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Solution properties of well-defined 2-(dimethylamino)ethyl methacrylate-based (co)polymers: A viscometric approach

Isabelle Ydens, Sébastien Moins, Philippe Degée, Philippe Dubois *

Laboratory of Polymeric and Composite Materials, University of Mons-Hainaut, Place du Parc 20, B-7000 Mons, Belgium

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Abstract

Well-defined poly(2-(dimethylamino)ethyl methacrylate)-based (co)polymers with various molar masses were synthesized by atom transfer radical polymerization (ATRP) using CuBr ligated with 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) as catalyst, and ethyl 2-bromoisobutyrate (EBiB) or α-methyl, ω-(2-bromoisobutyrate) poly(ethylene glycol) (mPEG$_x$-BiB) as (macro)initiator. The solution properties of these (co)polymers were investigated by viscometry either in pure water or in concentrated buffer solutions. It comes out that reduced viscosity in pure water is strongly affected by the molar mass of poly(2-(dimethylamino)ethyl methacrylate) block but also by the quaternization degree of tertiary amino groups. In fact, a polyelectrolyte effect can only be detected when the charge density per macromolecule reaches a critical value either in terms of molar mass or quaternization degree. Fitting of viscometry data according to either Huggins or Fuoss and Fedors equation also allows calculating the intrinsic viscosity and approaching the overlap concentration.

Keywords: 2-(Dimethylamino)ethyl methacrylate; Atom transfer radical polymerization; Viscometry behavior; Polyelectrolyte effect; Polycations

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1. Introduction

In recent years, much interest has been devoted to water-soluble cationic polymers, such as poly(L-lysine) [1,2], derivatized chitosan [3,4], 2-(dimethylamino)ethyl methacrylate-based [5–9] and 2-(diethylamino)ethyl methacrylate-based (co)polymers [10–14] that can be used as DNA binding agents in nonviral gene delivery systems. In this context, our group has recently reported a new strategy to introduce poly(ethylene glycol) sequences/grafts into 2-(dimethylamino)ethyl methacrylate (DMAEMA)-based polymer/DNA complexes in order to prepare hemocompatible particles, which can transfect cells in the presence of serum [15]. For that purpose, perfectly well-tailored (co)polymers in terms of architecture, molar mass and composition were highly desirable which explains why a controlled radical polymerization technique, i.e. atom transfer radical polymerization (ATRP), was considered. Indeed, ATRP is

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* Corresponding author. Tel.: +32 65 37 34 80; fax: +32 65 37 34 84.

E-mail address: philippe.dubois@umh.ac.be (P. Dubois).

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one of the most robust controlled/“living” radical polymerization methods since it can be applied to a wide variety of functional monomers such as DMAEMA [16–18] and provides well-defined polymers [19–24].

However to the best of our knowledge, there have been only a very limited number of studies on the viscometric behavior of such aminated (co)polymers. In the early nineties, the polyelectrolytic character of quaternary derived PDMAEMA has been demonstrated by Andonova and co-workers using polymers prepared by conventional free radical polymerization [25]. More recently, Li and co-workers reported the graft copolymerization of sodium carboxymethylcellulose with acrylamide and DMAEMA using ammonium persulfate (APS) and *N*,*N*,*N*′,*N*′-tetramethylene diamine (TMEDA) as initiating system [26]. The relationship between the reduced viscosity and pH for these (co)polymers in aqueous NaCl solution was briefly reported.

It must be emphasized that viscometry represents probably the most widely used experimental method to assess the conformational transition of polyelectrolytes in solution [27]. Indeed, viscometric behaviors are related to the chemical structure of the polycation, its size and charge density but also to the environment properties such as the ionic strength, pH and addition of salts [28].

In the present paper, viscometric properties of well-defined DMAEMA-based (co)polymers in salt-free solution are investigated. The influence of the macromolecular parameters such as composition and molar mass are described. In order to avoid limitations induced by the partial protonation of PDMAEMA chains in Millipore water, additional experiments have focused on the viscometric behavior of PDMAEMA homopolymers either in acetic acid/sodium acetate buffered solution or after quaternization of the pending tertiary amino groups.

2. Experimental part

2.1. Materials

Ethyl 2-bromoisobutyrate (EBiB, 98%), 2-bromo-2-methylpropionylbromide (98%), 2-(monomethoxy-capped-poly(ethylene glycol)) (mPEG$_x$ with $x = 10$ ($M_n = 480$) or 44 ($M_n = 1950$)), 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA, 97%) and copper (I) bromide (CuBr, 98%) were purchased from Aldrich and used as received. Triethylamine (from Fluka, 99%) was dried over barium oxide for 45 h at r.t. and distilled under reduced pressure. Tetrahydrofuran (THF, from Chem-Lab, 99+%) and 2-(dimethylamino)ethyl methacrylate (DMAEMA, from Aldrich) were passed through a column of basic alumina to remove out the stabilizing agents. The monomer was then stored under N_2 at −20 °C.

2.2. Synthesis of α-methyl-ω-(2-bromoisobutyrate) poly(ethylene glycol) (mPEG$_x$-BiB)

In a typical experiment, a solution of monomethoxy-capped-poly(ethylene glycol) (mPEG$_{10}$, 2 g, 4.1 mmol) and triethylamine (2.5 mL, 17.9 mmol) in 70 mL of anhydrous THF was cooled in an ice-water bath. Then, 2-bromo-2-methylpropionylbromide (2.2 mL, 17.9 mmol) was slowly added to the reaction mixture. The solution was warmed up to ambient temperature and stirred for 48 h. After filtration, the organic layer was evaporated under reduced pressure.

2.3. Synthesis of PDMAEMA and mPEG-b-PDMAEMA (co)polymers

In a typical experimental run, a dry glass-tube was charged with CuBr (34 mg, 0.24 mmol) and a magnetic stir bar. The tube was closed with a three-way stopcock capped by a rubber septum and purged by three repeated vacuum/nitrogen cycles. Separately, in a dry flask, HMTETA (0.109 g, 0.47 mmol), DMAEMA (4 mL, 23.73 mmol), and when needed, 4 mL of THF or toluene were introduced and bubbled with nitrogen during 5 min before transferring the mixture into the glass-tube placed in a water bath maintained at a given temperature. Finally, degassed EBiB or mPEG$_x$-BiB was added to the tube with a degassed syringe. The polymerization was stopped by immersing the tube into a liquid nitrogen bath and the (co)polymer was recovered by precipitation from cold heptane. Monomer conversion was determined by gravimetry. The catalyst was removed by taking advantage of the pH-dependence and thermo-responsive behavior of the PDMAEMA chains in water [29–31]. In practice, a crude polymer solution (1 g in 5 mL H_2O) was added drop by drop into 100 mL of an aqueous NaOH solution and the mixture was heated up to 65 °C for precipitating colorless (co)polymer chains.

2.4. Quaternization of tertiary amino groups in PDMAEMA homopolymer

Quaternization reaction of PDMAEMA was conducted using methyl iodide (CH_3I) as the quaternizating agent, according to a method reported previously [14]. Typically, 1 g of PDMAEMA homopolymer (6.3 mmol tertiary amine) was introduced in a round bottom flask and dissolved in THF (40 mL) under stirring at room temperature. Then, a defined amount of CH_3I (e.g., 1.6 mmol in the case of 25% quaternization) solution in THF (40 mL) was added drop wise. After 18 h, the quaternized homopolymer was recovered by volatilizing the solvent and residual CH_3I.

2.5. Characterization

^{1}H NMR spectrum was recorded using a Bruker AMX-300 apparatus at r.t. in $CDCl_3$ (30 mg/0.6 mL). Size exclusion chromatography (SEC) was performed in THF + 2 wt% NEt_3 at 35 °C using a Polymer Laboratories liquid chromatograph equipped with a PL-DG802 degasser, an isocratic HPLC pump LC 1120 (flow rate = 1 mL min^{-1}), a Marathon autosampler (loop volume = 200 μL, solution conc. = 1 mg mL^{-1}), a PL-DRI refractive index detector and three columns: a PL gel 10 μm guard column and two PL gel Mixed-B 10 μm columns. Poly(methyl methacrylate) standards were used for calibration. Viscometry was carried out at 25 °C using an Ubbelhode viscometer (inner diameter $\phi = 0.46$ mm). The (co)polymer solutions were prepared 24 h before measurements by dissolution in Millipore water (pH = 6.5) or in an acetic acid/sodium acetate aqueous buffer (0.5 mol L^{-1}) and then maintained at 25 °C for at least 30 min to reach equilibrium temperature.

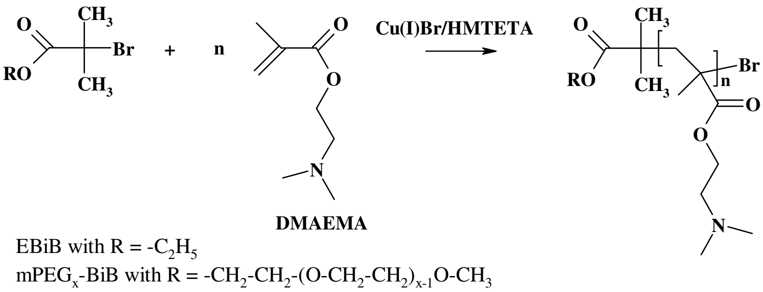
3. Results and discussion

Poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA)-based (co)polymers were synthesized by atom transfer radical polymerization (ATRP) under mild conditions using copper (I) bromide (CuBr) ligated with 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) as the catalyst, and ethyl 2-bromoisobutyrate (EBiB) or α-methyl-ω-(2-bromoisobutyrate) poly(ethylene glycol) (mPEG$_x$-BiB) as the (macro)initiator (Scheme 1).

Table 1 shows the experimental conditions for the synthesis of these (co)polymers to be used for the viscometric study as well as their apparent molecular characteristics (M_n (SEC) relative to PMMA calibration). Absolute molar mass (M_n) of PDMAEMA homopolymers have not been determined, except for Entry 3 with M_n reaching 26,700 as determined by vapor pressure osmometry in toluene. It is worth pointing out that this value is very close to the theoretical one, assuming a "living" radical polymerization (M_n (calcd) = $[DMAEMA]_0/[EBiB]_0 \times \text{conv.} \times MW_{DMAEMA}$). As far as PEG-*b*-PDMAEMA block copolymers are concerned (Entries 7–10, Table 1), the number-average molar mass has been estimated by ^{1}H NMR spectroscopy (M_n (NMR)) from the relative intensities of the α-amino methylene protons of DMAEMA derived repeating units at $\delta = 2.6$ ppm and the methylene protons of poly(ethylene glycol) sequence at $\delta = 3.65$ ppm ($CDCl_3$), knowing the molar mass of the PEG block (Fig. 1). These values are in rather good agreement with the expected values (M_n (calcd)) calculated from the initial DMAEMA to (macro)initiator molar ratio. For sake of comparison, a M_n value of 19,100 has been determined for Entry 7 by vapor pressure osmometry in toluene. Further confirming the control over the polymerization, monomodal and quite narrow molecular weight distributions (M_w/M_n, Table 1) have been reached by size exclusion chromatography (SEC) with polydispersity indices ranging mostly from 1.2 to 1.4. In a next part, these well-defined (co)polymers have been used to investigate their viscometric behavior.

3.1. Influence of the (co)polymer molar mass and composition on the reduced viscosity

In a first series of experiments, the effect of the PDMAEMA apparent molar mass (M_n (SEC)) on the reduced viscosity (η_{sp}/C) in pure water has been investigated. Fig. 2 shows the reduced viscosity of various homopolymers as a function of their concentration. As expected for non-ionized or poorly ionized polymer solutions, the reduced viscosity profile of PDMAEMA with apparent molar masses lower than 45,000 follows the Huggins relationship (Eq. (1)), i.e., no polyelectrolyte effect (see hereafter) can be detected but η_{sp}/C slightly in-



Scheme 1. Copper (I) mediated "living" radical polymerization of DMAEMA using alkylbromide (macro)initiator.

Table 1
Conditions for the synthesis of PDMAEMA-based (co)polymers by ATRP using CuBr/HMTETA catalytic complex and alkylbromide (macro)initiator

Entry	(Macro)initiator	$[DMAEMA]_0$/ $[(macro)initiator]_0$	Solvent	T (°C)	t (h)	M_n (calcd)[a]	M_n (NMR)[b]	M_n (SEC)[c]	M_w/M_n[c]
1[d]	EBiB	93	THF	60	16	14,600	–	14,000	1.19
2[e]	EBiB	100	Toluene	85	24	11,200	–	17,700	1.28
3[e]	EBiB	200	Toluene	85	1	26,200	–	23,100	1.29
4[f]	EBiB	180	Bulk	25	4	25,600	–	27,500	1.39
5[f]	EBiB	300	Bulk	25	16	38,300	–	41,000	1.41
6[d]	EBiB	500	THF	25	16	68,900	–	49,100	1.59
7[f]	$PEO_{10}BiB$	97	Bulk	25	1	13,500	16,900	16,100	1.28
8[f]	$PEO_{10}BiB$	192	Bulk	25	4	27,500	31,900	30,800	1.30
9[f]	$PEO_{10}BiB$	370	Bulk	25	4	53,500	43,000	41,800	1.50
10[d]	$PEO_{45}BiB$	100	THF	60	4	29,200	35,300	28,600	1.33

[a] As calculated from the following equation: $M_n\ (\text{calcd}) = MW_{PEO_xBiB} + ([DMAEMA]_0/[(macro)initiator]_0) \times \text{conversion} \times MW_{DMAEMA}$.

[b] As determined by ^1H NMR spectroscopy from the relative intensities of the α-amino methylene protons of DMAEMA derived repeating units at $\delta = 2.6$ ppm and the methylene protons of PEG sequence at $\delta = 3.65$ ppm ($CDCl_3$).

[c] As determined by SEC with reference to PMMA standards.

[d] $[DMAEMA]_0 = 2.95$ M, $[(macro)initiator]_0/[CuBr]_0/[HMTETA]_0 = 1/1/2$.

[e] $[DMAEMA]_0 = 2.39$ M, $[(macro)initiator]_0/[CuBr]_0/[HMTETA]_0 = 1/1/2$.

[f] $[DMAEMA]_0 = 5.93$ M, $[(macro)initiator]_0/[CuBr]_0/[HMTETA]_0 = 1/1/2$.

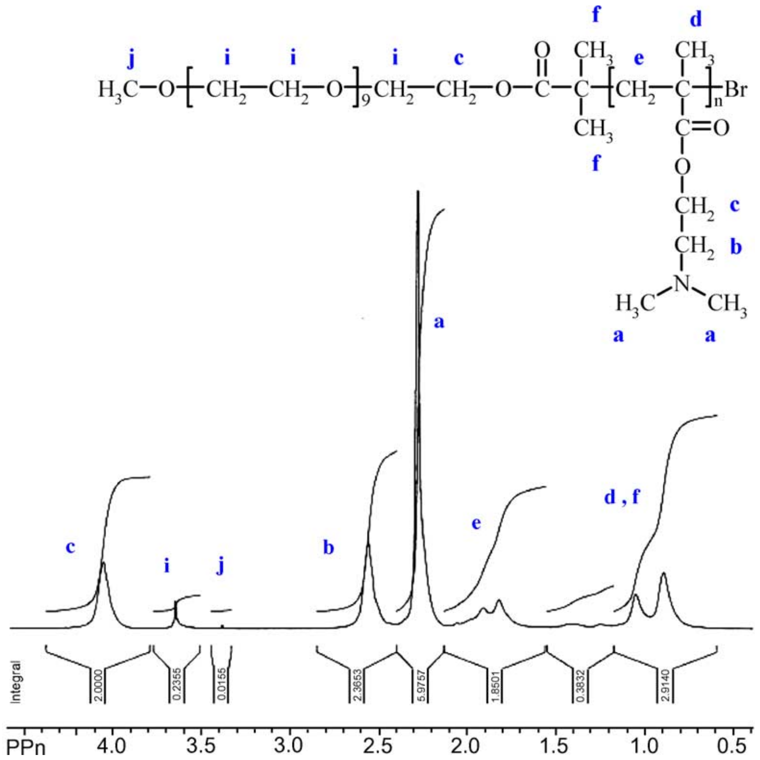


Fig. 1. ^1H NMR spectrum of mPEG$_{10}$-*b*-PDMAEMA diblock copolymer in $CDCl_3$ (Entry 8, Table 1).

creases with both polymer concentration and molar mass [32]. Eq. (1) reflects the net contribution from the hydrodynamic effect of a single polymer molecule and extrapolation to zero concentration corresponds to [η].

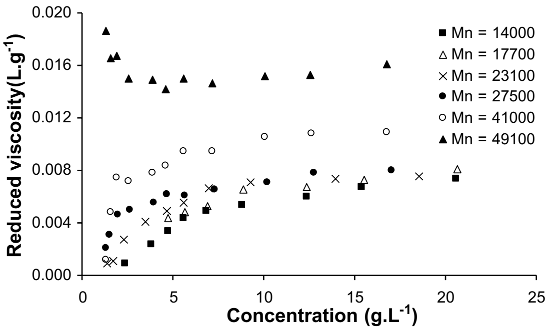


Fig. 2. Concentration dependence of the reduced viscosities of various PDMAEMA polymers in salt-free aqueous solution at 25 °C (Entries 1–6, Table 1).

$$\eta_{sp}/C = [\eta] + k'[\eta]^2C \tag{1}$$

where η_{sp}, C, $[\eta]$ and k', are the specific viscosity, the concentration of the polymer, the intrinsic viscosity and the Huggins constant, respectively.

Table 2 shows $[\eta]$ and k' values as calculated applying Eq. (1) to viscometric data of PDMAEMA homopolymers with apparent molar masses lower than 45,000. As could be expected, the intrinsic viscosity value increases with the M_n (SEC) while the Huggins constant shows positive values with a minimum for an apparent molar mass close to 23,000.

Very interestingly, one can also note that longer polymeric chains (with M_n (SEC) = 49,100) show a polyelectrolyte behavior characterized by a sharp increase of the reduced viscosity at low concentration range (Fig. 2). The polyelectrolyte effect is due to an expansion of the polyionic chain, which is caused by the progressively enhanced dissociation of ionizable groups as concentration decreases and therefore intensification of intramolecular repulsive interactions between ionized groups (i.e., protonated amino groups) spread all along the chain. These results highlight that a minimum chain length is necessary to display a polyelectrolyte effect likely due to the pK_a value of PDMAEMA in water (pK_a ~ 7.4) [33]. Indeed, dissolution of PDMAEMA in pure water only provides partial protonation of the amino groups pending onto the repeating monomeric units so that the polyelectrolyte behavior is only effective for a charge density per macromolecule high enough. The curve shown in Fig. 2 (corresponding to Entry 6 in Table 1) can be linearized applying the Fuoss (Eq. (2)) [34] and Fedors [28,35] (Eq. (3)) equations:

$$\eta_{sp}/C = [\eta]/(1 + kC^{0.5}) \tag{2}$$

$$1/[2(\eta_r^{0.5} - 1)] = 1/[\eta]C - 1/[\eta]Cm \tag{3}$$

where η_{sp}, η_r, C, $[\eta]$, k and Cm, are the specific viscosity, the relative viscosity, the concentration of the polymer, the intrinsic viscosity, the Fuoss constant and a polymer constant parameter, respectively.

Table 2
Effect of PDMAEMA apparent molar mass on the intrinsic viscosity $[\eta]$ and Huggins constant (k') at 25 °C in pure water

Entry[a]	$[\eta]$ (dL g^{-1})	k'
1	0.037	13.30
2	0.038	15.69
3	0.067	1.06
4	0.052	6.95
5	0.073	4.95

[a] Molecular characteristics are reported in Table 1 (same entry number).

Figs. 3 and 4 show that straight lines are obtained using both Fuoss and Fedors equations allowing to calculate intrinsic viscosity values of 0.18 and 0.13 dL g^{-1}, respectively. These values appear quite close to each other. The concentration range employed in this study include the overlap concentration, C^*, at which polymer coils begin to overlap each other (separating semi-dilute and dilute regimes) as is usually known for polyelectrolyte [36]. C^* can be approached from the reciprocal of the intrinsic viscosity ($C^* = 1/[\eta]$) [37] or experimentally as the concentration at which the viscosity is twice the

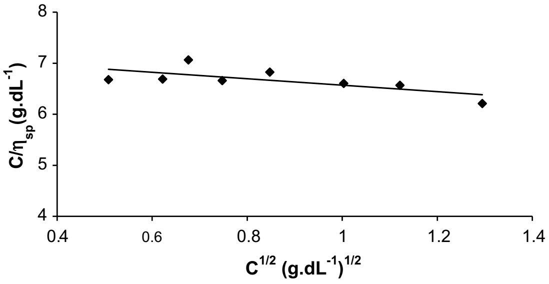


Fig. 3. Representation of the Fuoss equation for Entry 6, Table 1.

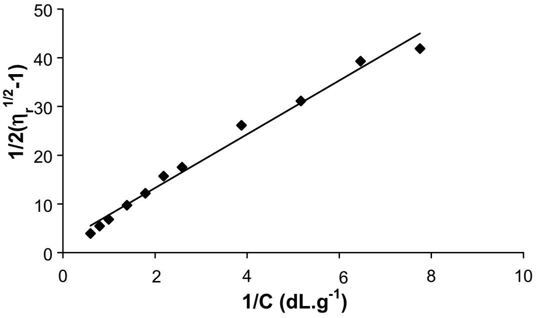


Fig. 4. Representation of the Fedors equation for Entry 6, Table 1.

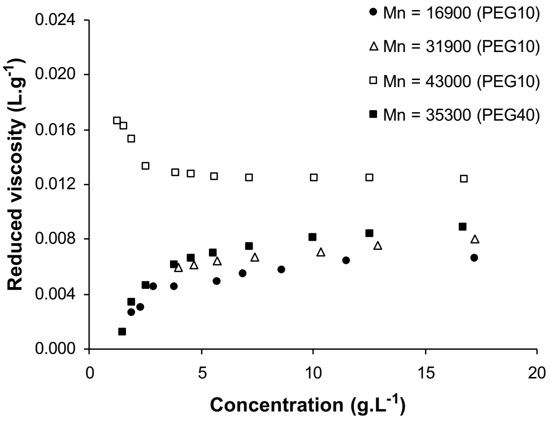


Fig. 5. Concentration dependence of the reduced viscosities of PDMAEMA copolymers in salt-free aqueous solution at 25 °C (Entries 7–10, Table 1).

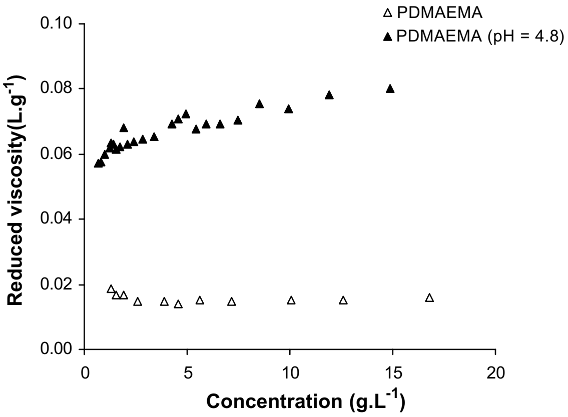


Fig. 6. Concentration dependence of the reduced viscosities of PDMAEMA polymer in salt-free aqueous and buffered (pH = 4.8) solutions at 25 °C (Entry 6, Table 1).

solvent viscosity [28]. The results obtained for C^* by means of the above mentioned methods are equal to 6.5 g dL^{-1} and 6.4 g dL^{-1}, respectively.

It is worth noting that a similar phenomenon has been observed for mPEG-*b*-PDMAEMA block copolymers (Fig. 5) for which a minimum apparent molar mass (M_n) in PDMAEMA block is again needed to display a polyelectrolyte effect. Indeed, the polyelectrolyte behavior is detected for the longer copolymer, i.e., characterized by a PDMAEMA block with a M_n as high as 43,000.

In order to avoid limitations induced by the partial protonation of PDMAEMA chains in Millipore water, additional experiments have focused on the viscometric behavior of the homopolymers in acetic acid/sodium acetate buffered solution as well as on the effect of quaternization of the amino groups.

3.2. Influence of the solution pH on the reduced viscosity

Due to the presence of weakly basic tertiary amino groups pending along the chains, the extent of ionization and solution properties should be strongly affected by substituting acetic/sodium acetate aqueous buffer (0.5 mol L^{-1}) for water. However, the concomitant enhancement of the ionic strength with the decrease of pH may also affect the layer of the bonded counterions around the chains, and accordingly trigger the chain contraction and even precipitation [38]. Such a behavior will depend on the nature and concentration of anions. Fig. 6 shows the concentration dependence of the reduced viscosity for a PDMAEMA sample (Entry 6, Table 1) solubilized in Millipore water and in an acetic/sodium acetate aqueous buffer (0.5 mol L^{-1}), respectively. An increase of the protonation degree of tertiary amino groups leads to higher reduced viscosity values due to higher hydrodynamic volume and some increase of long range repulsive interactions. However, no typical polyelectrolyte effect could be observed whatever the molar mass of the investigated PDMAEMA chains (not shown here). This is more likely due to the neutralization of positive charges by large acetate anions and therefore the decrease of short range repulsive interactions. The acetate counterions are weakly acidic groups which are not tightly bonded to the tertiary ammonium cations.

3.3. Influence of quaternization degree on the reduced viscosity

Quaternization reactions of a PDMAEMA homopolymer (Entry 1, Table 1) were carried out using various amounts of methyl iodide in tetrahydrofuran at room temperature for 18 h. Quaternization degree as determined by ^{1}H NMR spectroscopy in D_2O (from the relative intensities of α-amino methyl protons at 2.65 ppm (not quaternized) and 3.40 ppm (quaternized); NMR spectra not shown here) are in perfect agreement with the initial amino group-to-CH_3I molar ratios. Fig. 7 shows the variation of the reduced viscosity as a function of polymer concentration for different quaternization degrees. A polyelectrolyte behavior is clearly observed from quaternization yields higher than 25%. Moreover, one can note that the reduced viscosity increases with the quaternization yield, which results from the higher electrostatic repulsions and steric hindrance. The curves obtained by applying the Fuoss and Fedors equations to viscometric data for the quaternized PDMAEMA samples are presented in Figs. 8 and 9. As can be observed, straight lines are obtained for all the samples over a wide range of concentration allowing calculating the intrinsic viscosity values (Table 3). Analysis of these data shows that the intrinsic viscosity values obtained by the Fedors equation are much lower than

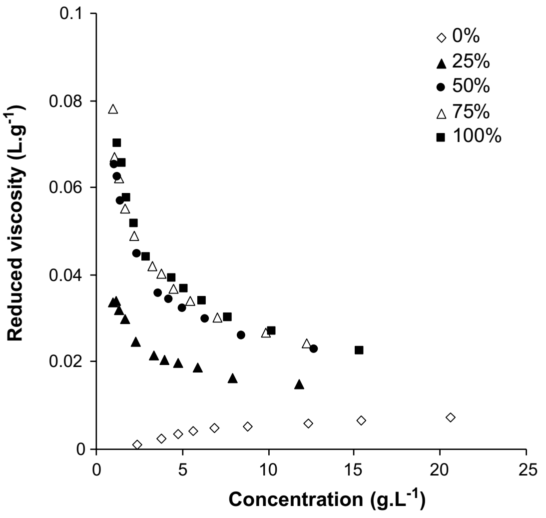


Fig. 7. Concentration dependence of the reduced viscosities of quaternized PDMAEMA polymers in aqueous solution at 25 °C (Entry 1, Table 1).

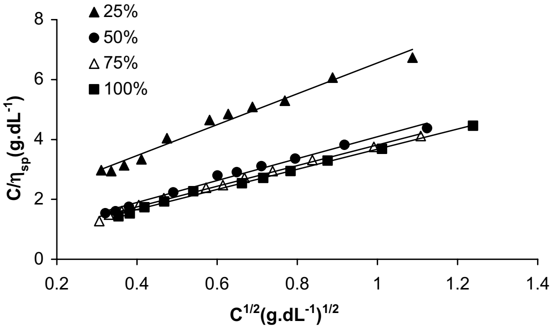


Fig. 8. Representation of the Fuoss equation for quaternized PDMAEMA.

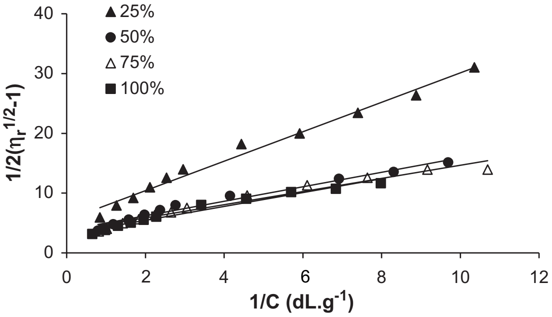


Fig. 9. Representation of the Fedors equation for quaternized PDMAEMA.

those obtained by the Fuoss equation as usually observed [28]. Furthermore, the [η] values as calculated by the Fedors equation lead to C^* values closer to values experimentally determined, than C^* obtained via the Fuoss equation. Finally, it is worth noting that [η] sharply increases when the quaternization degree passes from 25% to 50%, then it tends to level off whatever the method.

Table 3
Intrinsic viscosity and overlap concentrations for quaternized PDMAEMA (Entry 1 in Table 1)

Quaternization degree (%)	$[\eta]_{\text{Fuoss}}$ (dL g^{-1})	$[\eta]_{\text{Fedors}}$ (dL g^{-1})	C^*_{exp} [a] (g dL^{-1})	C^*_{Fuoss} (g dL^{-1})	C^*_{Fedors} (g dL^{-1})
25	0.71	0.41	7.4	1.4	2.4
50	2.32	0.83	4.9	0.4	1.2
75	2.69	0.91	4.6	0.4	1.1
100	3.15	0.86	4.9	0.3	1.2

[a] Determined as the concentration at which the viscosity is twice the solvent one.

4. Conclusion

Well-defined poly(2-(dimethylamino)ethyl methacrylate)-based (co)polymers with various molecular weights were synthesized by atom transfer radical polymerization (ATRP) using CuBr ligated with 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) as catalyst, and ethyl 2-bromoisobutyrate (EBiB) or α-(2-bromoisobutyrate)-ω-methyl poly(ethylene glycol) (mPEG$_x$-BiB) as (macro)initiator. The water solution properties of these (co)polymers were investigated by means of viscometric measurements. It comes out that PDMAEMA with apparent molar masses lower than 45,000 follows the Huggins relationship, i.e., no polyelectrolyte effect can be detected but η_{sp}/C slightly increases with both polymer concentration and molar mass. In contrast, a polyelectrolyte behavior characterized by a sharp increase of the reduced viscosity at low concentration range is observed for longer polymeric chains (e.g., M_n (SEC) = 49,100).

In parallel and in order to avoid limitations induced by the partial protonation of PDMAEMA chains in Millipore water, further studies have focused on the viscometric behavior of the homopolymers in acetic acid/sodium acetate buffered solution as well as on the effect of amino group quaternization. As a result, an increase of the protonation degree of tertiary amino groups leads to higher reduced viscosity values due to more expanded hydrodynamic volume and some increase of long range repulsive interactions. However, no typical polyelectrolyte effect could be observed whatever the PDMAEMA molar mass more likely due to the neutralization of positive charges by large acetate anions. On the other hand, polyelectrolyte behavior is observed for quaternization degrees higher than 25%. The Fuoss and Fedors equations were used to calculate the intrinsic viscosity values for these quaternized PDMAEMA chains. The analysis of these data showed that the intrinsic viscosity values obtained by the Fedors equation were much lower than those obtained by the Fuoss equation. Furthermore, the $[\eta]$ values calculated by the Fedors equation led to overlap concentration values (C^*) closer to experimentally determined C^*.

Acknowledgements

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References

[1] Kwoh DY, Coffin CC, Lollo CP, Jovenal J, Banaszczyk MG, Mullen P, et al. Biochim Biophys Acta 1999;1444:171.
[2] Wu GY, Wilson JM, Shalaby F, Grossman M, Shafritz DA, Wu CH. J Biol Chem 1991;266:14338.
[3] Lee KY, Kwon IC, Kim YH, Jo WH, Jeong SY. J Control Release 1998;51:213.
[4] Murata J-I, Ohya Y, Ouchi T. Carbohydr Polym 1996;29:69.
[5] Van de Wetering P, Moret EE, Schuurmans-Nieuwenbroek NME, Van Steenbergen MJ, Hennink WE. Bioconjugate Chem 1999;10:589.
[6] Niwa M, Ishida T, Kato T, Higashi NJ. Mater Chem 1998;8:1687.
[7] van Rompaey E, Sanders N, de Smedt SC, Demeester J, van Craenenbroek E, Engelborghs Y. Macromolecules 2000;33:8280.
[8] Rungsardthong U, Deshpande M, Bailey L, Vamvakaki M, Armes SP, Garnett MC, et al. J Control Release 2001;73:359.
[9] Bos GW, Trullsas-Jimeno A, Jiskoot W, Crommelin DJA, Hennink WE. Int J Pharm 2000;211:79.
[10] Mikaya M, Miwa N, Brautigam M, Akaike T, Maruyama A. J Biomed Mater Res 2000;49:390.
[11] Muller-Schulte D, Hodenius M. Radiat Phys Chem 2002;63:513.
[12] Asayama S, Maruyama A, Cho C-S, Akaike T. Bioconjugate Chem 1997;8:833.
[13] Dijk-Wolthuis WNE, Wetering P, Hinrichs WL. J Bioconjugate Chem 1999;10:687.
[14] Bütün V, Armes SP, Billingham NC. Polymer 2001;42:5993.
[15] Pirotton S, Muller C, Pantoustier N, Botteman F, Collinet S, Grandfils C, et al. Pharm Res 2004;21(8):1471.
[16] Zeng F, Shen Y, Zhu S, Pelton R. Macromolecules 2000;33:1628.
[17] Zeng F, Shen Y, Zhu S, Pelton R. J Polym Sci Part A: Polym Chem 2000;38:3821.
[18] Zhang X, Xia J, Matyjaszewski K. Macromolecules 1998;31:5167.
[19] Wang J-S, Matyjaszewski K. J Am Chem Soc 1995;117:5614.
[20] Kato M, Kamigaito M, Sawamoto M, Higashimura T. Macromolecules 1995;28:1721.
[21] Matyjaszewski K, editor. Controlled radical polymerization. ACS Symp Ser 1997:685.
[22] Matyjaszewski K, Xia J. Chem Rev 2001;101:2921.
[23] Kamigaito M, Ando T, Sawamoto M. Chem Rev 2001;101:3689.
[24] Patten TE, Matyjaszewski K. Adv Mater 1998;10:901.
[25] Bogoeva-Gaceva G, Andonova A. Polymer 1993;34:3934.
[26] Tan Y, Zhang L, Li Z. J Appl Polym Sci 1998;69:879.
[27] Forster S, Schmidt M. Adv Polym Sci 1995;120:51.
[28] Dragon S, Ghimici L. Polymer 2001;42:2887.
[29] Liu S, Weaver JVM, Tang Y, Billingham NC, Armes SP. Macromolecules 1998;35:6121.
[30] Pantoustier N, Moins S, Wautier M, Degée Ph, Dubois Ph. Chem Commun 2003:340.
[31] Ydens I, Moins S, Botteman F, Degée PH, Dubois PH E-polymers 2004:39.
[32] Huggins ML. J Am Chem Soc 1942;64:2716.
[33] Bütün V, Armes SP, Billingham NC. Macromolecules 2001;34:1148.
[34] Fuoss RM, Strauss UP. J Polym Sci 1948;3:246.
[35] Fedors RF. Polymer 1979;20:225.
[36] Mattoussi H, O'Donohue S, Karasz FE. Macromolecules 1992;25:743.
[37] Dobrynin VA, Colby RH, Rubinstein M. Macromolecules 1995;28:1859.
[38] Lee W-F, Chen Y-M. J Appl Polym Sci 2003;89:2261.