Colloid Polym Sci (2005) 284: 86–91
DOI 10.1007/s00396-005-1332-3

SHORT COMMUNICATION

J. V. Herráez-Domínguez
F. Gil García de León
O Díez-Sales
Marina Herráez-Domínguez

Rheological characterization of two viscosity grades of methylcellulose: an approach to the modeling of the thixotropic behaviour

Received: 28 December 2004
Accepted: 22 March 2005

J. V. Herráez-Domínguez (✉)
F. G. G. de León
Department of Thermodynamics,
Faculty of Physics and Pharmacy,
University of Valencia,
Av. Vicente Andrés Estellés, s/n,
46100 Burjassot, Valencia, Spain

O Díez-Sales · M. Herráez-Domínguez
F. G. G. de León
Department of Pharmacy and Pharmaceutical Technology, Faculty of Pharmacy,
University of Valencia, Av. Vicente Andrés
Estellés, s/n, 46100 Burjassot, Valencia,
Spain

Abstract The rheological behavior of two viscosity grades of methylcellulose (MC) (M-0262 and M-0512) was determined based on the dispersions of different polymer concentrations (from 0.1 to 5% w/w). In order to analyze the possible thixotropic character of the dispersions, the up and down curves of rheograms for several agitation times were plotted. In all cases, the Ostwald-De Waele rheological model (or Power Law model) was used. For both grades of MC, preparations of concentrations in the range of 0.1–1.0% (w/w) exhibited Newtonian behavior, while at polymer concentrations from 2–5% (w/w), pseudoplastic behavior was observed. The lower viscosity grade MC (M-0262) showed no thixotropy, while the higher viscosity grade MC (M-0512) exhibited thixotropic behavior from 2–5% (w/w). To analyze and define thixotropic behavior, we propose an equation model obtained from the values of consistence, *m*, determined for each of the curves in a flow diagram$\tau \rightarrow \dot{\gamma}$. The results obtained from the proposed equation model showed good correlation to those obtained with the thixotropic areas method, and thus could be used as an alternative model for analyzing thixotropy.

Keywords Methylcellulose · Consistency · Pseudoplasticity index · Thixotropy

Introduction

Rheological behavior is important at every stage in the lifetime of a pharmaceutical product—including its design, manufacture, transport, storage [1] and also its use because it could affect the therapeutic value, via the release rate of active ingredient from the pharmaceutical matrices [2, 3]. Thus, detailed characterization of flow properties is relevant for product reliability and quality control. Thixotropy is commonly used to describe the rheological behavior of materials exhibiting a reversible time-dependent decrease in apparent viscosity when subjected to a particular shear rate. The study of thixotropic systems is typically complicated, however. In general, determination of the areas enclosed between up curve rheograms obtained for increasing shear rates, and down curve rheograms obtained for decreasing shear rates, following different agitation times, is used. These areas are referred to as thixotropic areas. [4–6]. Cellulose derivatives and, particularly, cellulose ethers are a group of common excipients of pharmaceutical preparations. The aim of the present work is to characterize the rheological behavior of two viscosity grades of methylcellulose (MC) in order to functionalize the viscosity of the respective dispersions at different concentrations (from 0.1% to 5%), shear rates($\dot{\gamma}$), and shear times (t_a). Such a function could help define the conditions of interest for polymers of this kind and destined for a specific use. In addition, we propose an alternative method for studying thixotropic behavior on the basis of the consistence values, m, determined for each of the flow curves, $\tau \to \dot{\gamma}$, between the minimum($\dot{\gamma}_{\min}$) and maximum($\dot{\gamma}_{\max}$) shear rates, and for different agitation times (t_a) applied to the system.

Experimental

The two viscosity grades of MC used in this study were used as received from Sigma Chemical, Co. (Madrid, Spain). The approximate viscosity of 2% aqueous solutions of these products, at 25 °C, was 400 cps (M-0262) and 4,000 cps (M-0512), respectively.

Dispersions of the two grades of MC were prepared in bidistilled water at concentrations ranging from 0.1–5.0% (0.1, 0.3, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0% w/w). A total of 450 g of each dispersion was prepared as follows: the amount of polymer required to yield 450 g of the dispersion at the desired concentration was added to water under constant stirring at 800 rpm for 45 min. Then, the preparation was sealed, shielded from light and allowed to stand for 48 h to ensure complete humectation of the polymer molecules. Following this storage period, the viscosity measurements were made.

Rheological measurements were carried out with a Brookfield Digital DVII+ rotary viscometer. The viscosity was determined for the eight rotational speeds provided by the viscometer. Taking into account the experimental characteristics involved (cylindrical spindles of different standard sizes were used), shear rates of between 0.063 s^{-1} and 75.549 s^{-1} were employed to determine viscosity. The measurements of apparent viscosity were initially made with the non-agitated dispersions in increasing order of shear rate and at time intervals of 10 s, which enabled the corresponding up curve rheograms to be plotted. Then, after agitation times of 1, 2, 3, 5, 10, 15, and 20 min. at the maximum rotational speed (60 rpm), the apparent viscosity values corresponding to the shear rates in decreasing order were measured in order to obtain the down curve rheograms. The temperature was maintained at 25 °C throughout the measurement process by immersing the flasks in a thermostatic bath.

In all cases, the Ostwald-De Waele rheological model (or Power Law model) was used for data analysis: $\eta = m\,\gamma^{n-1}$, (Eq. 1), where m is the Power Law viscosity constant, which describes the consistency of the system, and n is the Power Law index, which describes the deviation from Newtonian behavior. When the value of n is >1, the type of flow is shear thickening, and when n is <1, the type of flow is shear thinning (pseudoplastic behavior). The values of m and n were determined using the KaleidaGraph fit program.

The consistency (m) values with growing dispersion concentration (c) could be expressed as a function of the general form: $m = m_o e^{f(c)}$ (Eq. 2), where m_o (equal to 9.10^{-4} Pa s^n at 25 °C and 1 atm of pressure) corresponds to the consistency of the aqueous medium for the concentration ($c = 0$) [7] and m corresponds to the consistency in function of the concentration assayed (c). The specific $f(c)$ should be defined for each particular system.

For thixotropy analysis the values of m calculated for the dispersions of greater viscous MC grade (M-0512) at the concentrations that show pseudoplastic behavior, from 2–5% (w/w), were fitted by means of a mathematical function of the form $m = m(t)$, which must satisfy defined limiting conditions. In effect, examination of the experimental rheograms of a thixotropic system shows that, for $t = 0$, m attains its maximum value, $m = m_{\max}$. In contrast, for very long agitation times ($t \to \infty$), m tends towards a minimum limiting value, $m = m_{\min}$. Thus, a simple expression for the function $m(t)$ is as follows [8] (Eq. 3):

$$m_t = m_{\min} + (m_{\max} - m_{\min})e^{f(t)}, \tag{1}$$

where $m_{\max}$ is the consistency value of the gel without agitation and thus corresponding to the up curve; and $m_{\min}$ is the corresponding value obtained for maximum agitation time, t. The difference $\Delta m = m_{\max} - m_{\min}$ represents the maximum decrease in consistency (m) induced by agitation. The specific $f(t)$ should be defined for each system. The values of m were fitted by the least-squares method using the KaleidaGraph fit program.

Results and discussion

Rheological behavior of methylcellulose dispersions

In many studies involving different types of hydrogels for which viscosity (η) is changed when shear stress (τ) is applied, the Ostwald-De-Waele model ($\tau = m\gamma^n$) has been shown to be appropriate [8–11]. Equation 1 was used to fit the experimental data obtained for viscosity. The values of parameters m (consistency) and n

Table 1 Values corresponding to consistency (m, Pa.s^n) and pseudoplasticity index (n) obtained for M-0262 at different concentrations (from 0.1–5%, w/w) by means of the Ostwald-De Waele rheological model (Eq. 1)

c (%, w/w)	Consistency (m,Pa s^n)	Pseudoplasticity index (n)
0.1	0.0017	1
0.3	0.0037	1
0.5	0.0081	1
1	0.0428	1
2	0.411	0.9746
3	2.382	0.9627
4	8.871	0.9057
5	45.321	0.7492

Table 2 Values corresponding to consistency (m, Pa s^n) and pseudoplasticity index (n) obtained for M-0512 at different concentrations (from 0.1–5%, w/w) and agitation times by means of the Ostwald-De Waele rheological model (Eq. 1)

t_a (min)	Concentration (%, w/w)							
	0.1	0.3	0.5	1	2	3	4	5
	Consistency (m, Pa s^n)							
0	0.0020	0.0061	0.020	0.170	5.02	67.2	156	420
1	0.0020	0.0061	0.020	0.170	4.10	55.9	125	358
2	0.0020	0.0061	0.020	0.170	3.96	51.6	115	341
3	0.0020	0.0061	0.020	0.170	3.83	50.3	108	331
5	0.0020	0.0061	0.020	0.170	3.74	50.0	107	320
10	0.0020	0.0061	0.020	0.170	3.60	47.4	103	306
15	0.0020	0.0061	0.020	0.170	3.59	45.2	102	291
20	0.0020	0.0061	0.020	0.170	3.50	44.5	101	290
	Pseudoplasticity index (n)							
0	1	1	1	1	0.85	0.50	0.48	0.39
1	1	1	1	1	0.88	0.56	0.53	0.45
2	1	1	1	1	0.88	0.58	0.55	0.45
3	1	1	1	1	0.87	0.58	0.56	0.45
5	1	1	1	1	0.87	0.61	0.55	0.45
10	1	1	1	1	0.87	0.61	0.55	0.45
15	1	1	1	1	0.87	0.61	0.55	0.45
20	1	1	1	1	0.87	0.61	0.55	0.45

(pseudoplasticity index) are shown in Table 1 for low viscosity grade MC (M-0262), and in Table 2 for high viscosity grade MC (M-0512) for all concentrations used in the study. In all cases, the correlation coefficients obtained were >0.99.

As can be seen (Table. 1 , 2), the values of the Power Law index (n) for dispersions of low concentration (from 0.1–1%) are equal to 1, indicating that diluted solutions of the two grades of MC exhibit Newtonian flow. In contrast, non-Newtonian flow, which is commonly attributed to chain entanglement, was observed at polymer concentrations from 2–5% w/w, for both grades of MC, for which the n value is <1, thus indicating pseudoplastic flow. These n values decreases as the polymer concentration increases for both grades of MC. It seems clear that in concentrated polymer dispersions, the degree of entanglement must be greater than in dilute solutions. On the other hand, and for a given concentration value, the high viscosity grade MC (M-0512) shows n values inferior to those of the low viscosity grade MC (M-0262).

In Fig. 1, experimental values of viscosity (η, Pa s) as a function of shear rate($\dot{\gamma}$.s^{-1}) are graphically represented: low viscosity grade MC (M-0262) (**a**, **b**) and high viscosity grade MC (M-0512) (**c**, **d**), at polymer concentrations of 2% and 5% (w/w), respectively, serve to represent dispersions showing non-Newtonian flow. In general, an important decrease in viscosity is observed with increasing shear rate - especially at the lower shear rates employed—followed by a less accentuated descent of the curves.

Consistency variation with methylcellulose concentration

The values obtained for consistency (m) in turn can be related to the concentration (c) of the dispersions evaluated in the present study (Eq. 2). In all cases, the correlation coefficients obtained were greater than 0.99, and the equations obtained for the two grades of MC are:

$$(\mathrm{M{-}0262}) \quad m = m_{\mathrm{o}} \cdot \mathrm{e}^{4.84\sqrt{c}} \quad (r = 0.996), \tag{2}$$

$$(\mathrm{M{-}0512}) \quad m = m_{\mathrm{o}} \cdot \mathrm{e}^{7.64\sqrt[3]{c}} \quad (r = 0.999). \tag{3}$$

In accordance with these equations, in the concentration range used, it seems possible to predict the consistency values of the gels that could be obtained at a given polymer concentration for these grades of MC, and which could be of interest for a given use or application. Such equations could also be used to establish the industry laboratory technical conditions required to obviate certain problems during product preparation or manipulation.

Thixotropic behavior

To analyze the possible thixotropic character of the dispersions studied, at the concentration values showing pseudoplastic flow (from 2–5% w/w), we obtained the up and down curves for the agitation times used in the experiments. For low viscosity grade MC (M-0202), all

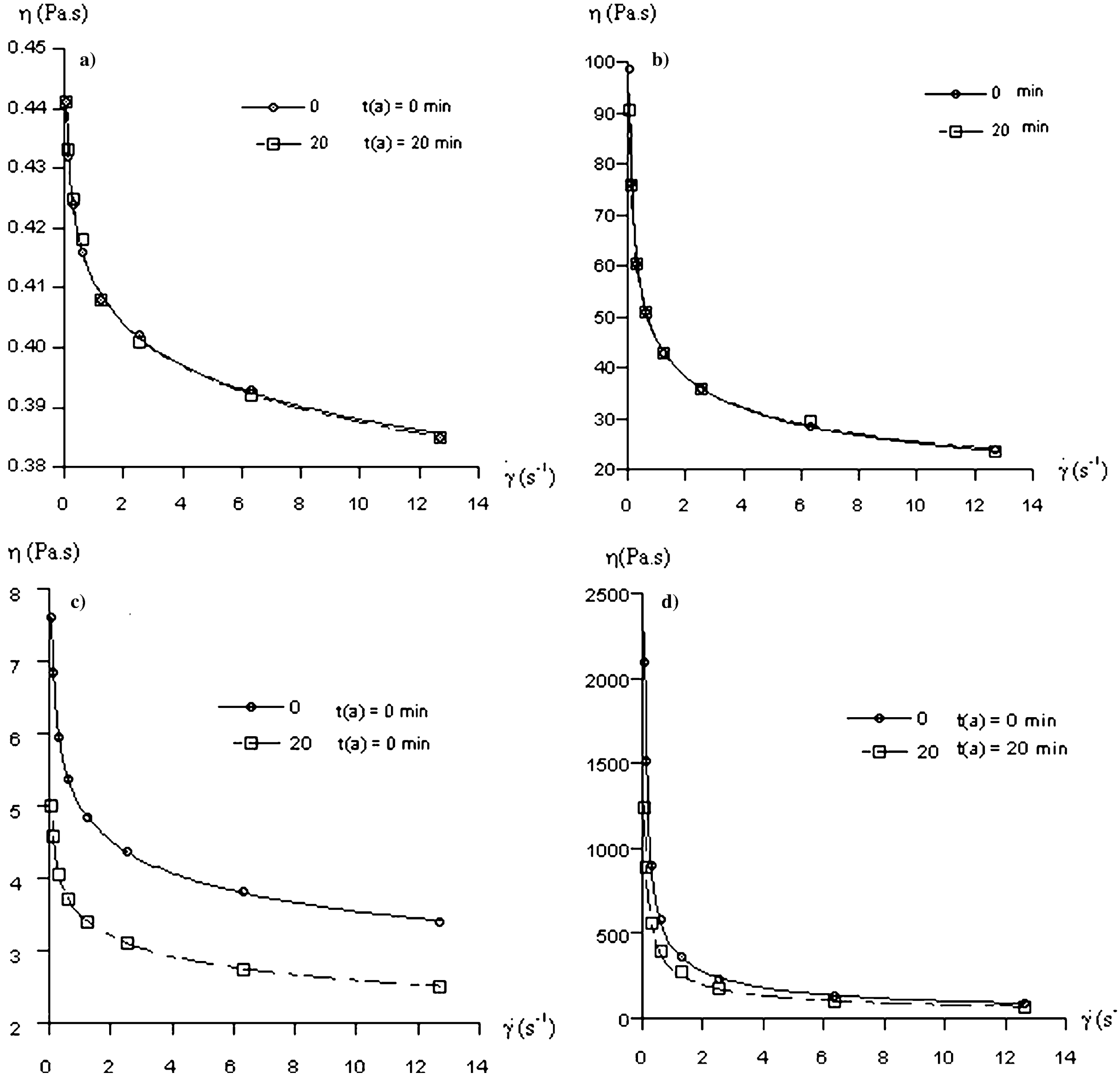

Fig. 1 Viscosity values as a function of shear rates (*up curve* –O– $t_a = 0$ min; *down curve* –□– for $t_a = 20$ min), for both viscosity grades of methylcellulose: M-0262 [2% (**a**), 5% (**b**)] and M-0512 [2% (**c**), 5% (**d**)]

of the rheograms obtained for each of the concentrations used in the study were practically superimposed. As an example, Fig. 1a, b includes the corresponding down curves (for 2–5% w/w dispersions, respectively) following the maximum agitation time (20 min)—clearly demonstrating the absence of thixotropy. We therefore can conclude that under the conditions of the experiments, this type of polymer shows no thixotropic behavior.

For high viscosity grade MC (M-0512), the down curves were displaced with respect to the up curve, i.e., the rheograms exhibited a hysteresis loop, thus indicating the thixotropic behavior of this grade of MC polymer. As an example, Fig. 1c, d presents the up ($t_a = 0$) and down curves obtained following the maximum agitation time ($t_a = 20$ min), for the dispersions prepared at polymer concentrations of 2–5% (w/w), respectively. This seems to indicate that the length of the methylcellulose molecules (molecular weight) is responsible for MC thixotropic behavior, attributable to secondary bond interactions between the molecules.

In order to analyze the thixotropic behavior of this grade of MC (M-0512), the consistency of hydrogels prepared at concentrations from 2–5% (w/w) was analyzed as a function of the agitation times (Fig. 2). It should be pointed out that in all cases the consistencies obtained remained practically constant after 5 min of agitation. All could be described according to a function of the form:

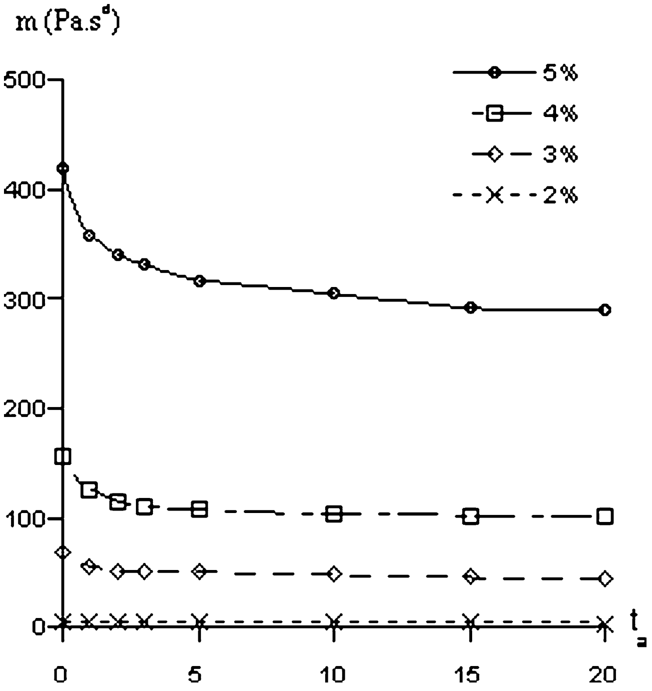

Fig. 2 Variation of consistency (m) as a function of agitation time (t_a) for dispersions of high viscosity grade MC (M-0512)

$$m_t = m_{\min} + (m_{\max} - m_{\min})e^{K\sqrt{t}}, \tag{4}$$

were m_{max} is the consistency value of the gel without previous agitation, and thus corresponding to the up curve; and m_{min} is the corresponding value obtained at the maximum agitation time, t, expressed in minutes. The difference [m_{max}–m_{min}] represents the maximum decrease in consistency m induced by agitation (Δm), which could be taken to be representative of the absolute thixotropy value of the system. Finally, parameter K characterizes the rate of variation of consistency, m, with agitation time. The correlation coefficients obtained for the fits were in all cases >0.99. The values of m_{max}, m_{min}, (Δm) and K are included in Table 3. As can be seen, the absolute thixotropy value (Δm) increases as the concentration and respective consistency values (m_{max}, m_{min}) of the dispersions increase. The influence of K upon the values of $m(t)$ is clearly conditioned by (Δm), which in turn depends on polymer concentration. The relationship between the absolute thixotropy values (Δm) and concentration from 1–5% (w/w) yields the following equation: $\Delta m = 1.429[e^{0.92c}-1]$, with a good correlation coefficient ($r > 0.998$).

In order to compare the utility of the method proposed, we determined the thixotropic areas, S_T, as a function of the corresponding agitation times [6]. The absolute thixotropy values, $S_T (= S_{max} - S_{min})$ calculated from the up and down curves after $t_a = 20$ min. are also included in Table 3. As could be expected, the S_T values also increase as the gel concentration increases. The relationship between the thixotropy values obtained by the two methods, S_T and Δm, is linear ($\Delta m = 0.058\ S_T$) with a good correlation coefficient ($r = 0.993$). This allowed us to conclude that is possible to analyze the thixotropy of a system by means of the consistency values obtained from the up and down curve rheograms.

On the other hand, knowledge of the absolute thixotropic value (Δm, or enclosed areas within the hysteresis loop) does not suffice to comparatively investigate systems with highly different viscosities. In fact, thixotropic systems with very high viscosities may exhibit down curves that differ relatively little from the corresponding up curves. In the same way, in less viscous systems, the differences in m (m_{max}, m_{min}) values (or the enclosed areas) can be very small. For this reason, and with the aim of comparatively studying the thixotropy of M-0512 gels obtained at different concentrations (2–5%, w/w), we calculated a new parameter that relates absolute thixotropy (Δm) to maximum consistency, determined by the up curves, corresponding to the different gels ($\Delta m/m_{max}$). This parameter could be taken as a relative value of thixotropy for each system. The corresponding values are also presented in Table 3. As can be seen, the relative thixotropy values show a tendency to increase as the concentration increases, until an asymptotic value is reached (Fig. 3). This tendency is expressed according to the following equation:

$$\frac{\Delta m}{m_{\max}} = 0.350 \cdot \left[1 - e^{-1.95\,c}\right] (r > 0.998) \tag{5}$$

This seems to indicate that the degree of breakdown and perhaps the degree of structuring by secondary bonds between molecules is a constant value for the polymer, corresponding to the asymptotic value (0.35), and is reached at a polymer concentration of approximately 3% (w/w).

In conclusion, there are important differences in the rheological behavior of aqueous dispersions of methyl-

Table 3 Values m_{min}, m_{max}, Δm, $\Delta m/m_{max}$ and K obtained from Eq. 3, and the absolute thixotropy values (S_T) for M-0512

C (%, w/w)	m_{min}(Pa s^n)	m_{max}(Pa s^n)	K (min$^{-1/2}$)	$\Delta m = m_{max} - m_{min}$(Pa s^n)	$\Delta m/m_{max}$	$S_T = S_{max} - S_{min}$(Pa s^{-1})
2	3.51	5.01	0.885	1.5	0.299	81.07
3	43.99	67.13	0.698	23.14	0.344	366.47
4	99.77	156.41	0.922	56.64	0.362	1,166.92
5	278.56	419.54	0.564	140.98	0.336	2,336.06

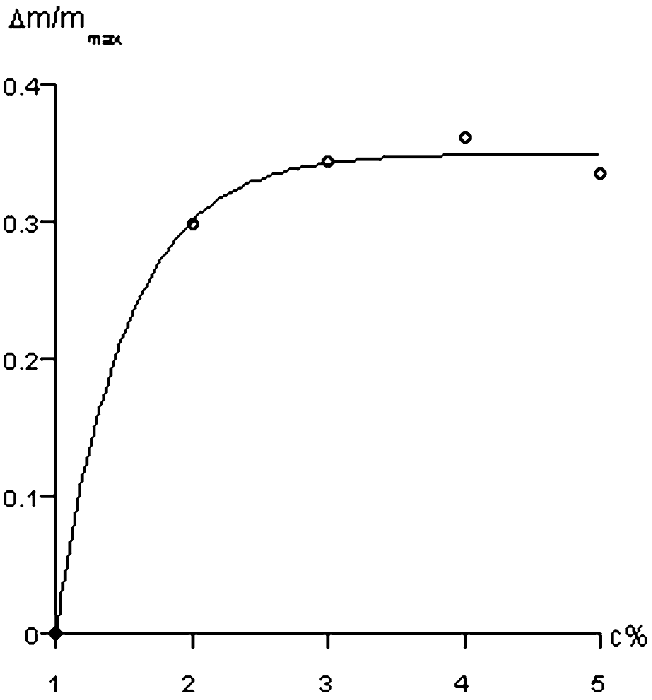

Fig. 3 Relationship of relative thixotropy ($\Delta m/m_{\max}$) as a function of concentration for dispersions of high viscosity grade MC (M-0512)

cellulose (in particular thixotropy), that are related to polymer molecular weight and concentration in the aqueous medium. When the polymer concentration in the medium is low (<1%w/w), the molecules behave as individual entities capable of Brownian motion, and the system exhibits Newtonian flow characteristics independently of the molecular weight of the polymer. When the molecular weight of the latter is high (M-0512) at a given concentration (>1%, w/w), the molecules are capable of interacting by secondary bonds to produce a loose three-dimensional structure, as a result of which the material is gel-like when unsheared. Shear stress disrupts these bonds, the flowing elements become aligned, and viscosity falls. When shear stress is removed, the structure recovers—though not immediately—(thixotropic behavior). In contrast, when the molecules are not sufficiently long (M-0262), at the same range of concentration the molecules are entangled—with the association of immobilized solvent—but no secondary bonds are implied in their association. Shear stress disentangles the molecules and releases the entrapped water. However, at any particular shear rate, an equilibrium is established between the shearing force and re-entanglement via Brownian motion (no thixotropy) [4].

References

1. Warburton B (1996) Encyclopedia of pharmaceutical technology, vol 13. M Dekker, New York
2. Alvarez-Lorenzo C, Gómez-Amoza JL, Martínez-Pacheco R, Souto C, Concheiro A (1999) Int J Pharm 180:91
3. Meyvis T, De Smedt S, Stubbe B, Hennink W, Demeester J (2001) Pharm Res 18:1593
4. Marriot C (1988) Pharmaceutics. Aulton ME (ed) Churchill Livingstone, New York
5. Dolz M, Gonzalez F, Belda R, Herráez JV (1988) J Pharm Sci 80:75
6. Dolz-Planas M, Roldan-García C, Herráez-Domínguez JV, Belda-Maximino M (1991) J Pharm Sci 77:799
7. Raznjevic K (1976) Handbook of thermodynamic tables and charts. McGraw Hill, New York.
8. Herráez JV, Dolz M, Sobrino P, Belda R, González F (1993) Pharmazie 48:359
9. Chu JS, Chadrasekharan R, Amidon GL, Weiner ND, Goldberg AH (1991) Pharm Res 9:1408
10. Hernandez MJ, Pellicer J, Delegido J, Dolz M (1998) J Disper Sci Technol 19:31
11. Sanz-Taberner T, Martin-Villodre A, Pla-Delfina JM, Herráez JV (2002) Int J Pharm 233:43