

## CHAPTER 1

### pH- AND IONIC STRENGTH EFFECTS ON INTERPOLYMER COMPLEXATION VIA HYDROGEN-BONDING

Vitaliy V. Khutoryanskiy<sup>1\*</sup>, Artem V. Dubolazov<sup>2</sup>, Grigoriy A. Mun<sup>2</sup>

<sup>1</sup>*Reading School of Pharmacy, University of Reading, Whiteknights,  
PO Box 224, RG6 6AD, Reading, United Kingdom*

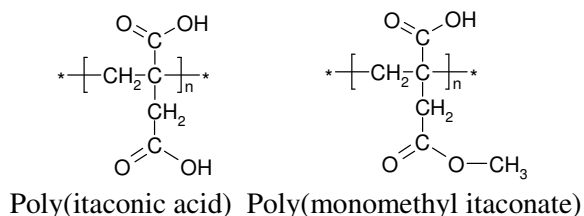
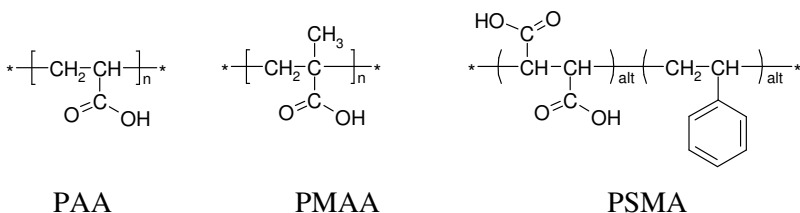
*\*E-mail: v.khutoryanskiy@reading.ac.uk*

<sup>2</sup>*Department of Chemical Physics and Macromolecular Chemistry,  
Kazakh National University, 95 Karasai Batyra Street,  
050012 Almaty, Kazakhstan*

When poly(carboxylic acids) are mixed with non-ionic polymers in aqueous solutions, a phase separation can be observed which is often accompanied by formation of precipitates. These precipitates are in fact novel individual polymeric compounds termed interpolymer complexes (IPCs) or polymer-polymer complexes. The precipitation in the mixtures of poly(carboxylic acids) with non-ionic polymers was reported for the first time in 1959 by Smith and co-workers,<sup>1</sup> when two water-soluble polymers (poly(acrylic acid) (PAA) and poly(ethylene oxide)) were mixed together in aqueous solutions resulting in immediate formation of insoluble IPCs. These precipitates were separated, dried and their physicochemical properties were examined by a number of techniques, including the study of mechanical properties at different temperatures and polymer ratios, X-ray patterns and heat stability evaluation. It was concluded that the unique properties of precipitates result from hydrogen-bonding between ether and carboxyl groups of the polymers. It was also pointed out that the complexes may be formed not only between PAA and poly(ethylene oxide) (PEO) but also by many other non-ionic polymers such as poly(vinyl ethers), cellulose ethers and a large variety of hydroxyl-containing polymers.

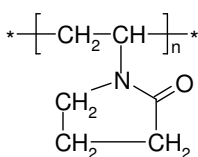
Few years later, Bailey and co-workers<sup>2</sup> published the second paper on the complexation between polymers via hydrogen-bonding. This study was also focused on the interaction between PAA and PEO with the aim to elucidate the effects of pH and composition on the solution viscosity of polymer/polymer mixture. They demonstrated that the product of interaction between PAA and PEO forms a precipitate at pH below 3.8, whereas at higher pH the polymers co-exist in aqueous solution. Depending on solution pH and PAA/PEO ratio the rheological properties of the polymers mixture displayed a varying degree of association between carboxyl and ether groups. Working with the relatively concentrated solutions of PAA and PEO (0.05–2 wt %) the authors<sup>2</sup> have demonstrated that their mixtures exhibit a higher viscosity compared to the pure components with a maximum corresponding to the IPC stoichiometry. It was demonstrated that the interaction between these polymers is driven by hydrogen-bonding and the IPC stoichiometry approaches 1:1. Whilst at low pH (pH < 3.8), the interaction results in phase separation, at higher pH, the polycomplex exists in solution. In the neutral pH region, they also observed some interaction between the two polymers.

At present, more than 50 poly(carboxylic acid) – non-ionic polymer pairs are known to form hydrogen-bonded complexes. The most commonly used water-soluble poly(carboxylic acids) include PAA, poly(methacrylic acid) (PMAA), styrene-maleic acid copolymer (PSMA) as well as poly(itaconic acid) and its derivatives:

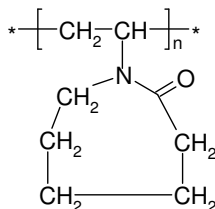


The list of non-ionic polymers forming IPC with poly(carboxylic acids) is more broad and includes several classes<sup>3</sup>:

1. *Polymers, containing lactame groups.*

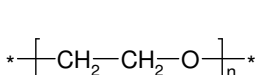


Poly(N-vinyl pyrrolidone) (PVP)

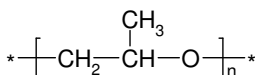


Poly(N-vinyl caprolactame)

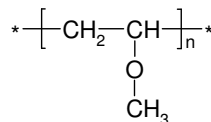
2. *Polymers containing ether groups either in the backbone (PEO, poly(propylene glycol) (PPG)) or as pendants (poly(vinyl methyl ether) (PVME)).*



PEO

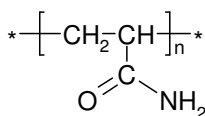


PPG

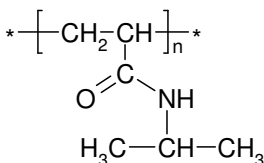


PVME

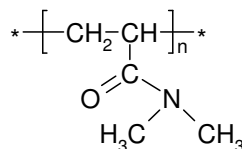
3. *Acrylic type polymers, such as polyacrylamide (PAAM), poly(N-isopropylacrylamide) (PNIPAAM) and poly(N,N-dimethylacrylamide) (PDMAA).*



PAAM

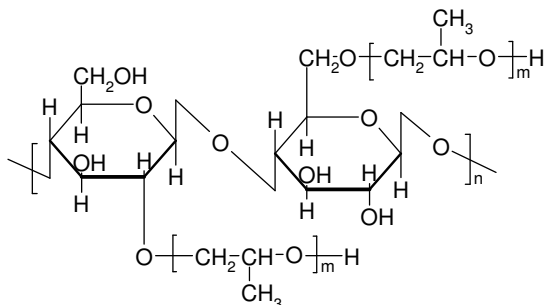


PNIPAAM

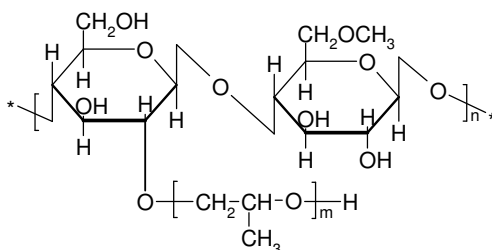


PDMAA



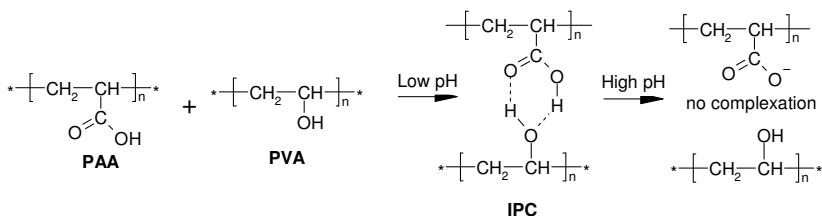


Hydroxypropylcellulose (HPC)



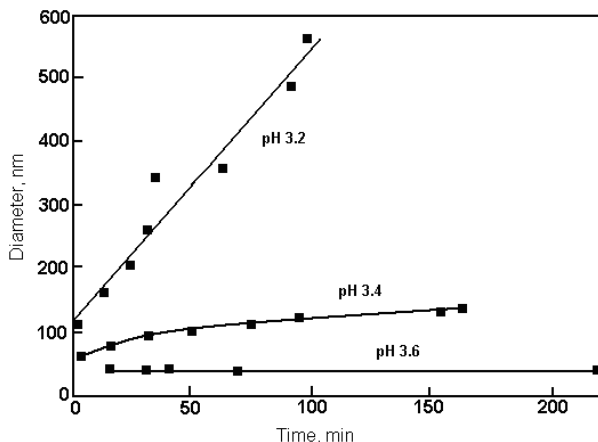
Hydroxypropylmethylcellulose (HPMC)

All poly(carboxylic acids) are weak polyelectrolytes, which ionisation is pH dependent. At low pH, they exist in non-ionised form and at high pH the carboxylic groups are fully ionised. Only unionised carboxylic groups can form hydrogen bonds with proton-accepting non-ionic polymers. By this reason, insoluble IPC may be formed under acidic conditions and dissociate upon increase in pH:



The complexation between poly(carboxylic acids) and non-ionic polymers occurs instantaneously upon mixing of solutions. This very fast process cannot be studied by conventional physicochemical techniques. However, the fast complexation can be followed by the aggregation of

primary complexes, which rate is strongly dependent on many factors including temperature, concentration and pH. Usaitis and co-workers<sup>4</sup> have studied the aggregation of IPC formed by PMAA and PVP at different pHs using dynamic light scattering (DLS). The most pronounced increase in the IPC particle diameter was observed for the complexation at pH 3.2, where the particle size increased from 100 to 550 nm within 100 min. At lower pHs (3.4 and 3.6), the aggregation was less intensive resulting in smaller IPC particles (**Fig. 1**).



**Fig. 1.** Average diameter of PMAA-PVP complex particles as a function of time at different pH. Reproduced from Usaitis A., Maunu L.S., Tenhu H. Aggregation of the interpolymer complex of poly(methacrylic acid) and poly(vinyl pyrrolidone) in aqueous solutions, *European Polymer Journal*, 33, 219-223 ©1997 (Ref. 4) with permission from Elsevier.

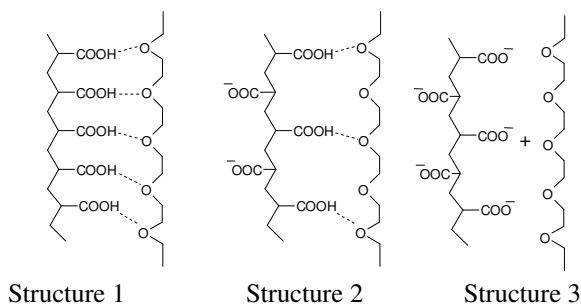
Ohno and co-workers<sup>5</sup> as well as Hemker and Frank<sup>6</sup> have studied the aggregation of complexes formed by PMAA and PEO by dynamic light scattering. It was demonstrated<sup>5</sup> that lower pH and higher temperature make the aggregation faster and spherical shape of aggregates was confirmed using scanning electron microscopy. A dramatic growth in light scattering was observed at  $\text{pH} < 3.0$ , whereas no significant changes in scattering-light intensity were detected at pH within 4.0–6.0. Similar observations were reported by Hemker and Frank,<sup>6</sup> however, in this study a significant increase in the IPC radius (from 50 to more than

200 nm) was observed at  $\text{pH} < 1.9$ . In the  $\text{pH}$  range 2.1–2.7, the radius remained unchanged at 48 nm. The difference of this result from the data reported by Ohno and co-workers<sup>5</sup> was explained by lower molecular weight of PMAA. The kinetics of IPC aggregation was also studied and it was demonstrated that the increase in size can be described by a power law relationship:

$$\langle R \rangle = R' \cdot t^b,$$

where  $\langle R \rangle$  is IPC radius (nm),  $t$  is time (min),  $R'$  and  $b$  are constants.

The effect of  $\text{pH}$  on the complexation of PEO with different poly(carboxylic acids) such as PAA, PMAA and PSMA in aqueous solutions has extensively been studied by Ikawa and co-workers.<sup>7</sup> They demonstrated that the yield of IPC increases drastically below a certain  $\text{pH}$  value, which was called critical  $\text{pH}$  of complexation ( $\text{pH}_{\text{crit}}$ ). It was shown that the  $\text{pH}_{\text{crit}}$  depends on the nature of poly(carboxylic acid) and increases with increase in dissociation constant ( $\text{pK}_a$ ). The composition and the structure of IPC were also found to be  $\text{pH}$ -dependent. The existence of a certain level of unionised carboxylic groups is necessary for PMAA and PEO to form stable IPC through hydrogen-bonding. A stable IPC with 1:1 molar stoichiometry is formed at  $\text{pH} < \text{pH}_{\text{crit}}$  (Structure 1), whereas at  $\text{pH}$  slightly higher than  $\text{pH}_{\text{crit}}$  the deviation from the 1:1 stoichiometry is observed (Structure 2). When the  $\text{pH}$  is high and carboxylic groups are fully ionised, the IPC is not formed (Structure 3):



Based on the studies discussed above, it can be concluded that the existence of a critical  $\text{pH}$  is a fundamental property of hydrogen-bonded IPCs, which determines the possibility of their formation, stoichiometry

and structure. In the following sections we will consider the physical methods used to determine  $\text{pH}_{\text{crit}}$  and factors affecting this value.

### 1. Methods used for determination of critical pH values

At present a number of methods are commonly used for determination of  $\text{pH}_{\text{crit}}$  values. All these methods are based on a measurement of a complexation parameter as a function of environmental pH.

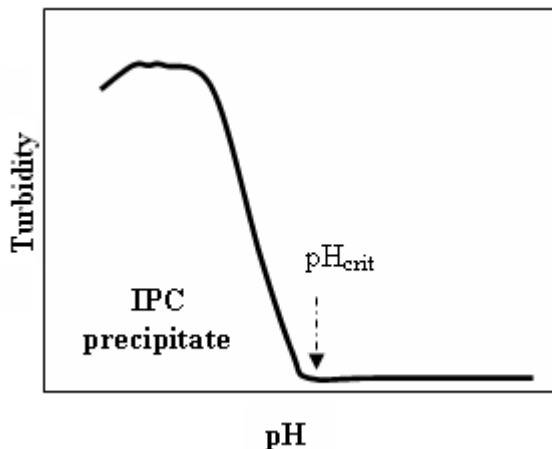
#### a) Yield of IPC precipitate as a function of pH

The gravimetric method suggested by Ikawa and co-workers<sup>7</sup> involves a mixing of the interacting polymers in solutions with different pH, separation of precipitate formed, drying and weighing of the final IPC. pH at which a drastic increase in the IPC yield is observed corresponds to the  $\text{pH}_{\text{crit}}$ . However, this method is time-consuming and centrifugation must be applied to ensure a complete isolation of insoluble complexes.

#### b) Turbidity of IPC solution as a function of pH

We suggested use of turbidimetry as a simple and fast alternative to the gravimetric method for determination of critical pH.<sup>8-11</sup> In this method, solutions of interacting polymers are mixed at pH 5–6 to make sure that insoluble complex is not formed. pH is then gradually decreased upon addition of small portions of 0.1 M HCl and solution turbidity is measured in parallel with pH control. The wavelength for measurement of turbidity can be in the range of 400–600 nm. The typical dependence of solution turbidity on pH is shown in **Fig. 2**. When pH is high enough and an insoluble complex is not formed, the turbidity readings remain low. However, when solution pH reaches  $\text{pH}_{\text{crit}}$ , the turbidity increases drastically, which can often be seen even by the naked eye. The drastic increase in solution turbidity within a narrow pH range is an indication of the cooperativity of the complexation process.

When pH is below  $\text{pH}_{\text{crit}}$ , the IPC continues to aggregate and forms larger particles. The aggregation process reaches saturation at some pH and then the turbidity does not change until the IPC particles start to precipitate, which may result in a slight decrease in turbidity.



**Fig. 2.** Typical dependence of solution turbidity on pH for the complexation between poly(carboxylic acid) and non-ionic polymer.

*c) Viscosity of IPC solution as a function of pH*

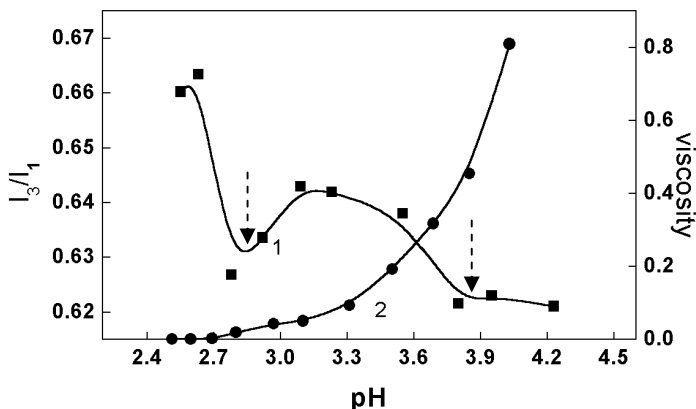
This method is based on the possibility to follow the conformational changes happening with the macromolecules upon complexation.<sup>12,13</sup> When the interacting macromolecules are mixed at relatively high pH, the solution viscosity is quite high. However, a gradual decrease in pH will lead to compaction of macromolecules, which is most pronounced when IPC is formed.

*d) Fluorescence spectra as a function of pH*

The fluorescent methods can be used for the study of interpolymer interactions when fluorescent molecules are either covalently linked with one of the interacting polymers or simply dispersed in the IPC solution. These methods will be considered in detail in Chapter 4. Here, we will briefly discuss the use of fluorescent methods for the study of pH effects in complexation.

The ability of the fluorescent probe pyrene to migrate into a more hydrophobic environment and change the intensity ratio of the third (383 nm) to the first (373 nm) vibronic peaks  $I_3/I_1$  in its emission spectra can be used to study pH-effects in the complexation between

poly(carboxylic acids) and non-ionic polymers and to determine the critical pH values. The  $I_3/I_1$  value for pyrene solubilised in distilled water is around 0.60-0.64. In more hydrophobic environment, this ratio increases, which may help to follow formation of non-polar domains upon complexation. In a series of studies,<sup>13-15</sup> we have demonstrated the possibility of using pyrene probe for determination of the critical pH. In these experiments free pyrene molecules were introduced to the IPC aqueous dispersion and pH of solution was varied to monitor how it affects the  $I_3/I_1$  ratio. **Figure 3** shows the dependence of pyrene  $I_3/I_1$  ratio and solution viscosity for PAA-PVA complexes as a function of pH.



**Fig. 3.** Dependence of pyrene  $I_{383}/I_{373}$  ratio (1) and specific viscosity (2) of PAA-PVA equimolar 0.01 base-mol/L solutions on pH. Reproduced from Nurkeeva Z.S., Mun G.A., Dubolazov A.V., Khutoryanskiy V.V. pH effects on the complexation, miscibility and radiation-induced crosslinking in poly(acrylic acid)-poly(vinyl alcohol) blends, *Macromolecular Bioscience*, 2005, 5, 424-432 (Ref. 13). Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

When pH is high (pH 3.75–4.25) and the IPC are not formed the  $I_{383}/I_{373}$  ratio approaches 0.62, the value typical for a polar, aqueous environment. A decrease in pH within 3.75–3.20 is accompanied by an increase in  $I_3/I_1$ , confirming the formation of more hydrophobic environment in the system. A further decrease in pH results in the lowering of  $I_3/I_1$  until pH 2.75, then this ratio increases again. We explained this complicated dependence of  $I_3/I_1$  by the existence of two

critical pH values ( $\text{pH}_{\text{crit1}}$  and  $\text{pH}_{\text{crit2}}$ ), which are shown by the arrows. Below  $\text{pH}_{\text{crit1}}$ , the hydrophobic IPC aggregate is formed; above  $\text{pH}_{\text{crit2}}$ , there is no interaction between macromolecules. At pH in between  $\text{pH}_{\text{crit1}}$  and  $\text{pH}_{\text{crit2}}$ , the product of interpolymer interaction exists in a more hydrophilic form. It should be noted that the values of  $\text{pH}_{\text{crit1}}$  determined by this fluorescent method are in good agreement with the values determined by turbidimetric and viscometric approaches.

Numerous attempts have also been made to study the pH effects on the complexation between polymers, when pyrene is covalently linked to macromolecules of one type.<sup>16</sup> However, in this case the complexation ability of modified macromolecules is enhanced greatly due to the contribution of non-polar pyrene groups to the stabilisation of IPC by hydrophobic effects. For example, according to Sivadasan and co-workers<sup>16</sup> the IPC formed by PAA and PAAM labeled with pyrene is characterised by  $\text{pH}_{\text{crit}}$  4–5, whereas the turbidimetric determination of  $\text{pH}_{\text{crit1}}$  carried out for PAA and unmodified PAAM by using the turbidimetric method gives  $\text{pH}_{\text{crit1}}$  2.5–3.5.<sup>17</sup>

## **2. Factors affecting the critical pH values**

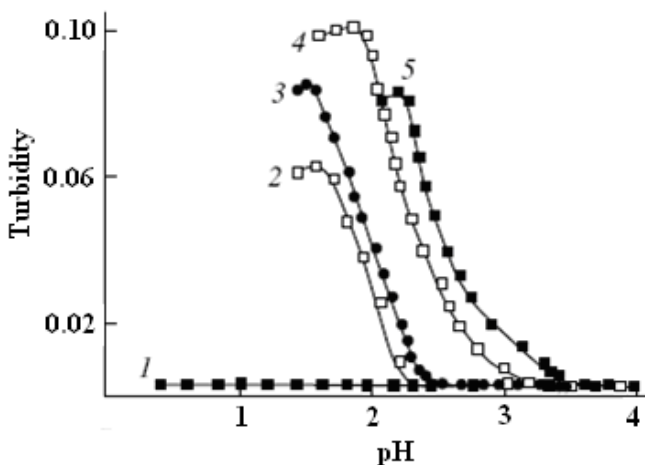
### *a) Concentration of polymers in solution*

In a number of studies, it has been shown that an increase in polymer concentration shifts the critical pH values to the higher region.<sup>9-11,17-19</sup> It is believed that an increase in the polymer concentration suppresses the ionisation of PAA, which favors the formation of intermacromolecular hydrogen bonds.

### *b) Molecular weight of polymers*

It is well known that the molecular weight of polymers affects the complexation. Kabanov and Papisov<sup>20</sup> have demonstrated the existence of a lower critical molecular weight of polymers, below which IPC are not formed. It was related to the importance of cooperative effects in complexation, which can be achieved only when the interacting macromolecules are long enough.

Critical pH values of complexation were also found to be affected by the molecular weight of the interactive polymers. **Fig. 4** shows the dependence of solution turbidity of 1:1 molar mixtures of PAA and HEC on pH for PAA samples with different molecular weight. An increase in PAA molecular weight within 250–1250 kDa leads to increase in the  $\text{pH}_{\text{crit}}$  values indicating an enhancement in the stability of IPC. However, the mixture of HEC with PAA 2 kDa remains fully transparent even at very low pH ( $\text{pH} < 1.0$ ). This behavior of the binary system can be due to the absence of the complexation because the chain length of PAA is lower than the minimal critical molecular weight.

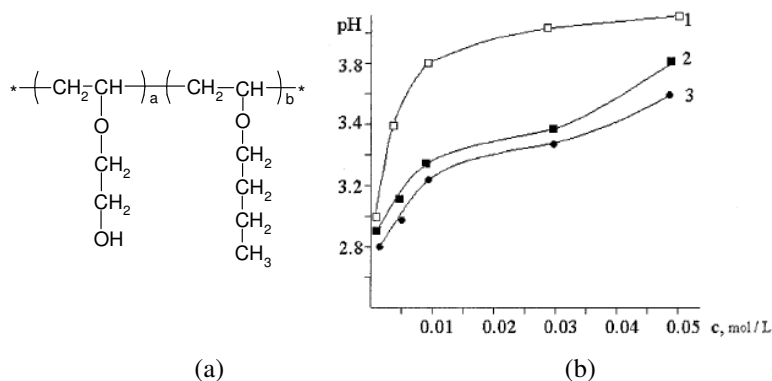


**Fig. 4.** Dependence of PAA-HEC (1:1 molar ratio) solution turbidity on pH. Molecular weights of PAA ( $M_w$ ): 2 (1), 250 (2), 450 (3), 750 (4) and 1250 kDa (5). The initial concentration of polymers is 0.01 base-mol/L. Reproduced with permission from Ref. 21.

### c) *Hydrophobicity of interacting polymers*

In addition to hydrogen-bonding, formation of IPC in aqueous solutions is stabilised by hydrophobic effects. As a result, the hydrophobic/hydrophilic properties of interacting polymers can affect the stability of IPC as well as the critical pH values. For example, PMAA, as a more hydrophobic polymer compared to PAA, forms stronger complexes, which  $\text{pH}_{\text{crit}}$  is generally higher.<sup>9, 11</sup>

An introduction of hydrophobic groups into macromolecules can also shift the  $\text{pH}_{\text{crit}}$  to higher pH values. In the study of the complexation of PAA with a series of vinyl ether copolymers it was found that an introduction of hydrophobic vinyl butyl ether (VBE) into the structure of PHEVE can enhance their complexation ability with respect to PAA in aqueous solutions.<sup>10, 22</sup> The copolymers containing more VBE exhibited higher critical pH values (**Fig. 5**).



**Fig. 5.** Structure of HEVE-VBE copolymers (a) and dependence of the  $\text{pH}_{\text{crit}}$  for the complexes of PAA and HEVE-VBE on the polymer concentration for the copolymers containing 22 (1), 12 (2) and 6 mol. % VBE (3). Reproduced from Mun G.A., Nurkeeva Z.S., Khutoryanskiy V.V., Bitekenova A.B.: Effect of copolymer composition on interpolymer complex formation of (co)polyvinyl ethers with polyacrylic acid in aqueous and organic solutions, *Macromolecular Rapid Communications*, 2000, 21, 381-384 (Ref. 10). Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

Unlike PHEVE homopolymer, the HEVE-VBE copolymers exhibit lower critical solution temperature (LCST) behaviour in aqueous solutions. It means that they can undergo phase separation upon heating. Staikos and co-workers<sup>23</sup> have previously demonstrated that non-ionic polymers with LCST are characterised by higher complexation ability with respect to poly(carboxylic acids) due to more effective stabilisation of IPC via hydrophobic effects. Indeed, the non-ionic polymers with a LCST form complexes with higher  $\text{pH}_{\text{crit}}$  as compared to their analogues without a LCST. For example, PVME,<sup>18</sup> PNIPAAm,<sup>19</sup> MC,<sup>24</sup> HPC<sup>15</sup> and

HPMC<sup>25</sup> have LCST in aqueous solutions and form stronger complexes with higher  $\text{pH}_{\text{crit1}}$  compared to PHEVE,<sup>9</sup> PAAM<sup>17</sup> and HEC<sup>26</sup> as LCST is not typical for the later group of polymers.

d) *Nature of non-ionic polymers*

The critical pH values ( $\text{pH}_{\text{crit1}}$ ), determined for complexes of PAA with different non-ionic polymers are summarised in **Table 1**.

**Table 1\***. Critical pH values ( $\text{pH}_{\text{crit1}}$ ) of some non-ionic polymers in 1:1 complexes with PAA ( $M_w$  450 kDa). The concentrations of both polymers in solution were 0.01 base-mol/L.

Non-ionic polymer	$M_w$ , kDa	$\text{pH}_{\text{crit1}}$	Comment
PHEVE	40	$2.45 \pm 0.05$	-
PVA	205	$2.67 \pm 0.05$	-
PHEA**	420	$2.75 \pm 0.05$	data taken from Ref. 27
HEC	100	$2.85 \pm 0.05$	-
PEO	20	$2.88 \pm 0.05$	-
PAAM	6000	$3.00 \pm 0.05$	-
HPC	100	$3.66 \pm 0.05$	LCST***
PNIPAAm	450	$4.60 \pm 0.05$	LCST
PVME	60	$4.85 \pm 0.05$	LCST
PVP	24	$4.85 \pm 0.05$	-

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\*\*Data listed for complexes with PAA ( $M_w$  250 kDa)

\*\*\*Non-ionic polymer exhibits LCST in aqueous solution

Although, a strict comparison of different polymers in this case is rather difficult as they have significantly different molecular weights, there is still a possibility to draw several conclusions. The lowest  $\text{pH}_{\text{crit1}}$  values are observed for the complexes of PAA with polymeric alcohols such as PHEVE, PVA, PHEA and HEC, which means that polymers bearing hydroxyl-groups have lower complexation ability. However, if hydroxyl-containing polymers exhibit LCST in aqueous solutions their complexation ability is greatly enhanced and these systems show significantly higher  $\text{pH}_{\text{crit1}}$  values. This phenomenon is observed for complexes of PAA with HPC. The polymers having either ether-groups such as PEO or amide-groups such as PAAM exhibit intermediate

complexation ability. Again, when the presence of ether-groups or amide-groups is additionally backed by LCST the complexation ability of the polymers is enhanced significantly; this is observed for PVME and PNIPAAm. The highest complexation ability is observed for polymers with lactame-groups such as PVP.

#### e) Presence of inorganic salts

Several authors reported different phenomena observed upon the addition of inorganic salts to the polymer solutions forming IPC. Bel'nikovich and co-workers<sup>28</sup> reported that increasing ionic strength suppresses the complexation of PAA with PVA and HEC. Chen and Morawetz<sup>29</sup> demonstrated that the addition of NaCl reduces the intensity of interactions of PAA with PVP and PEO. Sivadasan *et al.*<sup>16</sup> found that an increase in ionic strength leads to a decrease in pH at which the interpolymer interaction begins between PAA and pyrene-modified PAAM. However, Staikos *et al.*<sup>30</sup> showed that the presence of sodium bromide in solution favours the formation of a compact IPC between PAA and PEO. Iliopoulos and Audebert<sup>31</sup> studied the effect of tetramethylammonium chloride on the complexation between PAA and PEO by the potentiometric technique. They showed that the complexation degree is higher in salt solutions than in pure water, which was related to the change in the thermodynamic quality of the solvent. Indeed, deterioration in the thermodynamic quality of the solvent leads to more effective stabilisation of IPC through hydrophobic effects. Prevysht *et al.*<sup>32</sup> studied the effect of added salts on the stability of IPCs composed of PAA and PEO, PVP and HPC. It was demonstrated that the addition of NaCl results in IPC aggregation.

In fact, the influence of inorganic salts on the complexation between poly(carboxylic acids) and non-ionic polymers in aqueous solutions is associated with two opposite effects. The presence of inorganic salts in solution favours the ionisation of carboxylic groups of poly(carboxylic acids), which is unfavourable for hydrogen-bonding. On the other hand, the solvation of macromolecules is reduced in the presence of inorganic salts, which weakens polymer-solvent interactions and strengthens the intermacromolecular interactions between polymers. A prevalence of one

of these effects will lead either to stabilisation or destabilisation of IPC upon addition of inorganic salts.

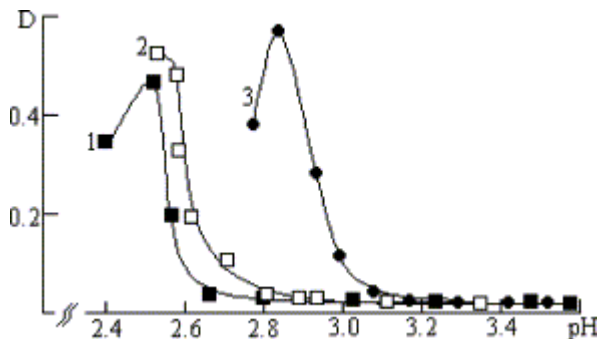
When analysing the effect of salt addition on the critical pH values ( $\text{pH}_{\text{crit1}}$ ), we have found that the IPC that have a relatively low  $\text{pH}_{\text{crit1}}$  (2.45–2.88) exhibit a tendency to have an increased  $\text{pH}_{\text{crit1}}$  upon the addition of inorganic salts.<sup>19</sup> This trend is observed for complexes of PAA with PHEVE, PVA, HEC and PEO (see **Table 1**). The stronger complexing systems with  $\text{pH}_{\text{crit1}}$  within 3.66–4.85 range show the opposite trend. The complexes of PAA with HPC, PNIPAAm, PVME and PVP decrease their  $\text{pH}_{\text{crit1}}$  upon addition of NaCl. Hence, the effect of ionic strength on  $\text{pH}_{\text{crit1}}$  depends on the pH at which the complexation is occurred.

Interesting phenomena were observed when transition metal ions such as  $\text{Cu}^{2+}$  and  $\text{Fe}^{3+}$  are added to poly(carboxylic acid) – non-ionic polymer mixtures.<sup>17,33,34</sup> A significant enhancement in the complexation ability of the polymers in the presence of these ions was detected and related to the formation of triple poly(carboxylic acid) – metal ions – non-ionic polymer complexes. Since the enhancement of the complexation in the presence of transition metal ions was reported for complexes of PAA with three different non-ionic polymers such as PVP,<sup>33</sup> PEO<sup>34</sup> and PAAM<sup>17</sup> it can be anticipated that this effect is common for all hydrogen-bonded IPC. However, further studies are required to clarify it.

#### *f) Presence of organic molecules in solution*

Only few studies reporting the effects of organic molecules on the complexation between poly(carboxylic acids) and non-ionic polymers in aqueous solutions have been published. In the study of the complexation between PAA and poly(vinyl ether of diethylene glycol) (PVEDEG), it was found<sup>35</sup> that the addition of phenol and hydroquinone shifts the  $\text{pH}_{\text{crit1}}$  to the lower pH region even at relatively low concentrations of the additives (**Fig. 6**). Phenol and hydroquinone are known to form complexes with a number of water-soluble polymers such as PEO, PVP and PVA.<sup>36,37</sup> Moreover, this complexation occurs more readily with polyphenols.<sup>38</sup> It was assumed that the strong influence of these

molecules on the complexation can also be related to the competitive interactions between phenols and individual polymers via hydrogen-bonding; this may affect the complexation between the polymers.



**Fig. 6.** Dependence of turbidity of PAA–PVEDEG (2:1 mol./mol.) solutions on pH in the presence of hydroquinone (1), phenol (2) and without additives (3). The concentration of added phenol and hydroquinone is 0.01 mol/L. The initial concentration of polymers is 0.01 base-mol/l. Reproduced from Nurkeeva Z.S., Mun G.A., Khutoryanskiy V.V., Sergaziev A.D. Complex formation between poly(vinyl ether of diethyleneglycol) and polyacrylic acid: I. Effect of low molecular salts and phenols additives, *European Polymer Journal*, 37, 1233-1237, ©2000, with permission from Elsevier (Ref. 35).

Drug molecules such as lidocaine hydrochloride (Lid·HCl) can also affect the complexation between PAA and PHEVE.<sup>39</sup> The presence of Lid·HCl in solutions of PAA and PHEVE shifts the  $pH_{crit1}$  to the higher pH region when the drug concentration is within 0.005-0.095 mol/L. It was found that this drug can interact with PAA via ionic contacts and with PHEVE via hydrogen-bonding. The mixing of PAA, Lid·HCl and PHEVE results in the formation of triple complexes with reduced solubility.

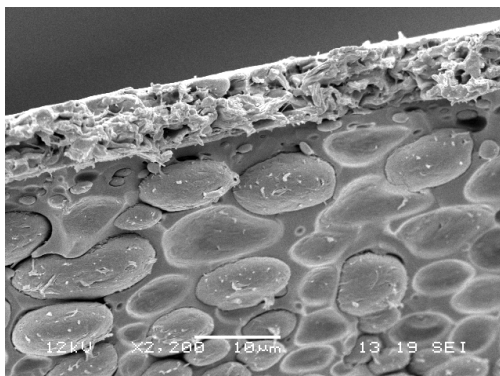
Cationic surfactants such as cetyl pyridinium bromide (CPB) can also affect the complexation due to the specific binding to PAA via ionic contacts.<sup>27</sup> Depending on the ratio between PAA and CPB the polycomplexes can form clear solutions, stable colloidal dispersions or precipitates. In order to study the effect of CPB addition on the  $pH_{crit1}$  for the complexation between PAA and PHEA the concentration of the surfactant was kept at very low level ( $1.5 \cdot 10^{-4}$  mol/L). It was found that the addition of CPB shifts the  $pH_{crit1}$  to the higher pH region and this

shift is more pronounced compared to the addition of NaCl of the same concentration.

### 3. pH-induced complexation – miscibility – immiscibility transitions

Formation of insoluble IPC between poly(carboxylic acids) and non-ionic polymers in aqueous solutions can be quite undesirable for the preparation of polymeric films. These films can be used for design of novel drug delivery systems (see Chapter 9), as packaging materials and as membranes in separation technologies. From a practical point of view, it is important to develop polymeric films with good mechanical properties and uniformity; however, the precipitation of IPC leads to the formation of uneven materials.

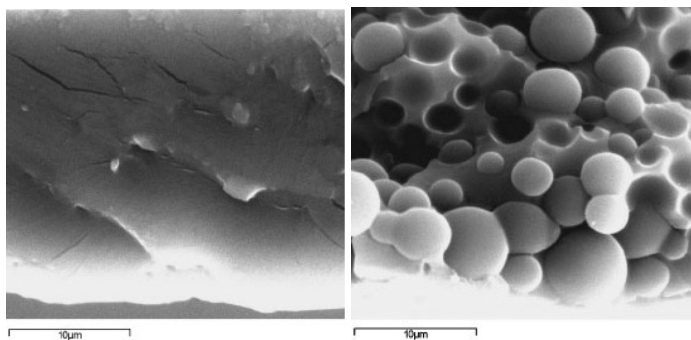
In the attempt to prepare the polymeric films based on PAA and HPC, we have tried to avoid the complexation by neutralising PAA with addition of NaOH.<sup>40</sup> A complete neutralisation of PAA helped to avoid the complexation and mixing the polymers has not resulted in the formation of a turbid IPC solution. However, after evaporation of water, the film formed had poor mechanical properties, was not fully transparent and had inhomogeneous morphology confirming a complete immiscibility between poly(sodium acrylate) and HPC (**Fig. 7**).



**Fig. 7.** Scanning electron microscopy image of the film based on the blend of HPC with poly(sodium acrylate) (33:67 mol. % ratio).

The immiscibility in this binary system was due to the lack of intermacromolecular hydrogen-bonding, which is known to facilitate the

formation of miscible blends.<sup>41</sup> In a later study<sup>15</sup> we have attempted to cast the polymeric films from PAA and HPC mixtures at varied pH and found that a miscibility window is observed at a casting solution pH higher than  $\text{pH}_{\text{crit1}}$  but lower than  $\text{pH}_{\text{crit2}}$ . Similar results were obtained for the blends of PAA with PEO<sup>14</sup> and PVA.<sup>13</sup> **Figure 8** shows the scanning electron microscopy images of the film cross-sections obtained by casting PAA-PVA mixtures at different pH.



**Fig. 8.** Scanning electron microscopy image of an equimolar PAA-PVA blend cast from a solution with pH 3.32 (a) and 4.6 (b). Reproduced from Nurkeeva Z.S., Mun G.A., Dubolazov A.V., Khutoryanskiy V.V. pH effects on the complexation, miscibility and radiation-induced crosslinking in poly(acrylic acid)-poly(vinyl alcohol) blends, *Macromolecular Bioscience*, 2005, 5, 424-432 (Ref. 13). Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

#### 4. Concluding remarks

pH plays an important role in the complexation between poly(carboxylic acid) and non-ionic polymers in aqueous solutions. The structure of IPCs, as well as their physicochemical properties, depends on the solution pH. Two critical pH values exist in binary poly(carboxylic acid)-non-ionic polymer mixtures. The formation of colloidal dispersions of hydrophobic interpolymer complexes and their further precipitation is observed below the first critical pH of complexation ( $\text{pH}_{\text{crit1}}$ ). Above this value, but below the second critical pH of complexation ( $\text{pH}_{\text{crit2}}$ ), the products of interaction are more hydrophilic. Above  $\text{pH}_{\text{crit2}}$ , the polymers do not interact with one another leading to homogeneous solution mixtures.

The  $\text{pH}_{\text{crit1}}$  depends on the concentration of polymers in solution, their molecular weight, the hydrophobic-hydrophilic balance, the nature of the functional groups in the non-ionic polymers, and the presence of inorganic salts or organic molecules in solution. The determination of  $\text{pH}_{\text{crit1}}$  allows the comparison of the complexation ability of different polymeric pairs. Higher  $\text{pH}_{\text{crit1}}$  corresponds to a stronger complexation ability between poly(carboxylic acid)s and non-ionic polymers.

A careful control of solution pH is also important for preparing polymeric films based on blends of poly(carboxylic acids) and non-ionic polymers. The films cast from solutions below  $\text{pH}_{\text{crit1}}$  are not uniform because of IPC precipitation. The films cast from solutions above  $\text{pH}_{\text{crit2}}$  are cloudy and have poor mechanical properties due to lack of intermacromolecular hydrogen-bonding and immiscibility between the polymers. The formation of miscible films is possible within the  $\text{pH}_{\text{crit1}}$ - $\text{pH}_{\text{crit2}}$  range, where the polymers form a hydrophilic associate and weak interpolymer hydrogen-bonding ensures the miscibility.

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