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Review

Methylcellulose, a Cellulose Derivative with Original Physical Properties and Extended Applications

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Abstract: This review covers the preparation, characterization, properties, and applications of methylcelluloses (MC). In particular, the influence of different chemical modifications of cellulose (under both heterogeneous and homogeneous conditions) is discussed in relation to the physical properties (solubility, gelation) of the methylcelluloses. The molecular weight (MW) obtained from the viscosity is presented together with the nuclear magnetic resonance (NMR) analysis required for the determination of the degree of methylation. The influence of the molecular weight on the main physical properties of methylcellulose in aqueous solution is analyzed. The interfacial properties are examined together with thermogelation. The surface tension and adsorption at interfaces are described: surface tension in aqueous solution is independent of molecular weight but the adsorption at the solid interface depends on the MW, the higher the MW the thicker the polymeric layer adsorbed. The two-step mechanism of gelation is confirmed and it is shown that the elastic moduli of high temperature gels are not dependent on the molecular weight but only on polymer concentration. Finally, the main applications of MC are listed showing the broad range of applications of these water soluble cellulose derivatives.

Keywords: methylcellulose (MC); cellulose derivative; synthesis; characterization; rheological properties; thermogelation; applications

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1. Introduction

Chemically modified polymers have been extensively investigated in order to develop new biomaterials with innovating physic–chemical properties. Important classes of modified polymers are cellulose ethers, such as methylcellulose (MC), hydroxypropylmethylcellulose (HPMC), hydroxyethylcellulose (HEC) and carboxymethylcellulose (CMC). Cellulose is the most abundant polysaccharide found in nature; it is a regular and linear polymer composed of (1→4) linked β-D-glucopyranosyl units. This particular β-(1→4) configuration together with intramolecular hydrogen bonds gives a rigid structure. Aggregates or crystalline forms are a result of inter-molecular hydrogen bonds occurring between hydroxyl groups. The water insolubility of cellulose is assigned to this association between the single molecules, leading to the formation of highly ordered crystalline regions [1]. This morphology, with the consequent low accessibility to reactants, is related to the origin of cellulose and controls its reactivity. Then, derivatives prepared under heterogeneous conditions have often an irregular distribution of substituents along the cellulosic backbone.

Methylcellulose (MC) is one of the most important commercial cellulose ethers and it has been used in many industrial applications [2,3]. MC is the simplest cellulose derivative, where methyl groups ($-CH_3$) substitute the hydroxyls at C-2, C-3 and/or C-6 positions of anhydro-D-glucose units (Figure 1).

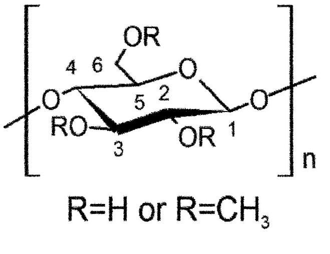

Figure 1. Repeating unit of methylcellulose: –OH or $-OCH_3$ at positions 2, 3 and 6 of the anhydro-D-glucose.

This cellulose derivative has amphiphilic properties and original physico–chemical properties. MC becomes water soluble or organo-soluble when the degree of substitution (DS) varies from 0 to 3. It shows a singular thermal behavior in which aqueous solution viscosity is constant or slightly decreasing when temperature increases below a critical temperature point (29 ± 2 °C). If temperature continues to increase, viscosity strongly increases resulting in the formation of a thermoreversible gel [4]. These characteristics classify MC as a lower critical solution temperature polymer (LCST).

The formation of the thermoreversible MC gels is a two-stage process as studied earlier and it is accompanied by an increase in turbidity of the solution and macroscopic phase separation at high temperatures (>60 °C) [5,6]. Although the gelation of MC has been studied extensively by various techniques, a variety of different gelation mechanisms has been proposed [4,7–15]. During the gelation process, the first step denominated "clear loose gel" (or pre-gel) is mainly driven by hydrophobic interaction between highly methylated glucose zones, and the second step, is a phase separation occurring at temperatures >60 °C with formation of a "turbid strong gel". Additionally, MC gelation is influenced by the substitution pattern [11] and co-ingredients like salts, sugars, and alcohols [16,17]. The influence of the molecular weight (MW) is still under discussion [6,7,18–20] as well as the structure of the strong turbid gel [15,21–23].

This review covers particularly the influence of the MW of methylcelluloses on their most original physical properties using MC with the same degree of substitution as described in our recent works [20,24].

2. Experimental Section

Commercial premium methylcelluloses given by Dow Chemical Company (Crossways Dartford, Kent, UK) were used as received: A15LV, A4C, A15C, and A4M. The samples were obtained under heterogeneous conditions, *i.e.*, resulting in irregular distribution of methyl groups along the chains. They were dissolved as follows: dispersion of the powder in hot water (around 80 °C) under vigorous stirring with a magnetic bar; then, after 15 min, the solution was stored at around 4 °C for 24 h followed by stirring and used at the desired temperature.

The molecular weight was calculated from the intrinsic viscosity values of the methylcellulose solution filtered on a 0.2 µm pore membrane at low concentration. A capillary viscometer Micro-Ubbelohde (SCHOTT Instruments GmbH, Mainz, Germany) with a diameter of 0.66 mm linked with a semi-automatic chronometer ViscoClock (SCHOTT Instruments GmbH) and a thermo-bath at 20 °C were used.

The degree of substitution was determined by ^{1}H and ^{13}C nuclear magnetic resonance (NMR) in DMSO-d_6 at 80 °C for sample concentration around 10 and 30 g/L respectively on a Bruker, Avance III 400 MHz spectrometer (Wissembourg, France). Analysis of the spectra was performed after identification of the different signals according to the literature [25–28].

Pictures of the MC solutions in water at 10 g/L at different temperatures were taken with a mobile device Samsung GT-I9195, ISO 125 (Seoul, South Korea) with exposure time 1/33 s and aperture f/2.6.

Rheological analysis was performed with an ARG2 rheometer from TA Instruments (New Castle, DE, USA) with a cone-plate geometry; the cone has a diameter of 60 mm, 1°59'13" angle and 54 µm gap. The temperature was controlled by a Peltier plate. The sample was left for 5 min before each experiment to attain thermal equilibrium. In order to prevent evaporation during the measurements, the system was isolated using a special cover including a small cup filled with silicon oil. An applied thermal program used for heating the sample imposed a 0.5 °C/min rate from 15 to 75 °C. Afterwards, the sample was stabilized for 3 min and cooled down from 75 to 15 °C at 0.5 °C/min. Flow and dynamic experiments were performed to cover different temperatures, shear rates, and frequencies respectively. All dynamic measurements were obtained in the linear domain along the temperature range from 15 to 75 °C with increasing and decreasing temperature ramps. Then, tests were carried out at a constant frequency of 0.5 Hz and constant strain of 1%.

3. MC Synthesis and Characterization

3.1. Industrial Preparation/Homogeneous Synthesis

Methylcellulose is usually synthesized by etherification of cellulose (reaction between cellulose, alkali and chloromethane or iodomethane). The hydrophilic character of the hydroxyl groups provides its solubility in aqueous systems and the methyl substituents prevent chain–chain packing forming in the cellulose crystalline phase. It is known that the solubility of MC depends on the degree of substitution (DS) and the distribution of methoxyl groups [12,29,30]. The rheological properties depend on the average degree of polymerization or molecular weight (DP or MW) but also on DS. These characteristics are imposed by the MC synthesis conditions [31–34].

Both methylcelluloses with a homogeneous and a heterogeneous blockwise distribution of substituents are known [12,29,35,36]. Commercial MC is usually synthesized through a heterogeneous route in a two-phase system. More specifically, since cellulose is insoluble in water and in most common organic solvents, an alkaline medium (NaOH) is used to swell cellulosic fibers and obtain the alkali-cellulose. This alkali-cellulose reacts with an etherifying agent such as iodomethane, chloromethane, or dimethyl sulfate. Then, purification and removal of by-products is applied by washing in hot water, followed by drying and pulverization of the prepared MC. Sometimes acetone, toluene, or isopropanol are also added, after the etherifying agent, in order to reach different substitution degrees [37–39]. Therefore, the heterogeneous route from cellulose semi-crystalline solid state produces a heterogeneous polymer, composed of hydrophobic highly substituted regions corresponding to the swollen amorphous zones in cellulose and more hydrophilic regions with lower average DS. In order to produce a MC with a homogeneous chemical structure [29], cellulose is solubilized in quaternary ammonium hydroxides (TMAH) [40] or in a mixture of dimethylacetamide and lithium chloride (DMA–LiCl) [12,29,41] or NaOH/urea [42] before the etherification step. This homogeneous process leads to better accessibility of free hydroxyls and a more regular distribution of methyl substituents along the chains which favors water solubility.

In order to synthesize di- or mono-*O*-methylcellulose regioselective protecting groups have to be used to get a uniform pattern of methylation. A variety of bulky groups are described in the literature depending on the carbon which has not to be methylated [35,43–45]. Regioselectively functionalized cellulose ethers were prepared under homogeneous and heterogeneous reaction conditions [46–48]. Furthermore, di-*O*-methylcelluloses did not show thermogelation in aqueous media, well known for methylcelluloses containing tri-*O*-methyl unit blocks [12,43–45].

The influence of the distribution of methyl groups along the chains has already been analyzed [12]. DS is the main structural factor that determines MC solubility: as usually accepted, MCs with DS between 1.3 and 2.5 are soluble in water, while those with DS > 2.5 are soluble in organic solvents [17]. It was demonstrated that for homogeneous substitution, water solubility occurs for DS ~ 0.9 whereas for heterogeneous samples (such as the commercial MC) solubility in water occurs over DS ~ 1.3 [12]. In addition to the control of solubility, DS is important when the amphiphilic properties are related to the interfacial properties [49,50]. Furthermore, it was deduced on the basis of comparison between heterogeneous and homogeneous samples having the same average DS, that thermogelation is directly related to the existence of highly substituted zones in the heterogeneous samples [12].

3.2. Characterization of MC

The most valuable techniques used for characterization of methylcellulose in terms of the degree of substitution and the molecular weight will be mentioned as well as difficulties related to their specific properties.

3.2.1. Substitution Pattern

DS determination can be carried out by ^{13}C-NMR analysis, to obtain not only the global DS but also the degree of substitution of each carbon (C-2, C-3, and C-6). The identification of different signals is performed as described previously [25–28]. Figure 2 shows the ^{13}C-NMR spectrum of a MC with an average DS (DS = 1.8). In the ^{13}C spectrum region between 59.5 and 58 ppm, three signals correspond to the methyl substituents at C-2, C-3 and C-6 positions, from low to high field respectively. The ratio between the integral of each methoxyl signal and that of anomeric signals at 103.8 (C-1) and 103.2 (C-1s) ppm (attributed to 4-linked β-D-glucopyranosyl units unsubstituted on C-2 and substituted on C-2 by methoxyl group, respectively) allows the determination of DS_2, DS_3 and DS_6 values and consequently the average DS.

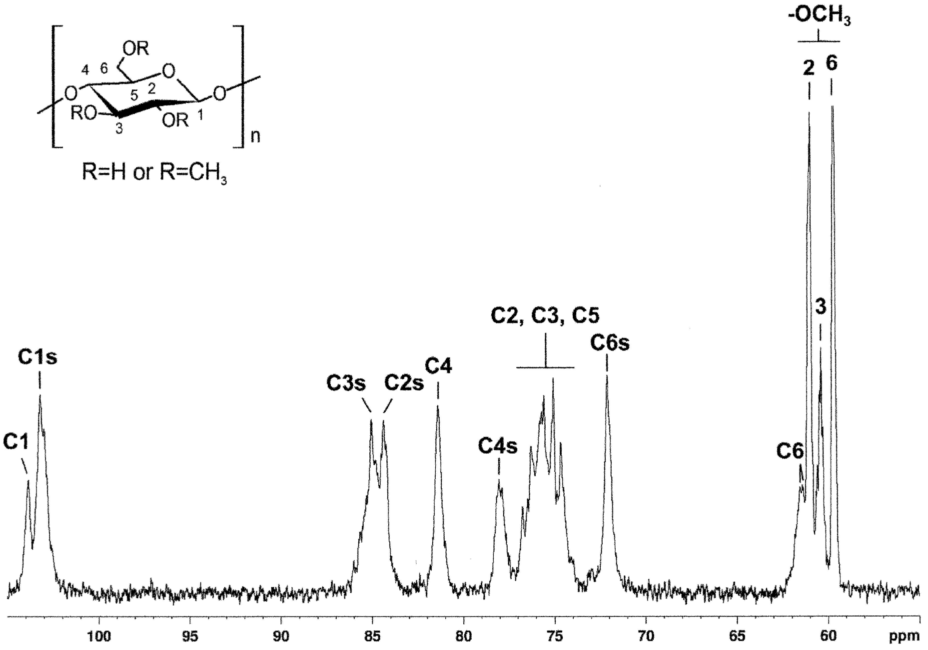

Figure 2. ^{13}C-NMR spectrum of methylcellulose A4C (30 g/L in DMSO-d_6 at 80 °C). C*x* and C*x*s correspond to the signals of carbon *x* unsubstituted and substituted, respectively. Reproduced with permission from Taylor & Francis Group, 2015 [20].

^{1}H-NMR spectroscopy may also be used to characterize methylcellulose. A ^{1}H-NMR spectrum of MC is shown in Figure 3 with the attribution of the main resonances [27,28]. The spectrum shows intense signals at 3.48–3.47 ppm corresponding to the overlapping of methyl protons at C-2 and C-3, and at 3.31 ppm attributed to methyl protons at C-6.

Using H-1 integral as reference and the proton integrals for 2-Me + 3-Me and 6-Me, it is possible to determine DS on C-2 + C-3 and C-6 positions for methylcellulose. Due to the overlapping, the DS obtained by ^{1}H-NMR gives some differences when compared with the DS obtained by ^{13}C-NMR (Tables 1 and 2).

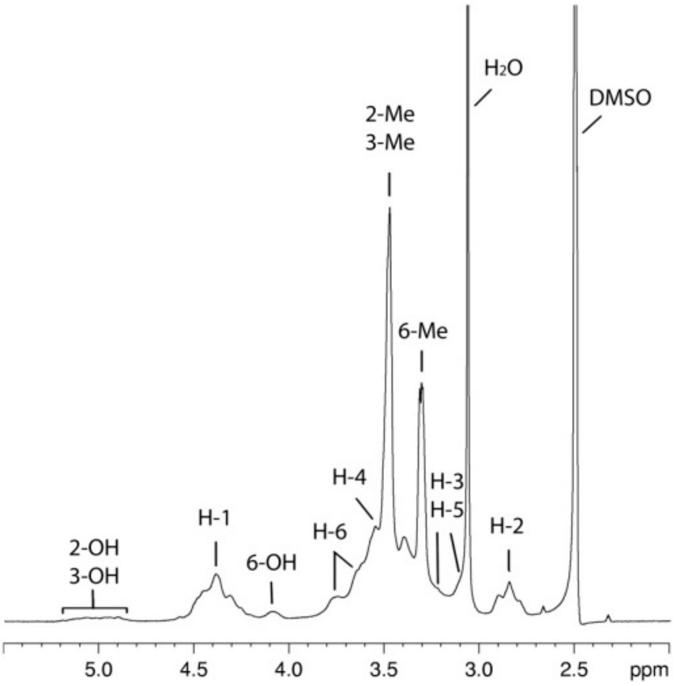

Figure 3. ^{1}H NMR spectrum of methylcellulose A15C (9 g/L in DMSO-d$_6$ at 80 °C).

Table 1. Degrees of substitution in C-2 + C-3 (DS$_{2+3}$) and in C-6 (DS$_6$) of commercial methycellulose (MC) dissolved in DMSO-d$_6$ at 80 °C.

DS	A15LV	A4C	A15C	A4M
DS$_{2+3}$	0.82	0.82	0.84	0.90
DS6	0.47	0.47	0.51	0.56

Table 2. Commercial methylcellulose characteristics. Reproduced with permission from Taylor & Francis Group, 2015 [20].

Samples	[η] [a] (mL·g^{-1})	*C** (g·L^{-1})	M_V [b] (g·mol^{-1})	DS [c]	DS$_2$	DS$_3$	DS$_6$
A15LV	193	5.18	42,100	1.8	0.8	0.4	0.6
A4C	573	1.75	212,000	1.7	0.7	0.5	0.5
A15C	740	1.35	304,600	1.8	0.7	0.5	0.6
A4M	933	1.07	423,400	1.7	0.7	0.5	0.5

[a] Intrinsic viscosity measured at 20 °C in water; [b] Viscometric-average molecular weight from relation 1; [c] Average degree of substitution; *C** is estimated as the inverse of [η].

The physicochemical characteristics of four methylcelluloses studied in our previous work are described (Table 2). It is noteworthy that the ^{13}C-NMR spectra of these commercial samples were similar, indicating that the distribution of methyl groups was nearly the same. Therefore, the four MC samples were used as models to study the role of MW on the physical properties of methylcelluloses.

The same samples have been fully hydrolyzed in acidic conditions and the composition of partially methylated monomeric units was established using liquid and gas chromatography [12,17,34].

The obtained results are given in Table 3. These data allowed the determination of the average degree of substitution (DS) which showed good agreement with the average DS calculated from ^{13}C NMR results. In previous work when establishing the substitution pattern of one commercial MC sample (DS ~ 1.9), the analysis by high performance liquid chromatography (HPLC) after complete hydrolysis revealed the following composition: 5.6% of unsubstituted, 25.4% of mono-substituted, 41.8% of di-substituted, and 27.3% of tri-substituted anhydro-D-glucose units [51]. These results are in good agreement with those given in Table 3.

Table 3. Degree of substitution (DS) and monomeric composition of commercial methylcelluloses expressed in number percents [17].

Data	A15LV	A4C	A15C	A4M
DS [a]	1.74	1.73	1.71	1.73
% NoS [b]	12	10	10	11
% MonoS [c]	26	29	27	27
% DiS [d]	38	39	39	40
% TriS [e]	24	22	24	22

[a] Average degree of substitution from additivity; [b–e] percentage of non-substituted, mono-substituted, di-substituted and tri-substituted units, respectively.

3.2.2. Macromolecular Characterization

It was found by small angle X-ray scattering (SAXS) that MC (M_W = 160,000 at 1 g/L concentration and 25 °C) behaves as a wormlike chain with a persistence length L_p = 5.8 nm in dilute solution [52]. Chatterjee *et al.* found by SANS (small angle neutron scattering) that L_p may be equal to even 13.6 nm [53]. It was also proven that chains associate into thin stiff fibrils when concentration increases (to 10 g/L) at 25 °C [52]. However, the same authors observed a significant increase of light scattering intensity only at 42 °C, which is tantamount with formation of aggregates [52]. In addition, it was shown, also from a light scattering study, that the apparent molecular weight increases from 20 to 50 °C at 5 g/L; this is interpreted as consistent with the progressive growth of clusters being formed (due to an increase of apparent molecular weight up to the gel point) [54]. It was concluded from rheology that methylcellulose solution (at 10 g/L, 20 °C), at equilibrium, forms a supermolecular structure maintained by weak reversible association caused by hydrophobic interactions. Interestingly, it was confirmed by dynamic light scattering (DLS): one relaxation mode appears at 20 °C in dilute regime which varies slightly near 55 °C due to aggregation at the phase separation but no gel is formed. A slower relaxation mode attributed to clusters appears in the semi dilute regime at 20 °C and these two modes persist up to 45 °C. When temperature continues to increase, the slow mode dominates the scattering intensity and moves to much lower frequencies until a strong gel is formed. This work is one of the very few clearly introducing the two step mechanism for gelation in semi dilute regime [54].

To conclude, macromolecular characteristics of single chains must be studied in dilute regime at temperatures lower than 25 °C when feasible. The molecular weight is usually calculated from the intrinsic viscosity determined on aqueous MC solutions at low polymer concentration ($C < C^*$). Then, the M_v is determined as a viscometric-average molecular weight using the relation given by Funami *et al.* [9] for MC in water at 20 °C:

$$[\eta] = 0.102 \cdot M_W^{0.704} \quad (1)$$

However other relationships were proposed by Uda and Meyerhoff to determine M_v [55] for aqueous MC solutions at 20 °C:

$$[\eta] = 0.28 \cdot M^{0.63} \quad (2)$$

and also by Keary [56] using steric exclusion chromatography (SEC) at 45 °C with multidetection equipped with a multiangle laser light scattering detector:

$$[\eta] = 3.2 \cdot 10^{-2} \cdot M_v^{0.80} \quad (3)$$

The use of pullulans as standards for molar mass determination of methylcelluloses was proposed by Sarkar and Cutié [57]. This technique is not valid as discussed by Poché *et al.* [58] who applied universal calibration to take into account the difference in the stiffness for the two series of polysaccharides. In addition, it is difficult to perform SEC analysis under valid conditions due to the ability of MC to form aggregates even at ambient temperature.

4. Physical Properties in Aqueous Solution

4.1. Solubility in Relation to Temperature

Preparing a solution of methylcellulose (an amphiphilic polymer) in cold water is delicate because when the powder comes into contact with water, a gel layer is formed. This decreases the diffusion of water into the powder and results in formation of macro-gelled particles with a very low dissolution rate. Therefore, it has been proposed to first disperse methylcellulose powder in hot water (around 75 °C) and then cool down to around 5 °C under continuous stirring. This method provides faster dissolution of the particles resulting in a homogeneous solution.

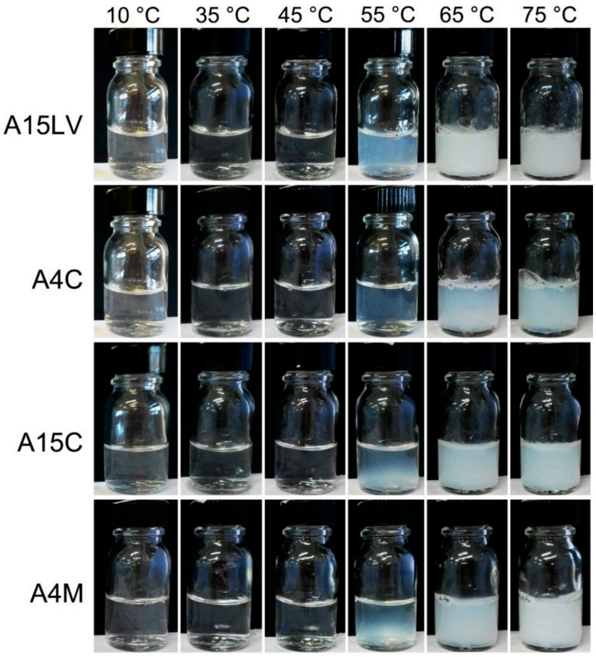

Figure 4. Influence of temperature and MW for 10 g/L aqueous solutions observed between 10 and 75 °C.

In previous work, methylcellulose was characterized by its phase diagram and by a lower critical solution temperature (LCST) at 29 ± 2 °C [4]. At temperatures below the LCST, it was easily soluble in water (higher solubility around 5 °C) whereas above the LCST, aggregates were formed with a clear phase separation around 55 °C (turbid system). This behavior is shown in Figure 4: the systems are transparent up to 45 °C and then become turbid due to phase separation independently of the MW in the covered range. It is interesting to compare this observation with rheological data and discuss in detail the mechanism of gelation as a function of temperature.

The temperature at which the phase separation occurs depends significantly on the DS-value. The higher the DS-values, the lower the solubility and additionally lower precipitation temperatures are observed due to a lower fraction of polar hydroxyl groups [53].

4.2. Rheological Behavior Up to Gelation

In dilute solution and at low temperatures (5 °C), the methylcellulose solutions exhibit Newtonian flow as shown in Figure 5. It is important to mention that the results given by flow experiments are superimposed with those provided by Cox–Merz transformation of dynamic experiments [59]. It enables the conclusion that the solutions are homogeneous [20]. At 20 °C, the steady state viscosity depends slightly on the shear rate. However, the viscosity is lower compared with the values obtained at 5 °C due to a decrease of the solubility parameter [4].

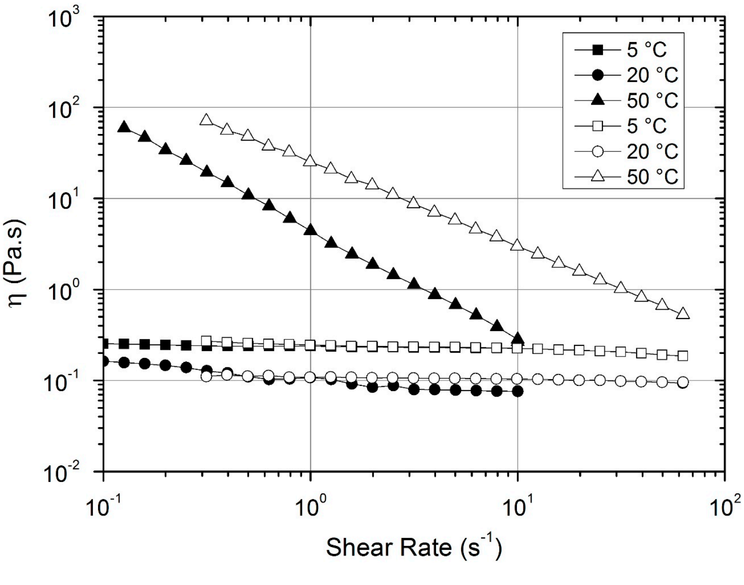

Figure 5. Viscosity as a function of the shear rate for methylcellulose A15C at 10 g/L. Open symbols are given for Cox–Merz transformation of dynamic measurements, filled symbols are for flow measurements. The lines are added to guide the eye.

When the temperature increases, over and around 30 °C, non-Newtonian behavior occurs corresponding to chain–chain interaction due to the hydrophobic character of methylcellulose even at a concentration lower than *C**. This behavior is in good agreement with the hypothesis of Kobayashi *et al.* [54] describing the pre-gel state by DLS. Rheological data show clearly a stronger dependence of viscosity with shear rate at 50 °C than at 20 °C. It can be seen from Figure 5 that the two series of measurements (flow and dynamic rheology) are separated and flow gives a much lower viscosity compared to the less disturbing dynamic experiments. In this case, Cox–Merz cannot be applied due to stronger perturbation of the loose network in the flow experiments.

The dependence of viscosity as a function of temperature was given at well-defined shear rates as shown in Figure 6 [24]. The behavior is Newtonian at temperatures lower than 30 °C (a critical temperature) and then becomes non-Newtonian when the shear rate increases. The critical temperature depends slightly on the MW of MC (Table 4).

Table 4. Critical temperature (T_c) of commercial methylcellulose in aqueous solution for the appearance of non-Newtonian behavior.

Critical Temperature	A15LV	A4C	A15C	A4M
T_c (°C)	40	40	35	30

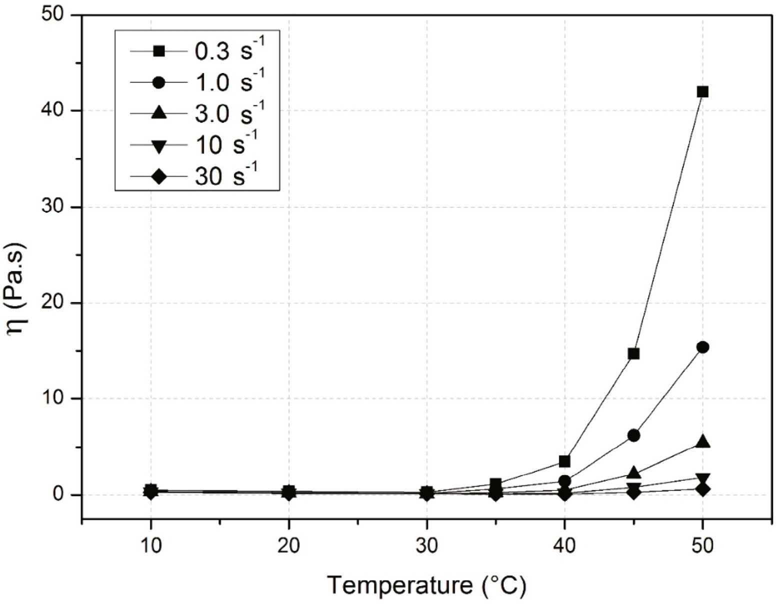

Figure 6. Influence of temperature on the viscosity of methylcellulose solution at different shear rates. Viscosities of a 10 g/L solution of A4M obtained using Cox–Merz transformation of dynamic measurements in the linear viscoelastic region. The lines are added to guide the eye [24].

The data given in Figure 6 indicate the formation of loose chain interaction over 30 °C which corresponds to the starting point of aggregation (pre-gel or loose gel domain). The higher the shear rate, the more the flow disturbs the loose reversible associations. These data support the shear-thinning behavior of the system while approaching the gel state. This association of amphiphilic molecules was also demonstrated by light scattering [54].

In dynamic rheology, at 20 °C, the MC solution behaves as a viscoelastic fluid with the storage modulus *G*' lower than the loss modulus *G*'' as shown in Figure 7. However, at 50 °C, the storage modulus *G*' becomes independent of the frequency and higher than *G*'', thus a gel is formed. These results are in agreement with the data from Knarr and Bayer [60]. All the experiments were taken in the linear viscoelastic region of the applied deformation in order to avoid a disruption of associations.

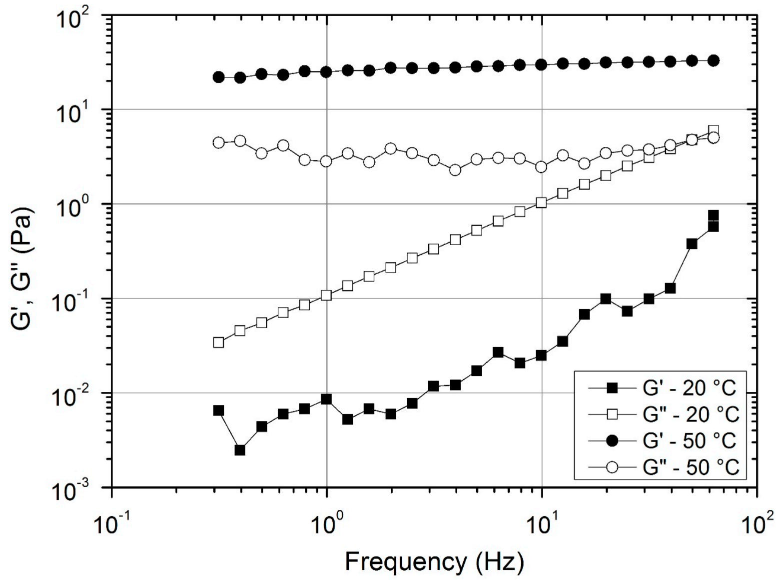

Figure 7. Dynamic behavior of methylcellulose A15C at 10 g/L in aqueous solution. *G*' filled symbols (at 20 °C, the values remain difficult to determine due to their magnitude around 10^{-2} Pa), *G*'' open symbols. The lines are added to guide the eye.

4.3. Influence of the Molecular Weight and Concentration on the Mechanism of Gelation

When the rheological behavior of methylcellulose is studied as a function of temperature, a large reversible hysteresis is observed between heating and cooling phases as often described in the literature [4,15,52,61–63]. An example is given in Figure 8 [20].

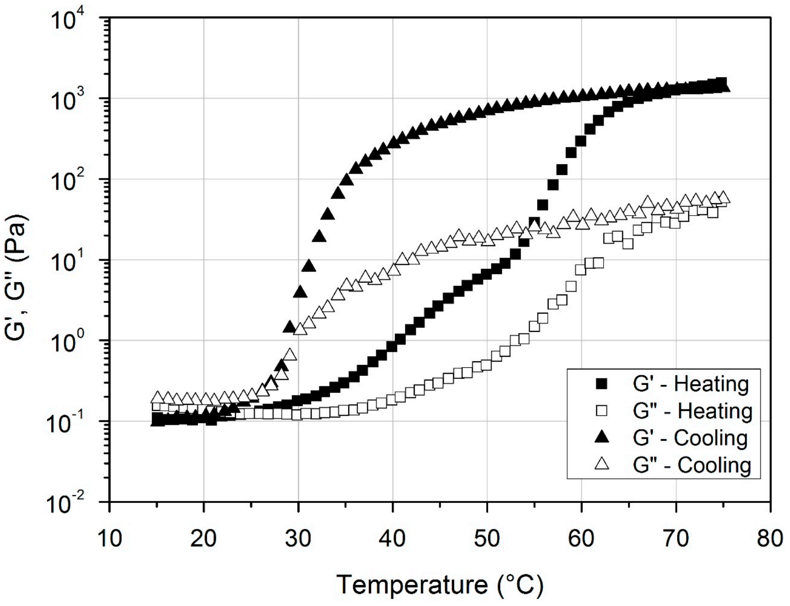

Figure 8. Temperature dependence of dynamic viscoelasticities for methylcellulose A4M at 10 g/L in aqueous solution. Constant frenquency of 0.5 Hz, strain of 1% and temperature rate of 0.5 °C/min. ■, □ heating; ▲, Δ cooling. *G*' full symbols and *G*'' open symbols. Reproduced with permission from Taylor & Francis Group, 2015 [20].

In order to analyze the MC viscoelastic sol–gel transition, dynamic oscillatory experiments were performed along a temperature cycle from 15 to 75 °C followed by decreasing to 15 °C at 0.5 °C/min for each methylcellulose sample dissolved in water at 10 g/L. An example of the viscoelastic evolution during the continuous temperature cycle is shown in Figure 8. The two-step gelation mechanism dependent on heating may be seen especially from *G*' variations. The same type of behavior observed during heating was described previously in many publications [15,20,54].

Solution with *G*'' > *G*' was observed at low temperature with rheological parameters depending on molecular weight; over around 30 °C, a gel-like behavior (*G*' > *G*'') was found up to around 50 °C corresponding to the first step of gelation. It is a clear loose gel or pre-gel domain where chain association progressively occurs [54]. A modification of the rate of increase of dynamic modulus at 0.01 rad/s for a methylcellulose at 49 g/L was determined at 42.5 °C by Li *et al.* [15]. At this point, the system starts to become turbid. This first gelation step may be interpreted as the association of the highly methylated zones (independently of concentration) in agreement with that described previously in the literature [10,15,54,64]. A scheme describing the evolution of the system with temperature was given by Li *et al.* [15] and is represented in Figure 9.

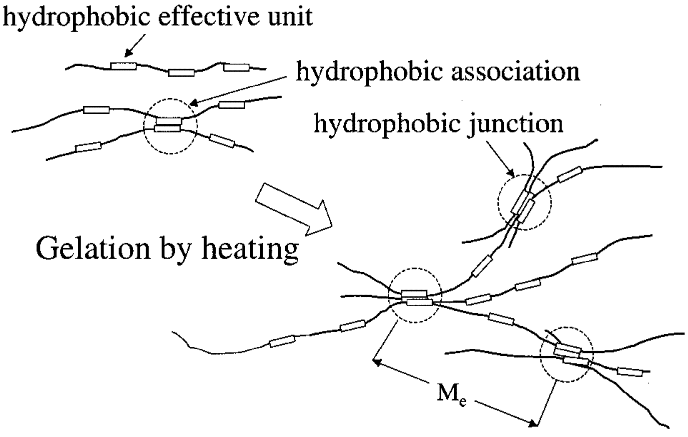

Figure 9. Schematic drawing showing gelation through the hydrophobic effective units of methylcellulose. At lower temperatures, the hydrophobic association is possible from the hydrophobic effective units. During heating, the gel is formed with the hydrophobic junctions consisting of such hydrophobic effective units and the mean length M_e between two junctions remains constant when the gelling temperatures are higher than 42.5 °C. Reproduced with permission from American Chemical Society, 2001 [15].

Between 55 and 75 °C, a large increase of *G*' is observed depending on the polymer concentration (when it is higher than *C**) and the turbid strong gel is formed corresponding to the second step of gelation, together with the phase separation [20]. This second step has been more widely studied in the literature [6,22,64]. The mechanism of phase separation observed over 50 °C, dependent on the chemical structure, polymer concentration and molecular weight, is still under discussion. A spinodal decomposition proposed by Fairclough *et al.* [62] increases concentration fluctuations during the phase separation trapped by gelation, the two processes occur almost simultaneously. On the contrary, Arvidson *et al.* [6] used rheological measurements and suggested that thermogelation of methylcellulose may proceed by a nucleation and growth mechanism.

In the case of the strong gels, the gel network structure may be formed on the basis of hydrophobically associating domains (the junctions) connected by a mean chain length of 27,500 g/mol as shown in Figure 9.

The elastic modulus *G*' was studied as a function of polymer concentration and molecular weight at 50 °C and 75 °C as shown in Figure 10. At 50 °C, corresponding to the end of first step of gelation, no clear dependency on molecular weight and concentration was noticed. It was shown that *G*' varies from 1 to 10 Pa for all tested systems [20].

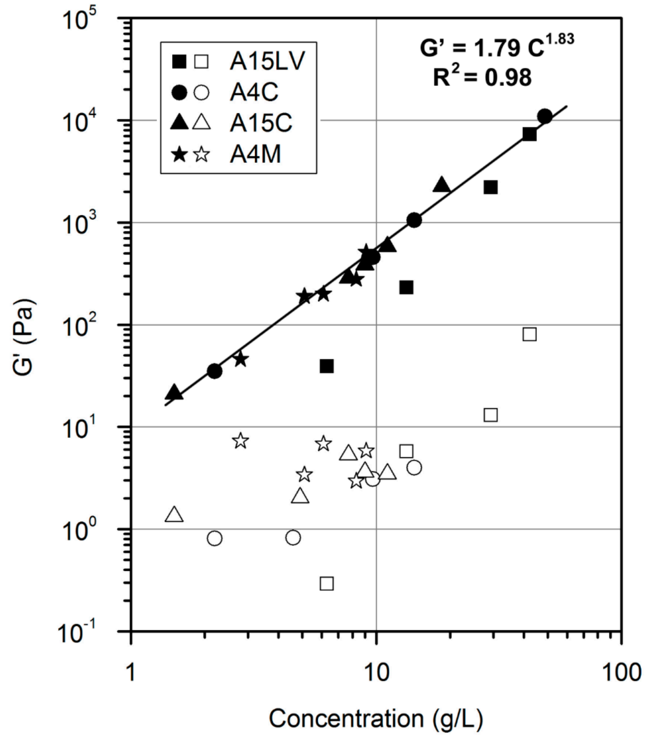

Figure 10. Storage moduli *G*' as a function of the polymer concentration at 50 °C (open symbols) and 75 °C (filled symbols) and 0.5 Hz for A15LV (M_v = 42,000), A4C (M_v = 212,000), A15C (M_v = 304,600) and A4M (M_v = 423,400) aqueous solutions. Reproduced with permission from Taylor & Francis Group, 2015 [20].

Aggregates are formed by finite and loose interchain interactions, which are too weak to stabilize a network. In addition, the probability of having multi-junctions per chain is low. At 75 °C, when the second step of gelation is stabilized, an interesting result was obtained. *G*' values are distributed on the same curve for all samples with different molecular weights, thus polymer concentration is the only one parameter which provides large variation of *G*' (10–10,000 Pa). Due to stronger interactions, the density of crosslink points is high and independent of the MW as soon as the distance between two of these cross-linkages is smaller compared with the chain length. It was found that the slope of the linear dependence is equal to $G' = 7.9 \times C^{1.83}$ (*C* expressed in g/L). This exponent is not far from the value of 2, usually obtained for many physical gels previously studied [65,66]. The sample A15LV, having the lowest MW, shows original behavior at the two temperatures compared with the other samples, based on the lower probability for network formation. This sample had a molecular weight in the same range as M_e given by Li *et al.* [15].

To conclude, the two characteristic domains may be described as follows:

- Firstly, at relatively low temperatures and low concentrations, a sol–gel domain corresponds to association of the most hydrophobic zones of few chains. The chain heterogeneity is caused by the highly methylated blocks.
- Secondly, at higher temperatures, a concomitant gel is formed corresponding to microphase separation in which polymer-rich microdomains prevent phase separation leading to a turbid gel. The mobility of the chains is reduced when the phase separation process is slow. This turbid gel is metastable and finally collapses with exclusion of solvent (syneresis process) especially at high temperature (>70 °C) and low concentration as also found on κ-carrageenan [4,10,13,67].

Finally, it is necessary to mention that methylcellulose solutions are stable at room temperature but that salts and additives may modify the gelling temperature [16,17]. The gelling temperature increases with the addition of organic polar solvents miscible with water such as alcohols and glycols, because these solvents enhance the aggregation between MC and water molecules through intermolecular hydrogen bonds [68].

4.4. Gel Structure and Hysteresis

The question of reversibility with temperature of gel formation and hydrophobic interactions was discussed by Chevillard and Axelos [4]. As pointed out previously, the chain associations involved in gelation occur slowly and usually a non-equilibrium state is studied. The existence of hysteresis is related to the formation of a stiff gel at high temperature (>70 °C) with fibril morphology proved by cryo-TEM (transmission electron microscopy), rheology and SANS [22,23]. This fibrillar network observed by cryo-TEM is heterogeneous and composed of hydrated fibrils with a diameter of 15 nm independently of the molecular weight. Bodvik *et al.* [52] observed, also by cryo-TEM, a dispersion of thread-like fibrils already at 45 °C on 1 g/L methylcellulose solution (chains ordered parallel to each other coming in close contact). The same observation was obtained at 60 °C for 0.2 g/L methylcellulose solution ($M_W = 530{,}000$) [21].

This structure, especially after syneresis, may contribute to decrease the gel dissolution rate when cooling and explain the importance of hysteresis. It also justifies the high elastic modulus at high temperature ($T > 70$ °C).

The fibrillar arrangement of chains may be the next step of association when compared with the Li *et al.* scheme given in Figure 9 [15]. The hydrophobic character is reinforced at higher temperature which increases the packing of the chains. In addition, structure rearrangement after phase separation due to the slow kinetic mentioned previously, may induce syneresis and the existence of hysteresis.

4.5. Interfacial Properties

Interfacial properties of amphiphilic polymers are interesting for many applications especially to stabilize foams and emulsion (food domain) or stabilize liposomes and solid dispersions [69–72]. Amphiphilic polymers reveal some advantages in comparison with small molecules of surfactants: the viscosity of the medium is higher, the thickness of the adsorbed layer at the interface is larger (as well as the van der Waals interactions) depending on the polymer structure. Among these polymers, non-ionic cellulose ethers (hydroxyethylcellulose (HEC), hydroxypropylcellulose (HPC), methylcellulose (MC), hydroxyethylmethylcellulose (HEMC), and hydroxypropylmethylcellulose (HPMC)) showed positive adsorption at the liquid/air and the other interfaces [49,73]. Mainly the role of methylcellulose and hydroxypropylmethylcellulose together with the influence of the molecular weight have been discussed in the literature [74–77]. They play a role not only due to their amphiphilic character (which depends on the microstructure such as the degree of substitution and the distribution of the substituents along the chains) but also by their water holding and viscosity enhancing properties [70,76,77]. It is important to mention that MC is often more surface active than proteins and dominates interfacial properties at higher concentration [74,76].

4.5.1. Surface Activity of Methylcelluloses

The surface activity of methylcellulose (MC) has been recently studied as well as the influence of the MC molecular weight on the air/water interface properties [24]. The experiments were performed with methylcellulose having a similar microstructure but different molecular weights allowing the influence of the molecular weight on the interfacial properties to be established.

Recent data obtained on methylcelluloses with different molecular weights are given in Figure 11 [24]. It demonstrates clearly that the MW has no influence on the surface activity of MC at equilibrium; the same conclusion was given on hydroxypropylmethylcelluloses by Gaonkar [75] but a slight impact was noticed for hydroxypropylmethylcelluloses by Sarkar [49]. The surface activity is mainly influenced by the chemical modification of cellulose and the distribution of hydrophobic groups along the polymeric chains [49].

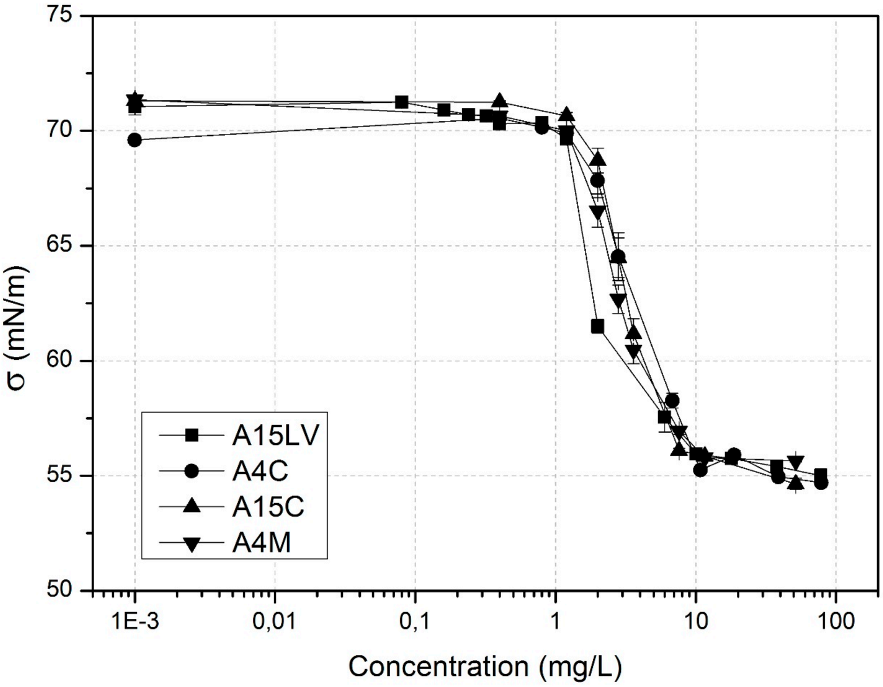

Figure 11. Influence of the molecular weight on the tension-active properties (σ in mN/m) of MC with different molecular weights as a function of polymer concentration at 20 °C. The lines are added to guide the eye [24].

Over 1 mg/L up to around 10 mg/L, the surface tension is decreased in relation to the progressive packing of amphiphilic molecules at the interface and to the orientation of highly hydrophobic blocks. In this concentration domain, a kinetic process was observed: for the higher molecular weight, stabilization of the surface tension takes more time than for lower molecular weight as discussed recently [24]. Concerning diffusion of molecules from the bulk, it is estimated that the bulk viscosity, which may play a role, is only slightly modified by the presence of the polymer (less than 1% compared to pure water). Then, the kinetic process is attributed to free diffusion based on the hydrodynamic volume of the polymer.

The critical aggregation concentration (CAC) around 10 mg/L is insensitive to the molecular weight as well as the minimum surface tension (55–56 mN/m). This value is in agreement with that given for methylcellulose A4M (52 mN/m on 3 g/L solution at 20 °C after 20 min) by Gaonkar [75]. The CAC was given previously at 10 mg/L and 50 mN/m for Methocel A15 (M_{W} = 14 kDa) [77]. This value is higher than that obtained usually for surfactant or for surfactant–polyelectrolyte complex tested previously (values obtained between 35 and 45 mN/m) [78–80].

From the literature, it was suggested that the polymers adsorbed at the interfaces form loops and trains based on the distribution of the hydrophobic blocks which are orientated into the air at the water/air interface [49]. Other papers have demonstrated that adsorption of hydrocolloids occurs with two consecutive or simultaneous stages: firstly, a slow diffusion of the coiled macromolecules from the bulk phase to the subsurface region occurs followed by adsorption of polymer segments at the surface with conformational change [76,81]. This allows the interpretation of our data in which only the fraction of hydrophobic zones (substitution degree around 3 being insoluble in water) is independent of the molecular weight.

4.5.2. Adsorption Isotherm

The mechanism of stabilization of colloidal systems is usually described in terms of DLVO theory (Derjaguin, Landau, Verwey and Overbeek) [82]. This theory predicts that the stability of colloidal suspension comes from the balance between two forces, electrostatic repulsion and van der Waals attraction. DLVO theory describes the interaction between two approaching particles having the same ionic potential. The potential distribution at the interface, electrical double layer and the slipping plane corresponding to the ζ-potential may be examined experimentally by electrophoresis.

The stability of colloidal particles may be controlled by polymer adsorption at the interfaces (oil/water, air/water or solid/water). Especially, when neutral polymers are used for coating a solid surface, the adsorbed layer (whose thickness increases when molecular weight increases) causes a steric stabilization. Then, in dilute solution, the ζ-potential of silica particles decreases and tends to zero due to a displacement of the slipping plane [83,84]. An example of such behavior is given in Figure 12.

It has been demonstrated that the interaction is very large for smaller amounts of added MC (lower than 5 mg/L). In addition, it has been shown that the behavior depends on the molecular weight, which is related to the adsorption of the molecule at the interface (loops and trains formation in relation to the surface free energy). Higher molecular weight corresponds to a thicker layer and lower ζ-potential. In the theoretical model, large loops with few adsorbed units occur for small adsorption free energies but small loops with more units are adsorbed for larger adsorption free energies when the chains are sufficiently flexible [85]. In the case of MC, trains probably consist of more hydrophobic zones (DS ~ 3) in contrast to loops, with lower DS, which rather expand into the aqueous medium.

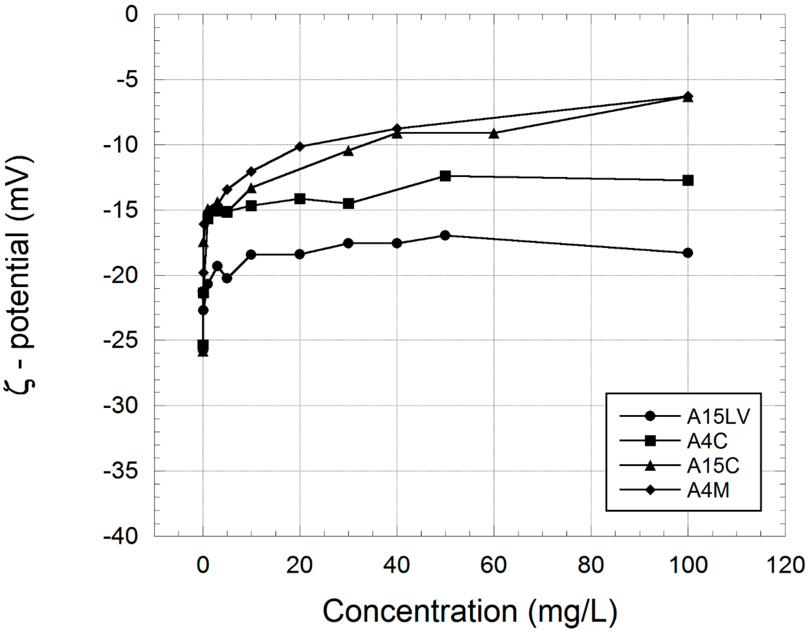

Figure 12. ζ-Potential (expressed in mV) of silica particles with an average 0.5-µm diameter dispersed in water at 20 °C in the presence of increased amounts of methylcelluloses with different molecular weights. The lines are added to guide the eye [24].

5. Applications

To our knowledge, the most important producers of MC are Hercules, Inc. (Wilmington, DE, USA). Aqualon division with Benecel A and Culminal, Dow Chemical Company with Methocel A and Shin-Etsu Chemical Company with Metolose SM. A variety of such cellulose derivatives exists mainly with different MW or viscosities in aqueous solution but only a slight variation in the degree of substitution. In the Benecel and Methocel cases, the characteristics are given by a specific code: A for methyl derivatives, a number indicating the viscosity (in mPa·s) of a 2% solution in water at 20 °C. This number for viscosity is followed by a letter *C* (indicating ×100) and *M* (×1000). The letters LV refer to a special low viscosity product. Methylcellulose is provided as a white powder (or sometimes as coarse particles) in pure form and dissolves in cold (but not in hot) water, forming a clear viscous solution or gel.

5.1. Main Properties

Methylcelluloses are water soluble but also soluble in mixed solvent (water/ethanol) and organic solvent (for higher DS). The most interesting properties and applications of water soluble methylcelluloses are described below.

In general, methylcelluloses are non-ionic polymers able to be mixed with other polymers (like polyvinyl alcohol (PVA) [86]), salt, and different ingredients. The viscosities are stable over a large range of pH (3–11) but degraded slowly in strong acids or bases. These polymers are enzyme resistant and are non-toxic for humans and plants (not cell permeable). They are not digestible in the body and cause no allergic reaction, consisting of an interesting dietary fiber. Methylcelluloses are provided mainly as a powder which is an efficient water retention agent.

The aqueous solutions are good thickening agents of which the rheological behavior may be controlled by the polymer concentration and molecular weight. Aqueous solutions allow the preparation of good transparent and flexible films preventing oil absorption. MC solutions enable the control of the settling of solid particles in dispersion, avoiding sedimentation. MCs have a protective colloid effect against droplets or particles agglomeration. MCs also stabilize emulsion and foams due to their surface and interfacial tensions. Possible MC adsorption at interfaces and the increase of interfacial film viscosity as well as increase of the medium viscosity reduce the particle diffusion. In the literature, the surface and interfacial tensions (against paraffin oil) of 0.1% aqueous solutions at 20° C are given: the average values for water are 72 and 45 mN/m respectively and for the methylcellulose solution, the values are 50–55 mN/m and 18–21 mN/m, respectively [87].

MC being an amphiphilic polymer is a binder for many types of systems: pigments, cellulosic fibers, pharmaceutical products, ceramics, and others [2,3,87,88]. In some of these cases, good adhesive character is obtained, methylcellulose is often more efficient than starch pastes and may be cleaned up with water. In addition, methylcellulose may be used at lower concentration than other additives.

An interesting development points towards film formation including different additives (as α-tocopherol) [89] for biodegradability and antioxidative properties, giving also excellent barriers against ultra-violet (UV) and visible light radiations.

All those properties make methylcelluloses applicable for many life areas. Selected applications are described below.

5.2. Main Applications

From technical notices [2,3,87,88], the main applications are summarized and displayed in the following sections.

5.2.1. Food

Methylcellulose is accepted for food applications in many countries over the world; it is identified as E461 in the European community as an emulsifier preventing the separation of two mixed liquids and texturing agents. However, it is also used as a thickener and gelling additive. Like cellulose, it is non-digestible, non-toxic, and non-allergic. It is a texturing agent especially in bakery products, to gain volume, texture, and improved freshness of pastes as well as for production of gluten free products. When frying frozen products like extruded croquettes, MC helps to retain their shape and the heat-gelling property and also reduces fat pick-up.

For example in ice-cream and other deep-frozen products, MC reduces the ice crystal growth during freezing and thawing. In mayonnaise, dressings, creams and sauces, MC allows the control of viscosity, emulsion stability, and the reduction of fat and egg content. As a result, MC may be recommended for dietetic products (low-calorie, *i.e.*, low fat yield and non-digestibility).

MC is also used to stabilize foams in cold drinks or for maintaining homogeneous dispersion of different components in food products.

5.2.2. Cosmetics and Personal Care

Methylcellulose is added to hair shampoos, hair styling products, liquid bubble bath concentrates, liquid soaps and body washes, lotions and creams, and toothpastes to generate their characteristic thick consistency.

MC has good skin and mucous membrane compatibility and has been used for many years in cosmetic preparations without any risks.

5.2.3. Pharmaceutical and Biomedical

MC is not metabolized in the digestive tract of the body, therefore it can be used as an additive for pharmaceuticals. High molecular grades control the release of the active ingredients in matrix tablets. Pharmaceutical grades of MCs have been used as thickeners, binders, emulsifiers, and stabilizers.

Methylcellulose is also used in the manufacture of capsules for nutritional supplements; its edible and non-toxic properties provide an alternative to the use of gelatin (animal source) [90].

The lubricating property of MC is of particular benefit in the treatment of dry eyes (Keratoconjunctivitis Sicca) [91]. Dry eyes are common in the elderly and often associated with rheumatoid arthritis. The lacrimal gland and the accessory conjunctive glands produce fewer tears. MC may be used as a tear and also saliva substitute.

MC is not absorbed by the intestines and passes through the digestive tract undisturbed. It attracts large amounts of water into the colon, producing a softer and bulkier stool as recommended to treat constipation, diverticulosis, hemorrhoids, and irritable bowel syndrome. Since it absorbs water and potentially toxic materials and increases viscosity, it can also be used to treat diarrhea.

Stewart *et al.* [92] used MC to restore the ability of human umbilical cord vein cells and to adhere the fibronectin after removal from substrata. MC also prevents human skin fibroblasts, human melanoma cells and mouse lung fibroblasts from losing adhesive properties as well as cell function in suspension.

Some examples recommend the use of MC instead of glycerol in a cryopreservation medium; a higher percentage of viability was noted for each organism tested in a 1% MC solution compared to a 15% glycerol solution [93].

MC was used in a semi-solid culture medium; plating cells in 1.2% MC with 10% fetal calf serum (plated over a layer of 0.9% agar or other concentrations) [94–97]. Human neuroblastoma cells were cloned and cultured successfully in a 1% methylcellulose medium [98]. Methylcellulose is used in the most common approaches to quantify multiple or single lineage-committed hematopoietic progenitors, called colony-forming cells (CFCs) or colony-forming units (CFUs), in combination with culture supplements that promote their proliferation and differentiation [3].

Sponges were also produced and saturated with coagulating agents to decrease the blood flow when placed on an incision [99].

5.2.4. Ceramics and Construction Materials

For ceramics processing, MC provides a better flow and uniform thickness; thermal gelation reduces binder migration. MC finds a major application as a performance additive in construction materials [100]. It is added to mortar dry mixes to improve the mortar properties such as workability, open and adjustment time, water retention, viscosity, and adhesion to surfaces [101].

The construction materials can be cement-based or gypsum-based. Examples of dry mixture mortars utilizing methylcellulose include: tile adhesives, insulating plasters, hand-trowled and machine sprayed plaster, stucco, self-leveling flooring, extruded cement panels, skim coats, joint and crack fillers, and tile grouts. The main advantage of MC is its ability to mix with other polymers such as PVA providing porous composites [39] with high performance mortars for laying tiles and coating walls and ceilings, with a larger resistance value of adhesion to traction.

These macromolecules also significantly increase water-retention capacity and paste viscosity. The mixtures can also reduce the risk of separation of the heterogeneous constituents of concrete during transport and storage, because they stabilize the concrete while fresh. Since they result in highly viscous systems with a good water retention capacity and adhesion, the polymers are often used to produce mortars for tile-laying. The mortars are more homogenous and cohesive with the polymers, thus having greater fluidity [101].

MC is used as paint rheological modifier and stabilizer to prevent paint sagging problems. MC is also used as a protective colloid and pigment suspension aid in latex paints.

5.2.5. Adhesives

MC is a weak adhesive with a wide variety of applications because it gives good films [3]. It is commonly used as a bookbinding adhesive for paper, as well as for sizing papers and fabrics, and thickening water baths for marbling paper. It helps to loosen and clean off old glue from spines and book boards, or together with PVA it decreases drying time. MC can be employed as a mild glue which can be rinsed with water. It may be used in the fixation of delicate pieces of art. It is not affected by heat or freezing and forms a highly flexible bond. MC is the main ingredient in many wallpaper pastes. It is also used as a binder in pastel crayons.

5.2.6. Agriculture

MC is used as suspending and dispersing agent for wettable pesticides and fertilizer powders. It favors adhesion to waxy plant surfaces [3]. In sprays, it is a seed sticker used to bind pesticides, and nutrients to seeds with low toxicity.

5.2.7. Other Applications

MC is used for sizing in the production of papers and textiles because it protects the fibers from absorbing water or oil. MC is also used as a suspending agent in PVC suspension polymerization [102]. It allows the control of rheology and is a colloidal stabilizer in epoxy, fiberglass, and urea-formaldehyde resins [3].

6. Conclusions

This review presents the main techniques for preparation and characterization of methylcelluloses. These cellulose derivatives are water soluble with amphiphilic properties due to methylation on the –OH groups of the anhydro-D-glucose units. Degrees of substitution larger than 1.3, with a heterogeneous distribution of the methyl groups, allows the formation of hydrophobic zones induced by hydrophobic interactions. They are involved in thermogelation which is often observed for commercial methylcellulose samples. Original physical properties, which are particularly attractive, are described in this paper: the gelation induced by temperature increase, surface activity at air/water interfaces and adsorption at solid/water interfaces. The role of the molecular weight of methylcellulose on these physical properties is discussed in detail.

Due to all the described properties, methylcellulose may be used in many applications of which the most valuable ones are presented in this review.

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Author Contributions

Pauline L. Nasatto, Frédéric Pignon and Marguerite Rinaudo have performed the bibliographic research taking into account their experimental results. The team from Brazil contributed to the article writing.

Conflicts of Interest

The authors declare no conflict of interest.

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