pH-Mediated Interactions between Poly(acrylic acid) and Methylcellulose in the Formation of Ultrathin Multilayered Hydrogels and Spherical Nanoparticles

Olga V. Khutoryanskaya, Adrian C. Williams, and Vitaliy V. Khutoryanskiy*

Reading School of Pharmacy, University of Reading, Whiteknights, PO Box 224, Reading RG6 6AD Berkshire, United Kingdom

Received July 24, 2007

ABSTRACT: Poly(acrylic acid) forms insoluble hydrogen-bonded interpolymer complexes with methylcellulose in aqueous solutions under acidic conditions. In this work the reaction heats and binding constants were determined for the complexation between poly(acrylic acid) and methylcellulose by isothermal titration calorimetry at different pH and findings are correlated with the aggregation processes occurring in this system. The principal contribution to the complexation heat results from primary polycomplex particle aggregation. Transmission electron microscopy of nanoparticles produced at pH 1.4 and 2.4 demonstrated that they are spherical and dense structures. The nanoparticles ranged from 80 to 200 nm, whereas particles formed at pH 3.2 were 20−30 nm and were stabilized against aggregation by a network of uncomplexed macromolecules. For the first time, multilayered materials were developed on the basis of hydrogen-bonded complexes of poly(acrylic acid) and methylcellulose using layer-by-layer deposition on a glass surface. The thickness of these films was a linear function of the number of deposition cycles. The materials were subsequently cross-linked by thermal treatment, resulting in ultrathin hydrogels which detached from the glass substrate upon swelling. The swelling capacity of ultrathin hydrogels differed from the swelling of the thicker films of a similar chemical composition.

Introduction

Layer-by-layer (LBL) sequential adsorption of polymers on solid surfaces is a simple and versatile technique for producing ultrathin polymeric films and coatings that essentially involves alternative exposure of surfaces to solutions of different polymers which can form insoluble interpolymer complexes (IPC). This approach, first described by Decher,[1] produces multilayered materials with well-controlled thickness and morphology and was initially based on complexation between oppositely charged polyelectrolytes via electrostatic attraction forces.

Association between poly(carboxylic acids) and nonionic polymers in aqueous solutions via hydrogen bonding has also been utilized recently in building novel multilayered materials with unique physicochemical properties.[2] Multilayered materials based on hydrogen-bonded interpolymer complexes between poly(acrylic acid) (PAA) or poly(methacrylic acid) (PMAA) and synthetic nonionic polymers such as poly(*N*-vinylpyrrolidone), poly(vinyl alcohol), poly(acrylamide), poly(ethylene oxide), poly(methyl vinyl ether), poly(*N*-isopropylacrylamide), poly(*N*-vinylcaprolactame), poly(4-vinylpyridine), and poly(2-hydroxyethyl acrylate) have been reported over the past 3 years.[3−12] This expanding area of science has recently been reviewed by Kharlampieva and Sukhishvili,[13] and it is clear that hydrogen bonding between poly(carboxylic acids) and nonionic polymers offers an excellent method to prepare multilayered materials with well-defined thicknesses.

Hydrogen-bonded IPC's were first described over 40 years ago (Smith et al.,[14] Bailey et al.[15]) with complexation between poly(carboxylic acids) and poly(ethylene oxide). Since then, the nature of interpolymer interactions and the physicochemical properties of these materials has been explored. In particular, it is well-established that hydrogen-bonded IPC tend to precipitate in low-pH solutions and redissolve quickly as pH increases,[16] which opens many interesting opportunities for application of these materials.

In contrast to the large number of studies into interpolymer complex formation, few attempts have been made to describe the thermodynamics of these processes.[17−19] Spontaneous complex formation requires the Gibbs energy of mixing (ΔG^M) to be negative:

$$\Delta G^M = \Delta H^M - T\Delta S^M \quad (1)$$

where ΔH^M and ΔS^M are the total heat (enthalpy) and total entropy of mixing, respectively. A negative value of ΔG^M can be achieved either when ΔH^M is negative or when ΔS^M is positive and high. In most studies into thermodynamics of complexation via hydrogen bonding, a potentiometric approach has been used.[18−20] A disadvantage of this strategy is the inability to estimate thermodynamic parameters of complexation in low-pH solutions because deprotonation of poly(carboxylic acids) caused by dissociation of hydrogen bonds is masked by the presence of a significant number of protons in solution.

A more universal approach for estimating thermodynamic parameters of interpolymer complexation is direct measurement of heat effects using calorimetric techniques. However, few studies describe this; Abe and co-workers[17] examined complexation between poly(methacrylic acid) (PMAA) and poly(*N*-vinylpyrrolidone) (PVP) in several solvents. The enthalpy of complexation in water at pH 3.0 was found to be positive (5.9 kJ/base-mol), whereas in dimethylformamide it was negative (−1.0 kJ/base-mol). It was suggested that the total heat of mixing (ΔH^M) can be considered as a sum of three different contributions:

$$\Delta H^M = \Delta H_1 + \Delta H_2 + \Delta H_3 \quad (2)$$

---

* Corresponding author: e-mail v.khutoryanskiy@reading.ac.uk.

10.1021/ma071644v CCC: $37.00

where ΔH_1 is the heat of desolvation, ΔH_2 is the heat of hydrogen bonding, and ΔH_3 is the heat of conformational change. The positive value of ΔH^M observed for the complexation between PMAA and PVP in water was attributed to hydrophobic effects, resulting in positive entropy changes (ΔS^M).

Baranovski et al.[21] studied thermodynamic parameters for complexation between PMAA and PVP using both potentiometric and calorimetric approaches. They found that both methods gave similar results ($\Delta H^M = 2.3$ and 2.0 kJ/base-mol, determined calorimetrically and potentiometrically, respectively). It was also demonstrated that the heat of the complex formation was invariant over the PVP molecular weight range 10−160 kDa. A calorimetric study of complexation between PMAA and a series of poly(ethylene oxides) with varying molecular weights (200−35000 Da) in water has also been reported;[22] the enthalpies of complexation were up to 0.35 kJ/base-mol and depended on the molecular weight of poly(ethylene oxide). Unfortunately, both the above studies used polymer solutions without pH adjustment; hence, the intensity of complexation was submaximal.

Our previous studies[16,23] have shown that the structure of IPC's is pH-dependent with possible pH-induced transitions between compact hydrophobic IPC particles and swollen hydrophilic interpolymer associates. However, at present no thermodynamic studies describe the effects of solution pH on the reaction heats since the literature reports employ either solutions without pH adjustment or solutions at fixed pH.[18−22]

Currently there is considerable interest in the complexation between poly(carboxylic acids) and water-soluble nonionic cellulose ethers such as methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, and hydroxypropylmethylcellulose,[23−31] particularly for pharmaceutical applications.[32] These studies focus predominantly on the formation and properties of complexes in aqueous solutions or at hydrogel−solution interfaces. Consequently, the thermodynamic parameters of complexation between of poly(acrylic acid) and cellulose ethers have not previously been reported.

Here we describe the use of isothermal titration calorimetry to probe heat effects on complexation between PAA and methylcellulose in aqueous solutions at different pH's. This information was correlated with IPC aggregation assessed by turbidimetric titration and transmission electron microscopy. These results were then used to optimize complexation conditions for building hydrogen-bonded multilayered materials via the layer-by-layer approach. The subsequent multilayered films were thermally treated, resulting in polymer cross-linking. The cross-linked materials were then exposed to aqueous solutions, resulting in swelling with subsequent detachment of ultrathin hydrogels.

Experimental Section

Materials. PAA (M_w 450 000) was supplied from Sigma-Aldrich (UK). Methylcellulose (Methocel 60 HG) with 28−30% methoxyl content was purchased from Fluka (UK). The viscosity of 2 wt % methylcellulose (MC) in water at 20 °C was 35−55 mPa•s. Both polymers were used without further purification. Super Premium microscope glass slides 76 × 26 mm used for layer-by-layer coating were purchased from BDH (UK). All inorganic chemicals such as hydrochloric acid, sodium hydroxide, and buffer solutions were purchased from Sigma-Aldrich (UK) and used without further purification.

Preparation of Solutions and Adjustment of pH. Polymer solutions were prepared by dissolving the required amounts of MC or PAA in deionized water at defined pH and leaving it stirring overnight at room temperature. The pH of the solutions was then further adjusted by adding small amounts of 0.1 M HCl or NaOH and was measured using a digital pH-meter (Metrohm, Switzerland).

Isothermal Titration Calorimetry (ITC). ITC experiments were performed using a Setaram CSC model 5300 Nano-ITC III instrument. Throughout the experiments, 0.2 wt % aqueous solutions of MC were titrated with 2.0 wt % solutions of PAA at different pH's. Before experiments, all polymeric solutions were degassed for approximately 1.5−2 h in a vacuum chamber equipped with a magnetic stirrer. All experiments were carried out at 25 °C under continuous stirring of the sample cell at 200 rpm. The titration experiment consisted of 24 injections (10 μL) at 180 s interval. For heat effect calculations, the concentrations of polymers were expressed in unit-mol/L. The repeating unit molecular weights of PAA and MC are 72 and 176, respectively. The molecular weight of the repeating unit of MC was calculated taking into account the 28−30% methoxyl content.

Turbidimetric Titration. Turbidity changes of aqueous mixtures of PAA and MC were examined at 400 nm with a V-530PC spectrophotometer (Jasco, UK). In these experiments, the 0.2 wt % solution of MC at a defined pH was titrated with 2 wt % PAA solution of the same pH, and turbidity readings were taken immediately after mixing.

Transmission Electron Microscopy (TEM). TEM images of IPC nanoparticles were acquired using a Philips CM20 Analytical TEM. For sample preparation, the copper grids were brought into 30 s contact with aqueous dispersions of IPC and dried off with a filter paper. IPC nanoparticles were prepared by mixing 0.2 wt % solutions of PAA and MC at a defined pH (1.4, 2.4, and 3.2) in 30:70 wt % ratios.

Multilayered Coatings. The multilayered films were developed on the surface of the microscope glass slides using 0.2 wt % solutions of PAA and MC at pH 2.0. Before layering, the glass slides were treated with 2 M NaOH solution at 60−70 °C for 30 min, then rinsed with deionized water thoroughly, and dried in air. A layer-by-layer deposition cycle involved immersion of a glass slide into PAA solution for 15 min, with subsequent dipping into deionized water for 1 min to wash out excessive unbound macromolecules, followed by immersion into MC solution for 15 min and then rinsing by dipping into deionized water for 1 min. This procedure was repeated the required number of times. After assembly, the multilayered coatings were dried in air.

Thickness of LBL Films. The thickness of multilayered coatings was determined by an electronic micrometer (Fowler IP 54). The area of each glass slide supporting the LBL film was divided into nine zones (3 × 3 grid) with thickness assessed three times in each zone. Data are reported as the mean thickness value from all sites. The thickness of LBL films was also measured by ellipsometry using a MM-16 spectroscopic liquid crystal modulation ellipsometer (Horiba Jobin Yvon Ltd).

Scanning Electron Microscopy (SEM). SEM experiments used an FEI Quanta FEG 600 environmental scanning electron microscope with an acceleration voltage of 20 kV. The surface of LBL coatings was sputtered with gold before analysis.

Thermal Treatment and Determination of Equilibrium Swelling Degrees. The glass slides coated with multilayered films were treated at 120 °C for 2, 4, and 6 h in an oven. After thermal treatment, the slides were weighed and immersed in water at pH 2.0 for 24 h. After removal they were blotted dry, reweighed, and immersed in borate buffer at pH 9.2. After another 24 h the samples were removed, blotted, and again reweighed. The equilibrium swelling degree (g of water absorbed per 1 g of dry polymer) was calculated by

$$\text{swelling degree} = (w_s - w_d)/w_d \qquad (3)$$

where w_s and w_d are the weights of swollen and dry samples, respectively.

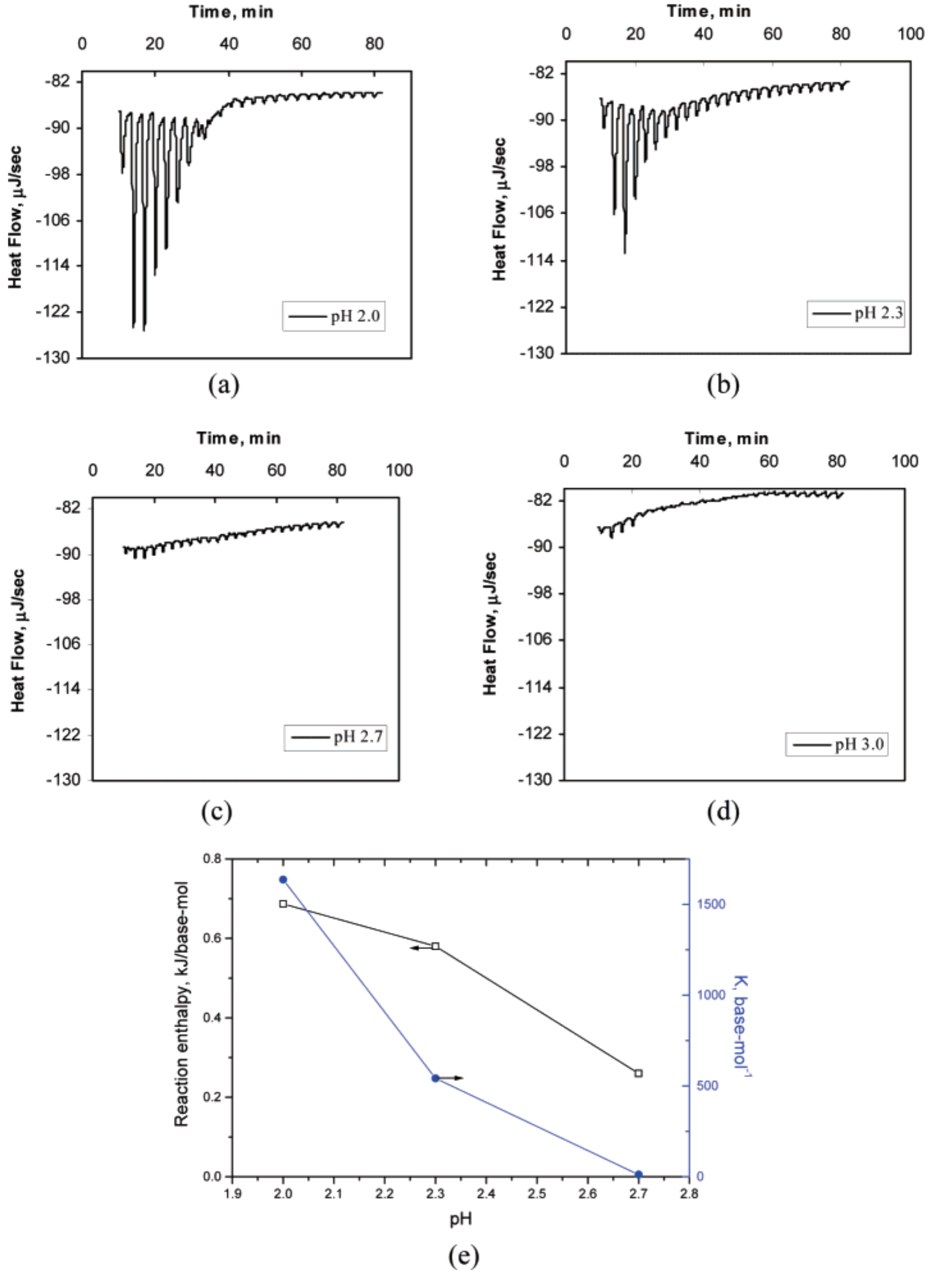


Figure 1. Isothermal titration calorimetry isotherms obtained by titration of 0.2 wt % methylcellulose with 2 wt % poly(acrylic acid) solution at different pH's (a−d); dependence of reaction enthalpy and binding constant on pH for the complexation between poly(acrylic acid) and methylcellulose (e).

Results and Discussion

Heat Effects in the Complexation between Poly(acrylic acid) and Methylcellulose. Isothermal titration calorimetry (ITC) directly measures heats generated in chemical reactions and has been widely used to study interactions involving biological molecules.[33−35] Recently, ITC was also used successfully to study complexation between oppositely charged polyelectrolytes[36] but to the best of our knowledge has not been used to probe reaction heats during hydrogen-bonded complexation between polymers.

Binding isotherms obtained by titrating 0.2 wt % MC solutions with 2 wt % PAA solutions at different pH's (pH 2.0, 2.3, 2.7, and 3.0) are shown in Figure 1a− d); titrations of water against 2 wt % PAA or 0.2 wt % MC at these pHs were also performed as control experiments. It can be clearly seen from the figure that stronger thermal effects are observed in solutions with lower pH. The enthalpy of complexation at different pH's was determined by BindWorks 3.1 software. Data fits were obtained using the independent set of multiple binding sites model. The changes in reaction enthalpy (ΔH) as well the binding constant (K) as a function of solution pH are shown in Figure 1e, and the numerical data are summarized in Table 1 (see Supporting Information). It should be noted that the experimental results obtained for the titration at pH 3.0, which demonstrated negligible thermal effects, could not be accurately fitted. These results show that the enthalpy of complexation between pH 2.0−2.7 is positive and that enthalpy decreases with increasing pH. The positive ΔH confirms the importance of hydrophobic effects in the complex formation. The heat effects found for the complexation between PAA and MC (0.26−0.69 kJ/base-mol) are consistent with values reported for complexes of PAA with poly(ethylene oxide)s (0.35 kJ/base-mol).[22]

The binding constants K = [IPC]/([PAA][MC]) for the complexes of PAA and MC range from 12 to 1637 base-mol^{-1}

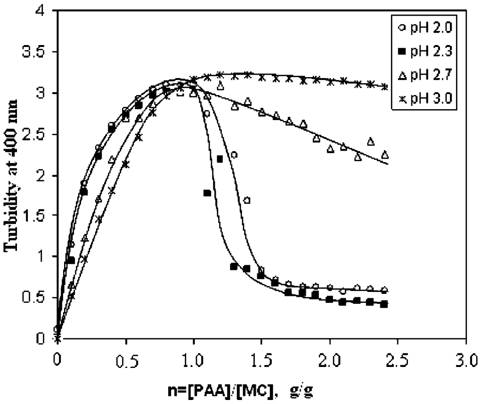


Figure 2. Turbidimetric titration of 0.2 wt % methylcellulose solution with 2 wt % poly(acrylic acid) solutions at different pH's.

and are also similar to the values reported by Eagland and coworkers,[22] although strict comparison of our results with this literature data is not possible because those experiments were performed in solutions without pH adjustment. The IPC stoichiometry n = [PAA]/[MC] was unaffected by changes in solution pH and remained at 1.5 ± 0.1. Thus, ITC is an excellent technique that can be used to estimate thermodynamic parameters of complexation between polymers via hydrogen-bonding and provides not only data regarding the strength of interaction but also IPC stoichiometry.

Aggregation of Complexes at Different pH. The formation of complexes in solutions was additionally studied by turbidimetric titration since mixing PAA with MC provides turbid solutions as IPC's form. Figure 2 shows the turbidimetric titration curves obtained by adding 2 wt % PAA solution to 0.2 wt % MC (as used for the ITC studies) at different pH's.

All the titrations performed at pH 2.0, 2.3, 2.7, and 3.0 are accompanied by increases in solution turbidity. The maximal turbidity values correspond with a 1:1 (g/g) stoichiometry of the PAA/MC complex, which is slightly lower than 1.5:1 (g/g) value determined by ITC. The difference in the IPC's stoichiometry may result from experimental differences since ITC data are composite and assess factors such as hydrogen bonding, desolvation, and compaction of chains and aggregation, whereas the turbidimetric method only monitors the aggregation processes. However, further addition of PAA decreases turbidity, most markedly at pH 2.0 and 2.3. This decrease is probably due to strong aggregation of IPC particles and their consequent rapid precipitation, an effect that would be expected to be more significant at lower pH's where surface charge of the complexes is reduced, which thus promotes aggregation. It is interesting to note that the ITC isotherms observed at pH 2.0 and 2.3 also show more pronounced peaks, i.e., demonstrate stronger thermal effects. It is well-known[32] that the formation of IPC's is a complex process, consisting of several stages (Figure 3): initially "ladder-type" structures form via hydrogen bonding (stage 1) followed by compaction of these structures into primary IPC particles (stage 2) which further aggregate (stage 3). It is likely that the major contribution to the strong thermal effects observed in ITC experiments at pH 2.0 and pH 2.3 is the further aggregation stage (stage 3) of complexation, which correlates well with the calorimetric data. The complexes formed at pH 2.7 and 3.0 are more colloidally stable, again largely due to surface charge effects.

To probe further the structural organization of IPC's, we prepared complexes by mixing PAA and MC (30:70 wt %) at three different pHs (1.4, 2.4, and 3.2). These pH values were chosen to cover a slightly broader pH range than we studied by ITC and turbidimetry, while the 30:70 wt % ratio was selected to ensure that the IPC's maintain good colloidal stability and do not precipitate for several days. The structure of the complexes was then examined by transmission electron microscopy (Figure 4a−c). The IPC's obtained at pH 1.4 and 2.4 are spherical nanoparticles, with diameters between 80 and 200 nm. It should be noted that these images were obtained without heavy metal salt staining, and the relatively good contrast of the IPC confirms that they are relatively dense nanoparticles, able to scatter electrons. The IPC's formed at pH 3.2 have a completely different structure to those formed at lower pH's; they are much smaller (20−30 nm) and less dense (poorer contrast of TEM images), and they appear to be linked by fibrous structures forming a network. These findings suggest that the complexes formed between pH 3.0 and 3.2 are primary IPC particles, whose aggregation is prevented by the network formed by uncomplexed macromolecules. This absence of aggregation also explains the negligible thermal effects observed at pH 3.0 using ITC. As pH decreases below 3.0, these uncomplexed macromolecules tend to form interpolymer hydrogen bonds and compact leading to further aggregation of primary IPC into larger nanoparticles with denser structures. These results provide the first data showing structural transitions in IPC organization at different pHs; previously, these structural transitions were predicted from indirect results.[16,23]

Multilayered Materials Based on Complexes of Poly(acrylic acid) and Methylcellulose. As was shown above, the strongest interaction between PAA and MC is observed in aqueous solutions at pH 2.0. These conditions were used to construct multilayered materials (layer-by-layer) on a glass substrate. The transparency of the dried coating decreased with the number of deposited layers. The thickness of the multilayered coatings was measured by two different techniques: a digital micrometer and ellipsometry. Figure 5a displays the dependence of multilayer coating thickness as a function of the number of monolayers, showing that both measurement techniques gave similar results.

The sample thickness obtained by micrometry provided broader standard deviations compared to ellipsometry because the measurements were performed at several contact points, and the results were statistically treated. Ellipsometric data were obtained by probing materials at single contact point. A linear relationship between the samples thickness and the number of deposited layers is evident, demonstrating good control of the deposition process. The surface morphology of dried multilayers was studied by scanning electron microscopy (Figure 5b), which clearly shows the presence of spherical IPC particles on the surface.

Ultrathin Hydrogels Based on Multilayered Materials. Multilayered materials deposited on flat surfaces are usually tightly bound to the substrate, which raises difficulties for obtaining free-standing films. Recently, Lutkenhaus and coworkers[37] and Jaber and Schlenoff[38] used neutral, hydrophobic substrates such as Teflon and polypropylene for LBL deposition to allow the multilayered assembly to be detached. Previously, it has been shown that thermal treatment of bulk PAA-MC films at 120 °C for 2−6 h results in the polymers cross-linking.[27] In the present study we have cross-linked multilayered PAA-MC coatings by a similar thermal treatment since such cross-linking with subsequent swelling in water will either form permanent hydrogel coatings on the surface of polar glass slides or will facilitate the detachment of multilayered ultrathin hydrogels.

Indeed, the thermal treatment of the glass slides coated with 10 monolayers resulted in polymer cross-linking; after heating

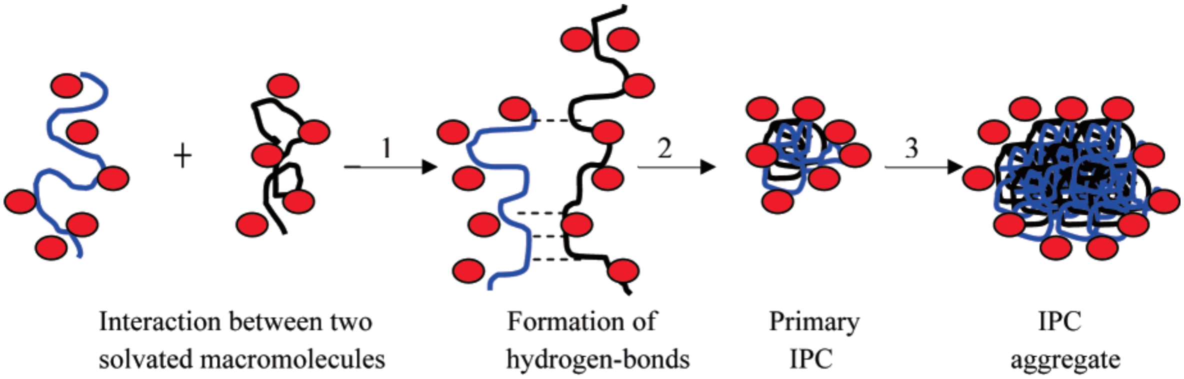


Figure 3. Scheme of IPC formation in solutions (circles are molecules of water).

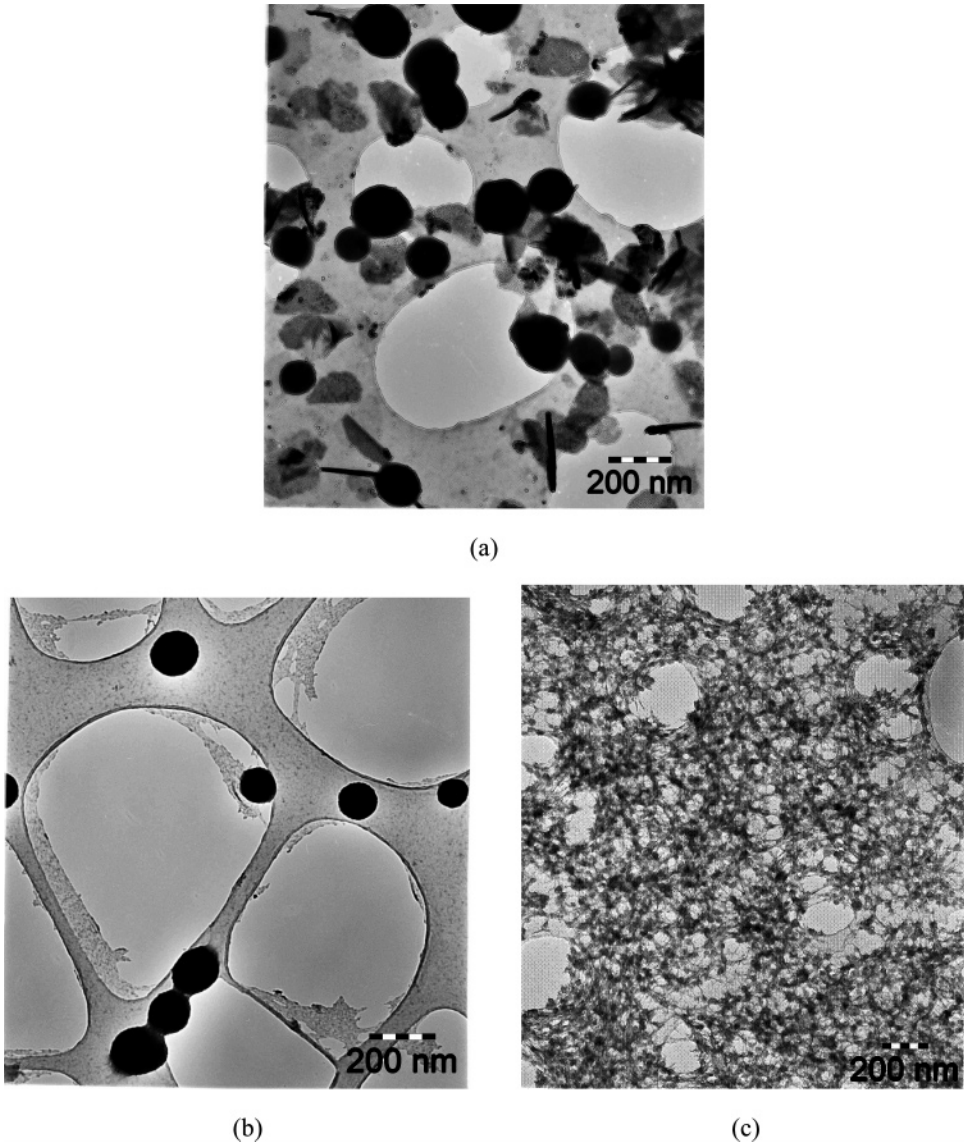
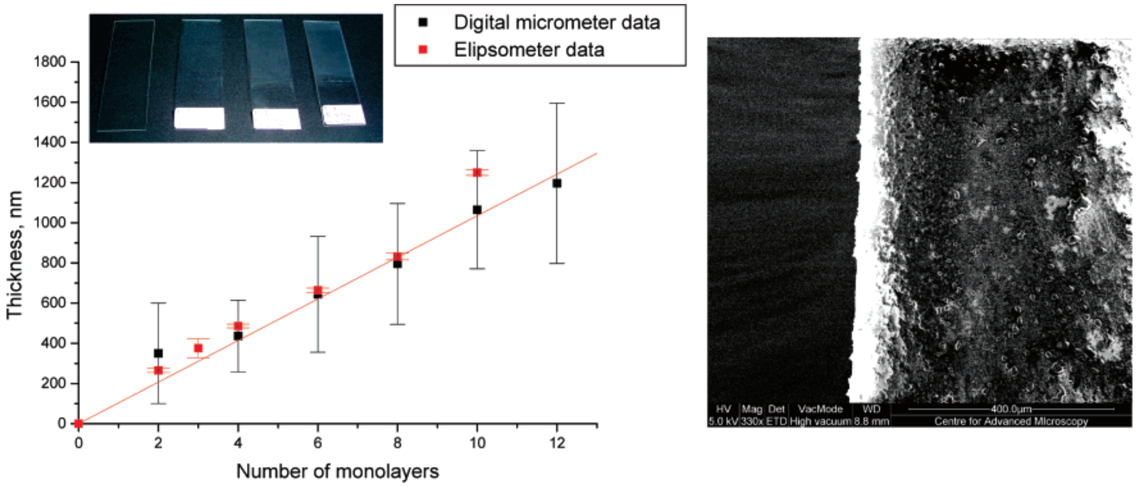


Figure 4. Transmission electron microscopy image of interpolymer complexes obtained from 0.2 wt % solution mixtures of poly(acrylic acid) and methylcellulose (30:70 wt %) at pH 1.4 (a), 2.4 (b), and 3.2 (c).

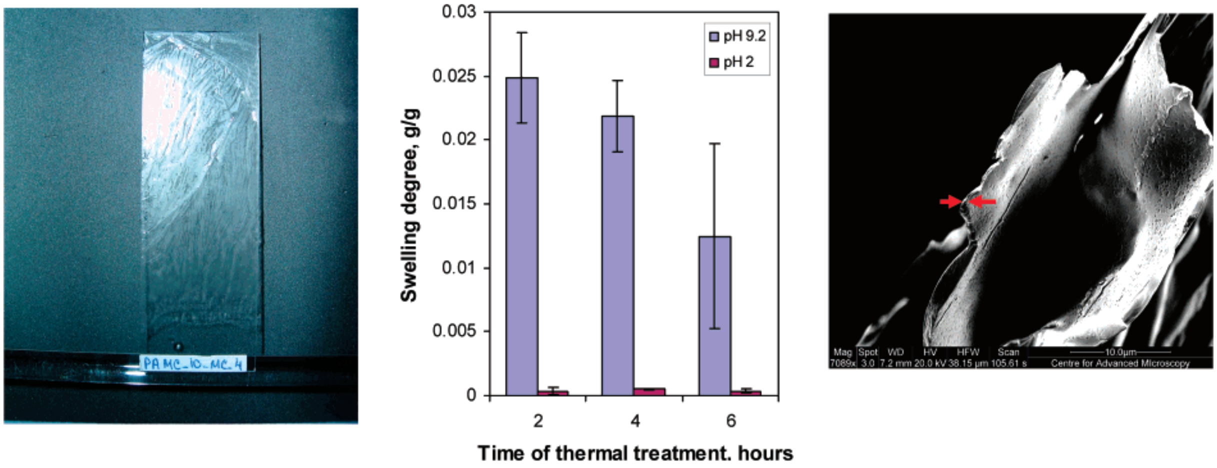
for 2, 4, or 6 h, the preweighed slides were immersed in water at pH 2.0 for 24 h, which caused neither polymer dissolution nor detachment of the ultrathin films. After blotting with a filter paper the samples were weighed again and then reimmersed in buffer solution at pH 9.2 for a further 24 h. This immersion resulted in immediate swelling of the polymer coating, which can be seen in Figure 6a.

The degrees of swelling on the glass surface in acidified water (pH 2.0) and alkaline buffer (pH 9.2) are presented in Figure 6b. It is apparent that increasing thermal treatment time reduced the swelling capacity of the hydrogels, which is likely to be due to increased cross-linking density of the polymers with time. Swelling of the LBL films is pH-dependent with essentially no swelling at pH 2.0, presumably because interpolymer hydrogen



(a) (b)

Figure 5. Multilayered poly(acrylic acid)−methylcellulose films on the surface of glass. Photoimage of multilayered coating (a, inset). Thickness of multilayered film as a function of monolayer numbers (a) and scanning electron microscopy image of multilayered film surface (b).



(a) (b) (c)

Figure 6. Image of swollen hydrogel layer on the surface of glass slide (a), degree of swelling of layer-by-layer hydrogel as a function of thermal treatment time (b), and scanning electron microscopy image of dry film detached from the glass (c).

bonding is facilitated under these conditions. Further, the hydrogen bonding between the LBL film and Si−OH groups on a glass surface does not allow the multilayer films to be detached. The swelling of multilayer coatings at pH 9.2 is caused by dissociation of carboxylic groups of PAA with subsequent disruption of hydrogen bonding. However, the degree of swelling of these ultrathin films is much lower compared to that of PAA-MC films obtained by casting from solutions and cross-linked thermally in a similar manner.[27] Perhaps, when the hydrogels thickness approaches micro- or nanometers, the samples can no longer be considered as 3-dimensional but rather as 2-dimensional materials with sorption capacity determined by surface area and not by sample volume.

The hydrogel coatings swollen at pH 9.2 were easily detached from the glass slides in the form of ultrathin hydrogel films (see Supporting Information). After drying, the multilayered films were analyzed by scanning electron microscopy (Figure 6c), which showed that the film thickness (arrows) is less than 1 μm, in good agreement with the thickness measured on the glass surface. Spherical IPC particles constituting this film can again be clearly seen. This material can be reswollen again upon immersion in water to form an ultrathin hydrogel. The presence of both PAA and MC in the detached film was confirmed by infrared spectroscopy (see Supporting Information); peaks at 1575 and 1074 cm^{-1} typical for carboxylate ions of PAA and ether groups of MC, respectively, are evident in the spectra of the cross-linked multilayered film, which was swollen at pH 9.2, detached from glass surface and dried. The multilayered film, which was simply scraped from glass surface, shows these spectral features at 1724 and 1062 cm^{-1}, corresponding to hydrogen-bonded undissociated carboxylic groups (−COOH) of PAA and ether bonds of MC, respectively.

Conclusions

Complexation between poly(acrylic acid) and methylcellulose via hydrogen bonding can be successfully utilized to prepare polymeric nanoparticles, multilayered coatings, and ultrathin hydrogel films. The pH of the polymer solutions plays an important role in the strength of interpolymer interactions. The calorimetric and turbidimetric data on the complexation between poly(carboxylic acids) and nonionic polymers can be used to optimize the conditions for preparation of nanoparticles in solutions or multilayered coatings on a glass surface.

The thickness of multilayered films assembled on the surface of glass slides via layer-by-layer deposition of interpolymer complexes is a linear function of the number of deposition cycles. These films can be further cross-linked by thermal treatment at 120 °C for 2−6 h. The cross-linked materials have poor swelling properties and do not detach from glass surface at pH 2.0 because this medium favors the formation of hydrophobic interpolymer complexes between the polymers and possibly facilitates noncovalent interactions with glass. At pH 9.2 the interpolymer complexes dissociate and cross-linked films start to absorb water and swell. The swelling results in formation of ultrathin hydrogel materials, which gradually detach from glass slides.

The polymers used in this study, poly(acrylic acid) and methylcellulose, are both biocompatible and nontoxic and widely used as pharmaceutical excipients, raising the possibility of preparing both nanoparticles and multilayered materials for advanced drug delivery systems or as selective membranes. One further advantage of using complexes based on this pair of polymers is their ability to cross-link through thermal treatment offers a simple control over the degree of cross-linking.

Acknowledgment. This work was supported by the Biotechnology and Biological Sciences Research Council UK (BBSRC project BB/E003370/1). The authors thank Dr. R. J. Green for helpful discussion on the use of isothermal titration calorimetry. Dr D. Sheppard and Dr. A. Holland (Horiba Jobin Yvon Ltd.) are gratefully acknowledged for their help in ellipsometric measurements. Dr. P. Harris and Dr. C. Stain from the Centre for Advanced Microscopy (University of Reading) are acknowledged for their help in TEM/SEM experiments.

Supporting Information Available: Complexation enthalpies and constants; image of swollen multilayered film detaching from the glass surface; FTIR spectra of methylcellulose powder, poly(acrylic acid) powder, LBL untreated, and LBL detached. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Decher, G. *Science* **1997**, *277*, 1232−1237.
(2) Sukhishvili, S. A.; Granick, S. *J. Am. Chem. Soc.* **2000**, *122*, 9550−9551.
(3) Kharlampieva, E.; Sukhishvili, S. A. *Langmuir* **2004**, *20*, 9677−9685.
(4) Kharlampieva, E.; Sukhishvili, S. A. *Langmuir* **2004**, *20*, 10712−10717.
(5) Bai, S.; Wang, Z.; Zhang, X.; Wang, B. *Langmuir* **2004**, *20*, 11828−11832.
(6) Yang, S.; Zhang, Y.; Yuan, G.; Zhang, X.; Xu, J. *Macromolecules* **2004**, *37*, 10059−10062.
(7) DeLongchamp, D. M.; Hammond, P. T. *Langmuir* **2004**, *20*, 5403−5411.
(8) Quinn, J. F.; Caruso, F. *Langmuir* **2004**, *20*, 20−22.
(9) Quinn, J. F.; Caruso, F. *Macromolecules* **2005**, *38*, 3414−3419.
(10) Kozlovskaya, V.; Yakovlev, S.; Libera, M.; Sukhishvili, S. A. *Macromolecules* **2005**, *38*, 4828−4836.
(11) Lee, D.; Rubner, M. F.; Cohen, R. E. *Chem. Mater.* **2005**, *17*, 1099−1105. Li, Z.; Lee, D.; Rubner, M. F.; Cohen, R. E. *Macromolecules* **2005**, *38*, 7876−7879.
(12) Tian, Y.; He, Q.; Cui, Y.; Tao, C.; Li, J. *Chem.*−*Eur. J.* **2006**, *12*, 4808−4812.
(13) Kharlampieva, E.; Sukhishvili, S. A. *Polym. Rev.* **2006**, *46*, 377−395.
(14) Smith, K. L.; Winslow, A. E.; Petersen, D. E. *Ind. Eng. Chem.* **1959**, *51*, 1361−1364.
(15) Bailey, F. E.; Lundberg, R. D.; Callard, R. W. *J. Polym. Sci., Part A* **1964**, *2*, 845−851.
(16) Khutoryanskiy, V. V.; Dubolazov, A. V.; Nurkeeva, Z. S.; Mun, G. A. *Langmuir* **2004**, *20*, 3785−3790.
(17) Abe, K.; Ohno, H.; Nii, A.; Tsuchida, E. *Makromol. Chem.* **1978**, *179*, 2043−2050.
(18) Staikos, G.; Karayanni, K.; Mylonas, Y. *Macromol. Chem. Phys.* **1997**, *198*, 2905−2915.
(19) Bokias, G.; Staikos, G. *Recent Res. Dev. Macromol. Res.* **1999**, *4*, 247−259.
(20) Tsuchida, E.; Osada, Y.; Ohno, H. *J. Macromol. Sci., Phys.* **1980**, *17*, 683−714.
(21) Baranovskii, V. Y.; Zenkov, I. D.; Kabanov, V. A. *Vysokomol. Soed., Ser. A* **1989**, *31*, 493−496.
(22) Eagland, D.; Crowther, N. J.; Butler, C. J. *Eur. Polym. J.* **1994**, *30*, 767−773.
(23) Dubolazov, A. V.; Nurkeeva, Z. S.; Mun, G. A.; Khutoryanskiy, V. V. *Biomacromolecules* **2006**, *7*, 1637−1643.
(24) Budtova, T. V.; Belnikevich, N. G.; Belyaev, V. M.; Panov, Y. N.; Frenkel, S. Y. *Vysokomol. Soed., Ser. B* **1991**, *33*, 520−524.
(25) Budtova, T.; Navard, P. *Macromolecules* **1996**, *29*, 3931−3936.
(26) Lu, X. H.; Hu, Z. B.; Schwartz, J. *Macromolecules* **2002**, *35*, 9164−9168.
(27) Khutoryanskiy, V. V.; Cascone, M. G.; Lazzeri, L.; Nurkeeva, Z. S.; Mun, G. A.; Mangazbaeva, R. A. *Polym. Int.* **2003**, *52*, 62−67.
(28) Nurkeeva, Z. S.; Mun, G. A.; Khutoryanskiy, V. V. *Macromol. Biosci.* **2003**, *3*, 283−295.
(29) Bumbu, G. G.; Vasile, C.; Eckelt, J.; Wolf, B. A. *Macromol. Chem. Phys.* **2004**, *205*, 1869−1876.
(30) Bumbu, G. G.; Vasile, C.; Chitanu, G. C.; Staikos, G. *Macromol. Chem. Phys.* **2005**, *206*, 540−546.
(31) Mangazbaeva, R. A.; Mun, G. A.; Nurkeeva, Z. S.; Khutoryanskiy, V. V. *Polym. Int.* **2006**, *55*, 668−674.
(32) Khutoryanskiy, V. V. *Int. J. Pharm.* **2007**, *334*, 15−26.
(33) Chen, W. Y.; Huang, H. M.; Lin, C. C.; Lin, F. Y.; Chan, Y. C. *Langmuir* **2003**, *19*, 9395−9403.
(34) Freire, E. *Drug Discovery Today: Technol.* **2004**, *1*, 295−299.
(35) Gourishankar, A.; Shukla, S.; Ganesh, K. N.; Sastry, M. *J. Am. Chem. Soc.* **2004**, *126*, 13186−13187.
(36) Bucur, C. B.; Sui, Z.; Schlenoff, J. B. *J. Am. Chem. Soc.* **2006**, *128*, 13690−13691.
(37) Lutkenhaus, J. L.; Hrabak, K. D.; McEnnis, K.; Hammond, P. T. *J. Am. Chem. Soc.* **2005**, *127*, 17228.
(38) Jaber, J. A.; Schlenoff, J. B. *J. Am. Chem. Soc.* **2006**, *128*, 2940−2947.

MA071644V