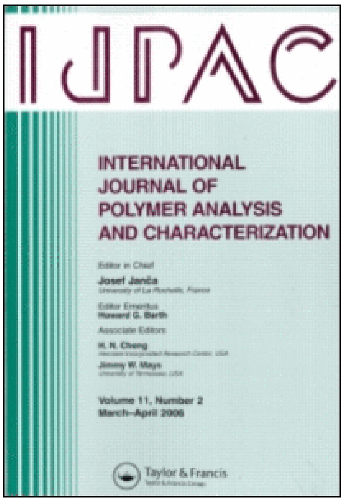

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Molecular Weight Studies on Hydroxypropyl Methylcellulose II. Intrinsic Viscosity*

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In order to obtain absolute molecular weight information for hydroxypropyl methylcellulose HPMC from viscosity measurements, the physics of the viscosity-increasing effect of particles with extended shape on a flowing suspension has been elaborated. It is suggested that the phenomenon causes orientation of the particles producing complete alignment of the longer axis with the flow direction at sufficiently high shear rate, and that the viscosity increment per volume unit of particles, that is, the unitless laminar intrinsic viscosity $[\eta]_{\phi}$, approaches the relative axial ratio $\mathbf{a}$ of the particle as compared to the liquid constituents with increasing particle length if the particle is a sufficiently large object. Hence, provided that the required liquid dynamic conditions are fulfilled, corresponding to laminar Newtonian flow, viscosimetry can be used as an absolute method for determination of $\mathbf{a}$. In the case of fully extended molecules, the weight-average molecular weight M_w can then be estimated as $M_w = ([\eta]100\rho - 1.5)\ M_u\mathbf{a}_l/\mathbf{a}_u$, where $[\eta]$ is in dL/g, ρ (conversion factor into volume fraction) in g/mL, M_u the molecular weight of the repeating unit (g/mol), $\mathbf{a}_u$ its axial ratio including solvation and $\mathbf{a}_l$ is the axial ratio of the liquid constituents. The theory is used to calculate M_w of various commercial HPMC viscosity grades (3–10,000 cP) of USP substitution type 2910 from capillary viscosimetry assuming complete extension as deduced from supplementing information obtained previously by osmometry. The value of ρ (g dry polymer/mL solvated polymer) is determined by a novel method based on the temperature influence on the specific viscosity under conditions of constant extension assuming that the solvation becomes negligible at a critical solution temperature T_θ, coinciding with phase separation. Furthermore, the proposed model for the laminar dynamics of suspensions appears to be generally applicable to polymers; the constant K of the empirical relation $[\eta] = KM^{\alpha}$, usually referred to as the Mark–Houwink equation, is derived as $K_w = \mathbf{a}_u M_u^{-\alpha}/(\mathbf{a}_l 100\rho)$, where K_w is in dL g^{-1} (g/mol)$^{-\alpha}$.

Keywords: Hydroxypropyl methylcellulose; Molecular weight; Intrinsic viscosity; Hydrodynamics; Polymer; Axial ratio

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INTRODUCTION

The viscosity-increasing effect of a polymer is its most characteristic solution property and has therefore since long been exploited as a reliable and highly discriminating descriptor of the molecular weight. In the case of cellulose and cellulose derivatives, the intrinsic viscosity and/or the viscosity grade (e.g., the viscosity η, in cP, of a 2% solution) is preferably employed.[1] Empirically, it was first demonstrated by Staudinger and Freudenberger[2] that the unitless specific viscosity $\eta_{sp} = \eta_{solvent}/\eta - 1$, increases approximately proportional to the molecular weight M (g/mol) for cellulose derivatives at equal concentrations c (g/dL);

$$\eta_{sp} = K_m cM \tag{1}$$

where K_m (dL mol g^{-2}) is a Staudinger-type constant. Equation (1) was subsequently improved[3–9] to encompass any macromolecule-solvent system, first into the form $\eta_{sp} = K_m cM^{\alpha}$ and then, into Equation (2), which through the introduction of the concept of intrinsic viscosity $[\eta]$ avoids difficulties due to the concentration dependence of η_{sp}/c;

$$[\eta] = KM^{\alpha}. \tag{2}$$

$[\eta]$ refers to infinite dilution as the result of its definition as the limiting reduced viscosity η_{sp}/c when the concentration c approaches zero. Equation (2) may hence be viewed as a modified Staudinger equation[10] and is commonly referred to as the Mark–Houwink, and sometimes as the Kuhn–Mark–Houwink,[11] the Mark–Houwink–Sakurada,[7,12] or the Mark–Houwink–Kuhn–Sakurada equation.[13,14] The exponent α is often observed to reach values as high as unity for cellulose in contrast to less extended polymers for which $\alpha < 1$.[9,12,15,16] In view of the widespread use of Equation (2), it is surprising that the correct dimensions of K, that is dL g^{-1} (g/mol)$^{-\alpha}$, appears not to be practiced in the literature but instead the units are either ignored[11,14,15,17–21] or insufficiently stated; as for example dL g^{-1} [7,12,16,22–24] or dL g^{-1} (g/mol)$^{-0.5}$,[25] which latter is valid for $\alpha = 0.5$ only. Both number-average molecular weight M_n and weight-average molecular weight M_w have been employed in Equations (1) and (2).

In order to establish the relation between $[\eta]$ and M for aqueous hydroxypropyl methylcellulose (HPMC), M_n was measured with an absolute method (osmometry) in the first article in this series.[26] This article continues with an analysis, using general liquid mechanic (hydrodynamic) concepts of suspended articles in liquids, on the viscosity increasing effect. Firstly, an attempt is made to give a rational explanation of the physical meaning of intrinsic viscosity and secondly, an investigation, both experimentally and theoretically, to which extent this quantity can be used to measure molecular weight.

EXPERIMENTAL

Materials

Commercial HPMC of USP-substitution type 2910 were obtained from the following manufacturers: The Dow Chemical Company, Midland, MI, USA (Methocel E3P and E6P) and Shin-Etsu Chemical Company, Naoetsu, Japan (Metolose 60SH-50 and 60SH-10000). The alkoxyl contents (% w/w) of the HPMC samples were $29.0 \pm 0.8\%$ methoxyl and $8.8 \pm 0.8\%$ hydroxypropoxyl which corresponds to a molar substitution of 1.90 ± 0.05 for the methyl and 0.23 ± 0.03 for the hydroxypropyl groups. Aqueous solutions were prepared by dissolving dried (at 80°C) HPMC samples followed by membrane filtration (Millipore, Molsheim, France; type AA, 0.8 μm).

Instruments

Capillary measurements of viscosity were performed with a Schott viscosity measurement system AVS300 + CT1150 (Schott Gerate GmbH, Hofheim a. Ts., Germany), supported by a prethermosetting water-bath Lauda RM6 (Lauda Dr. R. Wobser GmbH & Co. KG, Lauda-Königshofen, Germany) and equipped with an Ubbelhode viscometer Schott 501 with a capillary (no. I) having an inner diameter of 0.63 mm, an efflux volume V of 5.0 mL, and a capillary constant = 0.009947. The temperature was controlled to ± 0.05°C. Rotational viscometry was carried out using a Physica. Viskolab LC20 (Physica, Messtechnik GmbH, Stuttgart, Germany), equipped with a double-gap measuring system (Z1 DIN54453). The temperature was controlled within $\pm 0.1°C$ with a Lauda RM6 thermostat.

Measurements

Specific viscosity η_{sp} (dimensionless) was determined either from the time t (s) of the efflux through the Ubbelhode capillary or from the viscosity reading η (cP) of the rotational viscometer employing the following equations:

$$\eta_{sp} = (t_{corr} - t^0_{corr})/t^0_{corr} \tag{3}$$

where t_{corr} and t^0_{corr} are the capillary efflux times (averages of four determinations) of the solution and the solvent respectively, corrected for kinetic energy losses due to turbulence at the entrance and exit of the capillary[27,28] according to Hagenbach following the scheme provided with the instrument manual, or

$$\eta_{sp} = (\eta - \eta^0)/\eta^0 \tag{4}$$

where η and η^0 are the rotational viscosity of the solution and solvent respectively, at a given temperature.

Shear rate G (s^{-1}) was estimated[29,30] from the capillary efflux time t according to

$$G = 8V/(3\Pi r^3 t) \tag{5}$$

where G is the average velocity gradient, V (mL) the efflux volume, and r (cm) the capillary radius. Shear rates were also provided from the rotational viscometry instrument.

THEORY

The fundamental theory on the viscosity increasing effect of particles suspended in a flowing continuous liquid phase, applicable to large molecules in solution as a special case, stems from a treatment of the particles influence on the liquid movement. In this way Einstein[31,32] was able to derive an expression for the effect of hard particles with spherical shape which has been found to be valid independent of particle size, at low concentrations, as manifested both for extremely small particles of molecular size[31-33] as well as for extremely large objects with diameters in the 400 μm range.[34-38] Given below, an interpretation of the most important findings/assumptions and a suggestion for a generalization to rod shape.

Spherical Shape

1. The viscosity-increasing effect, per volume unit of suspended spherical particles, on a streaming incompressible liquid is independent of particle size as long as it is large in comparison with the liquid components (solvent molecules).
2. The interaction between the particle and the liquid (solvent) is entirely dynamical and the liquid can be regarded as a homogenous continuum (i.e., infinitely small constituents) without structure. The particle does not interact with the other particles and has a nonzero friction coefficient versus the liquid leading to adherence of liquid to the particle surface.
3. The liquid flow should be sufficiently slow so that the kinetic energy of the particle and of the liquid constituents are negligible (in relation to the frictional heat dissipation).
4. The proportionality between the viscosity increasing effect due to spherical particles, at sufficiently low collective particle volume fraction ϕ, is described by

$$\eta_{sp} = 2.5\phi \tag{6}$$

where η_{sp} is the specific viscosity of the suspension (solution).

Extended Shape

A generalization of Einstein's result for spherical shape into extended shape appears to be possible by the following additional assumptions:

5. The shape of the liquid constituents and of the particle is measured as their axial ratios $\mathbf{a}_l$ and $\mathbf{a}_p$, respectively.

6. The viscosity increasing effect per volume unit of a particle is independent of particle size for any shape as long as the shape is not altered.
7. The viscosity increasing effect per volume unit of the particles relative to the liquid equals a constant k if the particle shape is unchanged and k increases the more extended shape the particle has. The specific viscosity is then calculable according to

$$\eta_{sp} = (k - 1)\phi \tag{7}$$

   where $k = 3.5$ if both the liquid constituents and the particle are spherical.
8. The streaming of the suspension will adjust itself so as to minimize the viscosity increasing effect, that is to flow under minimum force and energy dissipation.
9. Laminar flow of the suspension is obtainable with a combination of sufficiently low concentration and suitable shear.
10. A laminar flow would affect the orientation of the particles so as to align their length axis with the flow direction while producing an inherent instability toward particle rotation.
11. Rotation of the particle is counteracted by the cohesive forces between particle and liquid.
12. Newtonian viscosity of the laminar flow would be indicative of liquid dynamic conditions of perfect alignment of the particles, having zero rotation transverse to its length axis, since this would result in a shear rate independence of the viscosity increasing effect provided that the particle shape is constant.

Rod Shape

Monodisperse axial ratio Imagine spheres which are elongated into rod-shaped particles, with an invariant cross-section (i.e., a cylinder), while retaining their volumes. As the axial ratio $\mathbf{a}_p$ increases the particles become increasingly one-dimensional with respect to their viscosity-increasing effect k under Newtonian conditions since their perturbation of the flow pattern of the liquid (i.e., liquid dynamic interaction) will be more and more dominated by the relative axial ratio $\mathbf{a} = \mathbf{a}_p/\mathbf{a}_l$ of the particles as compared with the liquid constituents. At sufficiently large $\mathbf{a}$, one therefore expects a proportionality

$$k = \xi \mathbf{a} \tag{8}$$

where ξ is a dimensionless proportionality constant. In addition, the proportionality must obey a size continuity requirement due to the assumption of a size independence. Therefore, one arrives at the conclusion that $\xi = 1$ if the particles were made up of the same constituents as the liquid so that it would be impossible to distinguish between the particles and the fluid itself, except for the difference in shape. Furthermore, it can be concluded that this latter case will be fulfilled for any real suspensions (solutions) as a consequence of the particle-liquid adherence condition. In such suspensions (solutions), all friction must then occur in the liquid since there will be no friction at the particle surface and hence the particle will have no other characteristic feature than the volume it excludes from the transport space of the liquid. This effect will be completely independent of the particle's adhesive properties versus the liquid as long as these are non-zero. The limiting case, where $\mathbf{a} \gg 1$, can hence be expressed as

$$[\eta]_\phi = \mathbf{a} \tag{9}$$

where $[\eta]_\phi$ is the dimensionless laminar intrinsic viscosity resulting from the use of volume fractions as used by Einstein (Equation (6)). It is obvious that, for real suspensions or solutions where $\xi = 1$, the intrinsic viscosity physically becomes identical with the relative axial ratio $\mathbf{a}$ of rod-shaped particles, at sufficiently large $\mathbf{a}$ under Newtonian liquid dynamics. The commonly used intrinsic viscosity $[\eta]$, which often is expressed in dL/g when the concentration c is measured in g/dL, is calculable by combining Equations (7) and (8) in such a way that it fulfills the two limiting cases of $\mathbf{a} = 1$ and $\mathbf{a} \gg 1$, resulting in the following general approximation for any $\mathbf{a}$ in this range:

$$[\eta] = (\mathbf{a} + 1.5)/(100\rho) \tag{10}$$

where the collective volume fraction ϕ of the particles is obtained from $\phi = c/(100\rho)$, where ρ is a conversion factor into volume fraction (g dry polymer/mL solvated polymer) of the suspended particle including any solvate which may be carried along as a particle entity.

Considering that the particle may be viewed as if it consists of $\mathbf{a}_p$ subunits, each with axial ratio = 1, linked together, its molecular weight M may be estimated according to

$$M = \mathbf{a}_p M_{\text{unit}} \tag{11}$$

where M_{unit} is the molecular weight of the subunit.

Polydisperse axial ratio For any suspension (solution) the measurement of $[\eta]_\phi$ or $[\eta]$ will indicate an average of the relative axial ratio $\mathbf{a}$ for the particles suspended. It can be shown that this, for particles with the same width but different length, corresponds to the weight-average relative axial ratio $\mathbf{a}_w$ by calculating the axial ratio from Equation (9) as follows:

$$\text{relative axial ratio} = \sum \eta_{sp,i} / \sum \phi_i = \sum f_i \mathbf{a}_i^2 / \sum f_i \mathbf{a}_i = \mathbf{a}_w \tag{12}$$

assuming that the increments in η_{sp} and the collective volume fraction ϕ, due to each particle, both are additive. The frequency (number per volume unit) of particles having relative axial ratios $\mathbf{a}_i$ is denoted with f_i.

Molecular Weight of Fully Extended Polymers

For polydisperse suspensions (solutions) of rod-shaped polymers characterized by the particle weight-average axial ratio $\mathbf{a}_p = \mathbf{a}_w \mathbf{a}_l$ one may estimate M_w according to

$$M_w = \mathbf{a}_w \mathbf{a}_l M_{\text{unit}} \tag{13}$$

where M_{unit} is the molecular weight of the subunit having, by definition, an axial ratio $\mathbf{a}_{\text{unit}} = 1$. In case of fully extended and single stranded polymers M_{unit} equals the molecular weight of the repeating unit M_u of the polymer divided with the axial ratio $\mathbf{a}_u$ of the solvated repeating unit. In this case M_w is calculable from $[\eta]$ according to

$$M_w = ([\eta]100\rho - 1.5) M_u \mathbf{a}_l / \mathbf{a}_u. \tag{14}$$

In the case of aqueous celluloses, where the repeating units consist of solvated entities of derivatized glucose units, both $\mathbf{a}_l$ and $\mathbf{a}_u$ are approximately 1. It follows from Equation (14) that the weight-average degree of polymerization DP_w can be calculated as

$$DP_w = ([\eta]100\rho - 1.5)\mathbf{a}_l/\mathbf{a}_u \tag{15}$$

and that $[\eta]$ is given by

$$[\eta] = (M_w\mathbf{a}_u/(M_u\mathbf{a}_l) + 1.5)/(100\rho). \tag{16}$$

At sufficiently large $\mathbf{a}_w$, $[\eta]$ can be approximated by

$$[\eta] = M_w\mathbf{a}_u/(M_u\mathbf{a}_l 100\rho) = K_w M_w \tag{17}$$

where $K_w = \mathbf{a}_u/(M_u\mathbf{a}_l 100\rho)$ is a constant, in $\mathrm{dL\,mol\,g^{-2}}$, referring to weight-average molecular weights. A theoretical derivation of the Staudinger findings for celluloses,[2] that is a linear relation between $[\eta]$ and M_w, is thus achieved. Furthermore, the results can be expressed as follows: an exponent $\alpha = 1$ in the Mark–Houwink relation (Equation (2)) indicate full extension of the polymer provided that the conditions of laminar Newtonian flow are fulfilled.

RESULTS AND DISCUSSION

Intrinsic Viscosity

The best accuracy in the determination of intrinsic viscosity $[\eta]$ is likely to occur under such conditions where extrapolation of the reduced viscosity η_{sp}/c to zero concentration can be made in a linear fashion. Linear relations are usually observed at sufficiently low concentrations for both small solutes[39] and polymeric solutes[40,41] and can hence be described by a truncated power function

$$\eta_{sp}/c = A + Bc \tag{18}$$

where the first virial coefficient can be identified as $A = [\eta]$. The second virial coefficient can be written in the form $B = k_H[\eta]^2$ and the constant

k_H (dimensionless) is usually referred to as the Huggins constant or the interaction constant[42] and may be viewed as reflecting the combined liquid dynamic and chemical interaction. A useful approximation of Equation (18) for numerical analysis is

$$c/\eta_{sp} = 1/A + k_H c. \tag{19}$$

The value of η_{sp} depends upon the applied shear rate, as observed and reviewed by Timell,[43] and hence the values of A and B will depend on the liquid dynamic conditions. Therefore, in order to be able to apply the theory presented in this work one has to carry out the extrapolation under such liquid dynamic conditions where the flow is laminar and Newtonian. It will be shown more explicitly using rotational viscometry in a subsequent article that such conditions were met in the measurements reported here, but suffice it for the time being, laminar Newtonian conditions are likely to be fulfilled for the entire set of HPMC viscosity grades since they could be characterized by a common interaction constant k_H, Figures 1 and 2, and Table I.

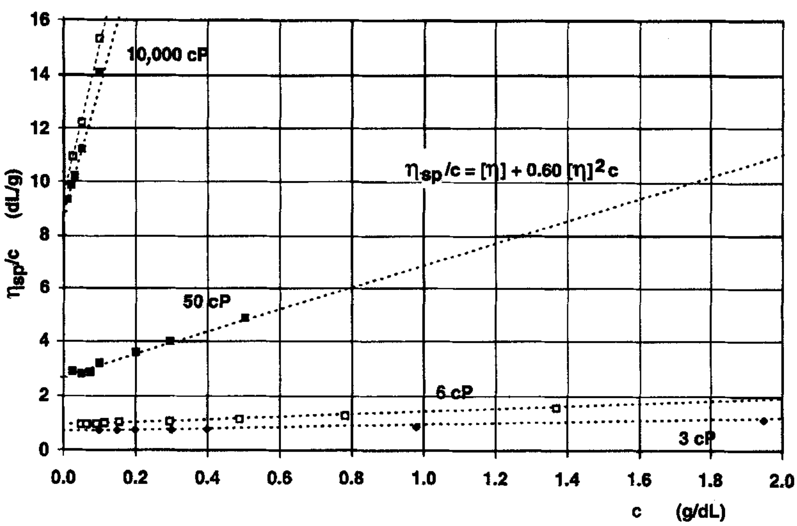

FIGURE 1 Reduced viscosity η_{sp}/c as a function of concentration c for aqueous HPMC (USP type 2910) of various viscosity grades at 20°C (two samples of 10,000 cP). The lines are calculated according to Equation (18) using a single value for the Huggins constant resulting in a complete data reduction model for $k_H = 0.60$.

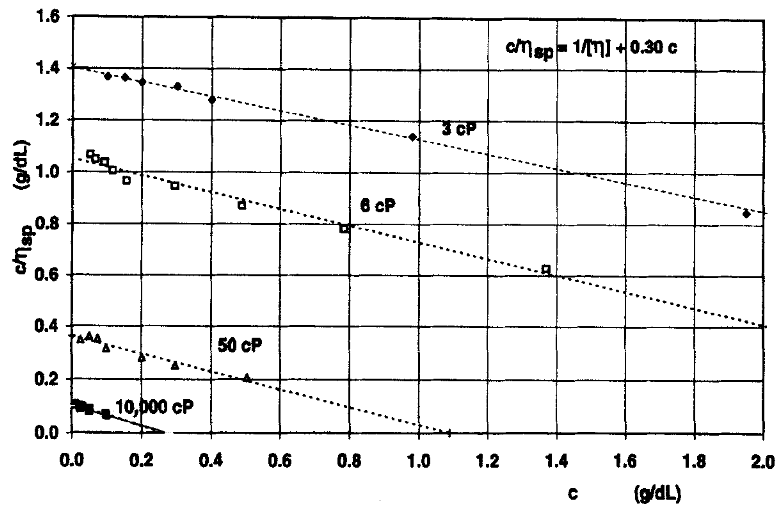

FIGURE 2 Inverse reduced viscosity c/η_{sp} as a function of concentration c for the same data as in Figure 1. The lines are calculated according to Equation (19) and the resulting $k_H = 0.30$ reflects a systematic divergence from Equation (18) with increasing concentration.

TABLE I Intrinsic viscosity $[\eta]$ and k_H for HPMC (USP-type 2910), determined with Equation (18) under conditions of laminar Newtonian flow and linear concentration dependence of the reduced viscosity, using capillary measurements of aqueous solutions at 20 and 7°C. Units: $[\eta]$ in dL/g, conc. in g/dL, shear rate in s^{-1}, k_H is dimensionless

*Viscosity grade**	3 cP	6 cP	50 cP	10,000 cP
$[\eta]$ (20°C):	0.69 ± 0.02	0.92 ± 0.02	2.65 ± 0.05	8.85 ± 0.09
k_H (20°C):	0.45 ± 0.08	0.56 ± 0.08	0.63 ± 0.10	0.66 ± 0.06
Conc. range:	0.1–1.5	0.05–1.67	0.025–0.50	0.01–0.074
Shear rate:	1235–560	1270–350	1271–390	1208–709
$[\eta]$ (7°C):			3.01 ± 0.06	9.5 ± 0.1
k_H (7°C):			0.63 ± 0.06	0.7 ± 0.1

*cP, 2% w/v @ 20°C.

The concentration ranges employed in the capillary measurements were determined by experimental accuracy and precision. While low concentrations improve the accuracy, by high shear rate governing laminar Newtonian conditions, the precision depreciates as a result of small differences between the efflux times t_{corr} and t^0_{corr}, *cf.* Equation (3).

The maximum concentration employed was determined by the limit of linearity of the concentration dependence of the reduced viscosity. The investigated ranges of concentration and shear rate, and the observed limit of the concentration dependency together with the calculated k_H and $[\eta]$ are collected in Table I. All data are presented in Figure 1 showing the observed reduced viscosity η_{sp}/c as a function of concentration. It can be seen that the calculated linear functions, according to Equation (18) with $k_H = 0.60$, appears to fit the entire set of viscosity data. Careful examination, however, indicates a small deviation from linearity at the highest concentrations, beginning at *ca.* 0.07% for 10,000 cP, *ca.* 0.45% for 50 cP, *ca.* 1.7% for 3 cP, and *ca.* 2% for 6 cP (see also Table I). It can therefore be concluded that all the linear parts of the functions can be described by a common k_H and this is further supported by the parallel slopes in Figure 2 of the plot according to Equation (19). However, although this equation, if applying linear regression, yields nearly the same values of $[\eta]$, as compared with Equation (18) $[\eta]$ is systematically overestimated while k_H is grossly underestimated, indicating the approximative character of Equation (19).

The obtained values of $[\eta]$ using Equation (18) agree well with previous values reported, *cf.* Table II. An estimate of $[\eta]$ representative for each HPMC grade has been made by averaging the values from different batches and literature values, Table II. The agreement with literature on k_H values: 3 cP ($k_H = 0.55$ for 0.6–2.0% at 25°C),[44] 6 cP ($k_H = 0.80$ for 0.6–2.0% at 25°C[44]; $k_H = 0.96 \pm 0.04$ for 0.2–0.5% at 20°C[45]), and 50 cP ($k_H = 0.61$ for 0.1–0.5% at 25°C)[44] is less impressive, probably, as discussed above, due to limited precision. Hence, while this work numerically indicates $k_H = 0.63 \pm 0.06$ using Equation (18), it is only reasonable to conclude that the true uncertainty probably is larger.

Volume Fraction

In order to appraise the collective volume fraction ϕ it is necessary to consider that the particles may be solvated. Hence, the analytical concentration c, measured in units of g dry substance (i.e., desolvated particles) per mL suspension (solution), must be supplemented with information about the solvation of the substance. A method for the

TABLE II Weight-average molecular weights of HPMC (USP type 2910) calculated from viscosity measurements of aqueous solutions at 20°C. $M_w = ([\eta]100\rho - 1.5)\ M_u \mathbf{a}_l / \mathbf{a}_u$ where $M_u = 203 \pm 3$ g/mol, $\mathbf{a}_u = 0.9 \pm 0.1$, $\mathbf{a}_l = 1$, and $\rho = 1.04 \pm 0.04$ g dry polymer per mL solvated polymer

*Viscosity Grade**	$[\eta]$, dL/g 20°C	$[\eta]$, dL/g 20°C *grade average*	M_n Ref. [26]	M_w *grade average*	M_w/M_n	M_n *static* LS	M_w *static* LS
3	0.69 ± 0.02^a 0.483^d 0.54 ± 0.05^e	0.65 ± 0.07	9,300	15,000	1.6		
6	0.92 ± 0.02^a 0.91 ± 0.03^b 1.089^d 0.85 ± 0.03^e	0.91 ± 0.10	12,000	21,000	1.8		
50	2.65 ± 0.05^a 2.67 ± 0.05^g 2.56 ± 0.06^e	2.7 ± 0.3	31,000	63,000	2.0	25,000[f]	132,000[f]
4,000	7.40^c	7.4 ± 0.4	100,000	170,000	1.7	117,000[f]	225,000[f]
10,000	9.58 ± 0.12^g 9.49 ± 0.12^g 8.85 ± 0.09^g	9.4 ± 0.6	120,000	220,000	1.8	158,000[f]	309,000[f]

*cP, 2% w/v @ 20°C
[a] This work, Table I.
[b] Lit.[45]
[c] Lit.[95]
[d] Lit.[126] (25°C).
[e] Lit.[44] (25°C).
[f] Single samples,[54] (FFF-MALS).
[g] This work.

measurement of solvation must be chosen that is uniformly sensitive to the total coordination (inner and outer-shell coordination) of contributing solvated volumes. Generally, methods related to transport properties will reflect such total solvation while other methods may be predominantly sensitive to a part of the solvation, for example, the inner-coordinated solvates.[46,47] Therefore, an attempt to utilize the viscosity effect for the determination of the conversion factor ρ (g unsolvated polymer/mL solvated polymer) into volume fraction will be made here. It is essentially derived from the temperature dependence of η_{sp} under conditions of invariant extension utilizing the fact that solvation often changes with temperature. It is assumed that a critical temperature T_θ is known or can be determined, at which solvation is negligible so that ρ_θ can be equal to the partial specific density ρ_s at T_θ (or approximated by the solid state density). Although T_θ sometimes is defined[48] as the critical solution temperature at which "the excess free energy of dilution is zero", which latter relates to the

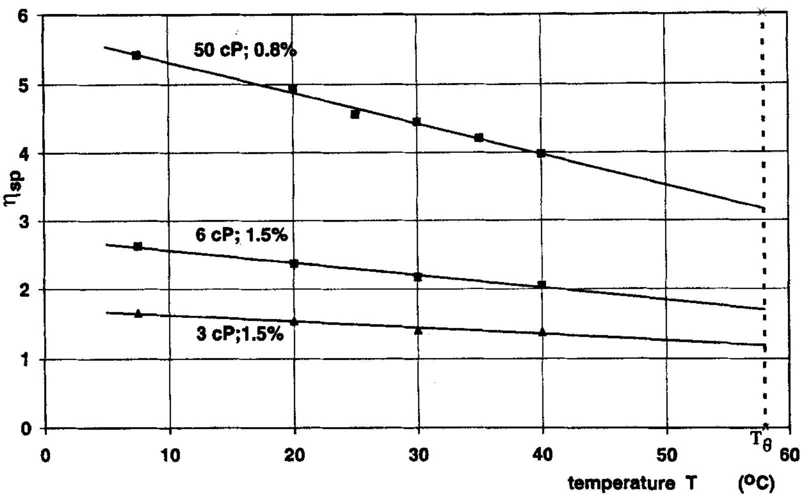

FIGURE 3 Temperature dependence of specific viscosity η_{sp} at laminar Newtonian conditions obtained by rotational viscometry of aqueous HPMC (USP type 2910) of various viscosity grades and concentrations (3 cP at 1.5% w/w; 6 cP at 1.5% w/w; 50 cP at 0.8% w/w). The linear relations for 7.5–40°C are extrapolated to the critical solution temperature $T_\theta = 58°C$, allowing the conversion factor ρ to be calculated; $\rho = 1.04 \pm 0.04$ g dry polymer/mL solvated polymer.

Hildebrand concept of ideal solution[49] (zero enthalpy of dilution for same size components) it appears more appropriate to assume that T_θ is the critical solution temperature at which the miscibility approaches zero rather than infinity, leading to zero solvation and phase separation.

Figure 3 shows the influence of temperature T on η_{sp} under laminar Newtonian conditions, obtained at a combination of sufficiently high shear rate and low temperature, using rotational viscometry on viscosity grades (3, 6 and 50 cP) of HPMC. The η_{sp} decreases linearly with increasing temperature, from 7.5°C to *ca.* 40°C, due to decreasing solvation. Further increase in temperature results in deviations from Newtonian behavior caused by beginning interactions between the polymer molecules. Extrapolation is made to $T = T_\theta = 58°C$, sometimes referred to as the cloud-point C_p, obtained from turbidity measurements at similar concentrations.[50]

Assuming that $\rho_\theta = \rho_s = 1/V_s = 1.304$ g/mL, using the value $V_s = 0.767$ mL/g for the partial specific volume in water for HPMC of USP substitution-type 2910,[50] one may calculate ρ at another temperature ($T < T_\theta$) according to

$$\rho = \rho_\theta[\eta]_\theta/[\eta] \tag{20}$$

where $[\eta]_\theta$ and $[\eta]$ are calculated from η_{sp} using Equation (18) assuming that k_H is independent of the temperature. It is found that ρ (20°C) = 1.04 ± 0.04 g/mL. If it is assumed that the solvation is independent of shear rate, the value should be representative for all viscosity grades of HPMC of the USP substitution-type 2910. The ρ value at 20°C corresponds to a hydration number $h = 2.2 \pm 0.1$ moles of water per repeat unit of the polymer assuming that the temperature dependence of V_s can be neglected. In fact, the indicated invariance of the hydration with the viscosity grade is supported by a constant value of $T\delta[\eta]/([\eta]\delta T) \approx \delta \ln[\eta]/\delta \ln T = -1.56 \pm 0.25$ (unitless) calculated from Figures 3 and 4 for T in Kelvin. The negative temperature dependence of $[\eta]$ appears to be typical for aqueous cellulose based systems: $\delta \ln[\eta]/\delta \ln T = -1.4 \pm 0.4$ for hydroxyethylcellulose (HEC)[51] (0–25°C); $\delta \ln[\eta]/\delta \ln T = -2.2 \pm 0.5$ for sodium carboxymethylcellulose (NaCMC) in 0.2 M NaCl[52] (0–40°C); $\delta \ln[\eta]/\delta \ln T = -1.6 \pm 0.2$ for chitosan in

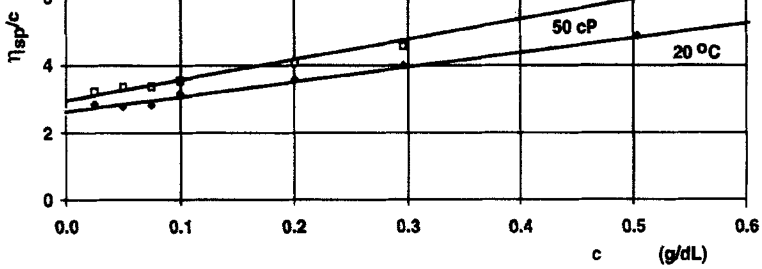

FIGURE 4 Influence of temperature on the concentration c dependence of the reduced viscosity η_{sp}/c at laminar Newtonian conditions of aqueous HPMC (USP type 2910) of 50 and 10,000 cP viscosity grade.

0.33 M acetic acid + 0.3 M NaCl (10–65°C).[53] Differences between the present study and the previous reports may partially be attributed to departures from the required laminar Newtonian conditions.

Figure 4 shows the concentration dependence of the reduced viscosity at two different temperatures, 7 and 20°C. The results, Table I and Figure 4, further support the above assumption that k_H is independent of temperature. Since no effect on k_H due to the change in solvation is evident this indicate that k_H is entirely due to liquid dynamic interactions provided that laminar Newtonian conditions are fulfilled.

Molecular Weight

The weight-average molecular weight is calculable from $[\eta]$ according to Equation (14) assuming full extension of the polymer. The extent of extension for aqueous HPMC may be concluded from Figure 5 in which the relation between $[\eta]$ and M_n at 20°C, obtained previously with osmometry[26] is shown. The relation is principally linear, both for HPMC and methylcellulose (MC) (MC data[1] included for comparison) suggesting full extension in both cases and hence applicability of

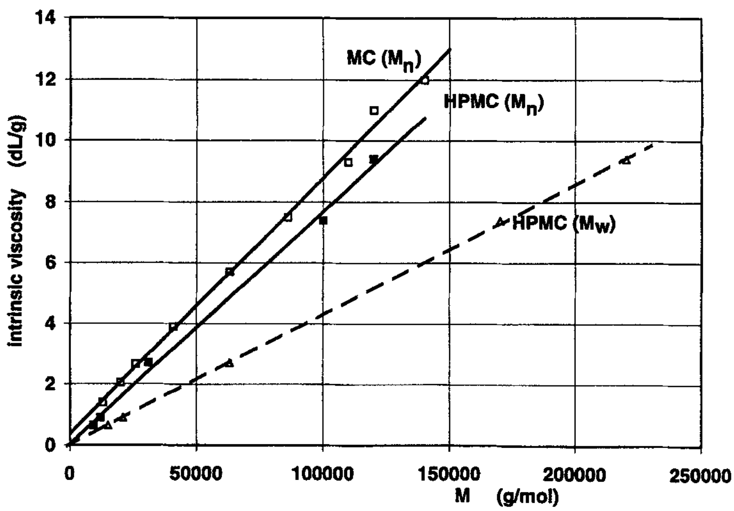

FIGURE 5 Relations between $[\eta]$ and osmometrically determined M_n for HPMC (USP substitution type 2910)[26] and MC.[1] The broken line represents M_w calculated from the theoretical Mark–Houwink constant $K_w = \mathbf{a}_u(M_u)^{-\alpha}/(\mathbf{a}_l 100\rho)$, where $M_u = 203 \pm 3$ g/mol, $\mathbf{a}_u = 0.9 \pm 0.1$, $\mathbf{a}_l = 1$, $\rho = 1.04 \pm 0.04$ g/mL, and $\alpha = 1.00 \pm 0.02$ (from the relation between $[\eta]$ and M_n). Separate M_w for HPMC represents grade averages (Table II).

Equation (14). Table II summarizes the calculated M_w for the different viscosity grades of HPMC based on a grade-average $[\eta]$ at 20°C estimated from this work and literature data. M_w is derived using this grade-average $[\eta]$ combined with the following values of the constants: $M_u = 203 \pm 3$ (g/mol), $\rho = 1.04 \pm 0.04$, $\mathbf{a}_u = 0.9 \pm 0.1$ and $\mathbf{a}_l = 1$. The axial ratio $\mathbf{a}_u$ of the repeating unit is only roughly estimated and constitutes the largest uncertainty.

The calculated M_w can be compared with the M_n measured by osmometry[26] by calculating the ratio M_w/M_n. It is found that the polydispersity is practically the same, around 1.8 ± 0.2, for all tested grades. A polydispersity of 2 is consistent with a broad but essentially monomodal molecular weight distribution invariantly observed for commercial HPMC as a single elution peak using analytical separation techniques, such as aqueous SEC used in our laboratory or field flow fractionation (FFF).[54] For polysaccharides, multimodal peaks do not occur unless due to presence of an impure polymer (mixture of different polymers), which has been recognized since Svedberg's work on their sedimentation properties.[55]

For comparison, some recent measurements on single samples of three viscosity grades using static light scattering combined with FFF[54] has been included in Table II. The agreement is acceptable, particularily for M_n, but it appears that the static light scattering tends to overestimate M_w as compared with the calculated grade-average M_w. The benefit of the presented viscosity method is that it is unusually robust. The accuracy depends primarily only on the accuracy of the estimation of $[\eta]$, $\mathbf{a}_u$, $\mathbf{a}_l$, and ρ giving a total accuracy of *ca.* 10% in the present work. However, the uncertainty is not very high for aqueous HPMC since any of the values of $\mathbf{a}_u$, $\mathbf{a}_l$, and ρ may not deviate much from unity. Generally, the precision obtainable is very high or *ca.* 1% since it is only dependent on $[\eta]$ as the other parameters are constant for a given combination of substitution grade and solvent.

CONCLUSION

Laminar Intrinsic Viscosity

Since the pioneering work of Einstein in 1906 on the hydrodynamics of suspended particles, resulting in the famous expression for spherical shape given in Equation (6), numerous attempts has been made to extend this relation to particles with extended shape as manifested by the many theories[2,4,6,33,36,37,40,56–114] and reviews[7,11–25,111,115–118] on the concept of intrinsic viscosity. However, it appears that all investigators have chosen to treat the boarder case of zero flow, that is, suspension at rest, leading to what has been called[90,98] stationary intrinsic viscosity. This case corresponds to what is now[113,114] referred to as Brownian dynamics. In contrast, the present work treats another case which corresponds to sufficiently high flow to produce what may be termed laminar dynamics. The major advantage of laminar dynamics versus Brownian dynamics is that the complicating effect on the suspended particle (i.e., rotation and frictional drag) due to Brownian motion of the liquid constituents is eliminated. Rotation (in the flow direction) is completely prevented, at adequate liquid flow to approach laminar streaming, due to adhesive forces between particle and liquid, which also causes zero shear between the surface of the particle and the liquid. The latter effect, which is recognized as the "no-slip" condition,[119,120] simplifies the hydrodynamic problem to a particle which is under zero net force and therefore does not have any net movement relative to neither the bulk liquid nor to the immediate surrounding liquid. All frictional energy dissipation must then occur between the liquid constituents only. An analogous concept is the boundary layer of Prandtl[119,120] with the exception that in laminar dynamics the particle is not moving through the fluid but rather moves with it.

Hence, application of Stokes law of friction will not provide any information for laminar dynamics and will be meaningless for the description of laminar $[\eta]$. It may be deduced directly from Equation (6), that the Stokes transport property (i.e., size) of the particle has no influence on $[\eta]$ for spherical particles and it is assumed in this work that this is true for any shape. The absence of rotation is experimentally verified by the occurrence of flow birefringence upon subjecting a suspension (solution) of anisotropic particles having any size or shape to flow. The effect has been recognized and is interpreted as an orientation of the particles with their length axes becoming parallel with the flow direction at sufficiently high shear rate.[60–62]

The most important additional convenience with respect to literature[7,11–14,16,21–25,113,114,118] chain dynamics is that a real volume concept is used. The present model, in analogy with Einstein's, retains the physical volume of the particle as identical with the hydrodynamically effective volume instead of the expanded volume concept.[3,15,17,61,84–86,88,89,91,98] Here, the viscosity-increasing effect is assumed to be dependent on the shape of the particle rather than on the virtually expanded volume. The unit of measurement of intrinsic viscosity used by Einstein and also employed in this work is the dimensionless volume fraction. The common practice to measure in units of dL/g, has the advantage of simplifying the determination but has the drawback of being difficult to interpret mechanistically since it varies with the experimental parameters, such as shear rate, temperature, and solvent. In contrast, the unitless laminar $[\eta]_\phi$ is invariant with these parameters and can be identified with the simple physical meaning of relative axial ratio.

Negative Intrinsic Viscosity

As discussed above, the dimensions of the particle is of no importance for its laminar dynamics as long as the particle is larger than the liquid constituents and therefore the laminar $[\eta]_\phi$ is limited to values greater than or equal to unity. However, since it is arbitrary which object is viewed as the particle or the liquid constituent, the reciprocated model should work also for particles smaller than the liquid constituents, but the effect would be opposite; a decrease in viscosity would occur so that the laminar $[\eta]_\phi$ would become negative. Support for this expectation, that is, $k < 1$ in Equation (7), is that negative intrinsic viscosities have, in fact, been observed for binary mixtures of small solutes and solvents, both nonpolymeric solutes[121,122] and oligomers[123,124] and these results may then be explained as being largely due to the solute molecules being the smallest of the solute–solvent pairs.

Solvent Molecular Shape

Anisotropy of the solvent molecules, that is, an axial ratio $\mathbf{a}_l > 1$ of the liquid constituents, is expected from Equation (8) to have exactly the inverse effect as compared with the axial ratio $\mathbf{a}_p$ of the suspended particle so that for $\mathbf{a}_l = \mathbf{a}_p \gg 1$, the laminar $[\eta]_\phi$ will be zero. In the present study of aqueous systems $\mathbf{a}_l$ can be approximated by unity.

Polymer Shape and Size

The proposed model for the laminar dynamics of suspended particles might be useful, under certain conditions discussed below, as a general tool for studying polymer conformation in flowing solutions. It is not only applicable to stiff polymers like the celluloses (e.g., HPMC and MC) as shown here but also to flexible polymers if such shear conditions can be created where the polymer approaches rod shape despite being completely extended. In such cases, the axial ratio $\mathbf{a}_w$ should be estimable from viscometry, according to Equation (10). In case the M_w is known then the value the weight-average number of strands ψ_w (dimensionless) (equal to the number of repeating units in a cross-section of the rod or the number of repeat units per M_{unit}) may be estimated as follows:

$$\psi_w^2 = M_w\mathbf{a}_u/(\mathbf{a}_w M_u) = M_w\mathbf{a}_u/(M_u[\eta]100\rho\mathbf{a}_l) \tag{21}$$

allowing the particle length l_w (Å) and diameter d_w (Å) to be calculated as

$$l_w^2 = (\psi_w\mathbf{a}_w l_u/\mathbf{a}_u)^2 = M_w[\eta]100\rho\mathbf{a}_l l_u^2/(M_u\mathbf{a}_u) \tag{22}$$

$$d_w = \psi_w^{1/2} l_u/\mathbf{a}_u \tag{23}$$

where l_u (Å) is the length of the repeat unit.

Furthermore, if there exists a limited range of large M_w where Equation (2) is valid then the corresponding value of the Mark–Houwink constant K can be derived exactly if combined with appropriate information. The supplemental information is offered by the laminar dynamic model for the hypothetical case that both the mechanism of the monotonical decrease in the relative extension of a rod-shape particle and ξ were the same for $M_w = M_u$ as in the above range of M_w. For this case, the normalized value of the intrinsic viscosity for the hypothetical monomer for which $\xi = 1$ can be calculated as

$$[\eta]_u = \mathbf{a}_u/(\mathbf{a}_l 100\rho) \tag{24}$$

which inserted into Equation (2) gives

$$K_w = \mathbf{a}_u(M_u)^{-\alpha}/(\mathbf{a}_l 100\rho) \qquad (25)$$

where K_w, in units of dLg^{-1} $(mol/g)^{-\alpha}$, is constant as long as the polydispersity P is kept constant. The corresponding constant for the number average K_n is obtained as $K_n = K_w P$.

Equation (25) is applicable to HPMC as shown in Figure 5 and gives reasonable agreement with the experimental values of K according to a set of recommended values for various polymer–solvent combinations at different temperatures,[7] even when using crude estimates of ρ, $\mathbf{a}_l$ and $\mathbf{a}_u$ and despite that the postulated liquid dynamic requirements may not have been completely fulfilled. Hence, further support for the validity of the suggested model of laminar dynamics is indicated. It is proposed that polymers in general will be subject to alignment with the flow of a suspension (solution) and tend to assume an extended shape which, although not completely extended, can be approximated with a rodlike shape at sufficiently high shear rate.

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