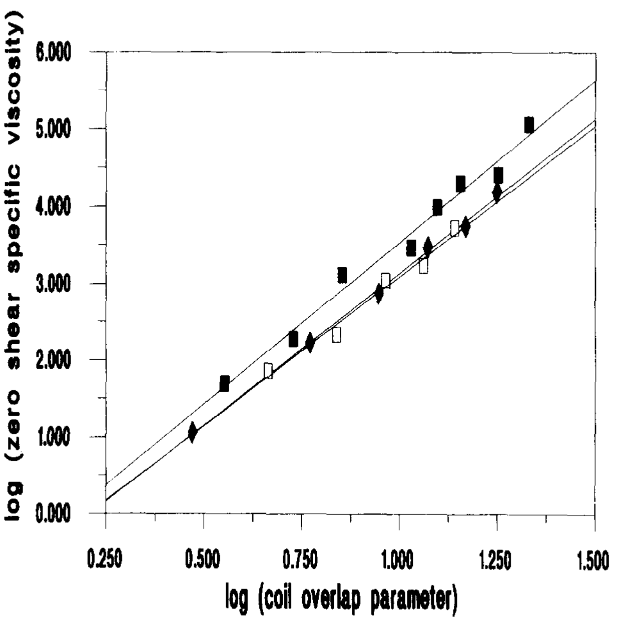

**Fig. 4.** Double logarithmic plot of zero shear specific viscosity versus the coil overlap parameter $c[\eta]$. The intrinsic viscosity, $[\eta]$ used was that obtained in water. Lines are least squares fits to the data points ◆: K15M; □: K8515; ◇: XU40468.

of the intrinsic viscosity against the molar mass of the three samples gave (0.50±0.10) and (0.41±0.02) using the intrinsic viscosities obtained in buffer and water respectively for the exponent "a" in the Mark–Houwink–Kuhn–Sakurada relationship ($[\eta] = K'M^a$) where K′ is a constant and in this case $M$ is taken as the weight average molar mass (see e.g. Harding, 1995). Although clearly not too much reliance should be placed on data obtained from three points, these values are close to the poor solvent ("0.5 end") of the exponent "a" expected for random coil polymers. This is consistent with the view that these polymers are prone to inter- and intra-chain association, which may be enhanced when these relatively stiff polymers are aligned as a result of being forced to close pack on drying. These values are also smaller than values of "a" for cellulose in cadoxen (Henley, 1961) and would appear to confirm the importance of substituted groups (and solvent conditions) on hydrodynamic properties.

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