

POLYIONIC COMPLEXES DERIVED FROM POLYVINYL ALCOHOL

II. WATER ABSORBILITY AND ANTITHROMBOGENECITY OF PVA-TYPE POLYIONIC COMPLEXES*

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ABSTRACT

Effect of both structure of substituents and degree of substitution of polyions derived from polyvinyl alcohol on water-absorbility and antithrombogenicity of formed polyionic complexes (PIC) have been investigated. It was found that the water content of the PIC formed from *p*-formylbenzenesulfonic acid substituted PVA was higher than that of the PIC formed from *p*-formylbenzoic acid substituted PVA. When the substitution degree of polycation increased from 27% to 64%, the water content of the formed PIC increased from 170% to 1270%. Effect of water content and net charge of PVA-type PIC on the antithrombogenicity was also investigated by plasma recalcification method.

Polyionic complexes (PIC), a category of hydrogel which contain appreciable amount of bonding-water that is different from the common free water when in wet state, have some advantages such as good biocompatibility with living tissue, high permeability to water and most of the microsolute found in body fluids, without any degeneration for proteins or enzymes, with satisfied antithrombogenicity, etc., therefore, be widely used as biomaterials. There are many reports concerning with the investigation of PIC as biomaterials^[1-5]. However, most of these works are only within the limits of polystyrene derived polyionic complexes. Nakajima et al.^[6,7] have reported the preparation and antithrombogenicity of polyionic complexes derived from slightly substituted polyvinyl alcohol (PVA), but the effect of structure of substituents and degree of substitution of PVA derivatives on the water-absorbility and antithrombogenicity of the formed polyionic complexes and the relationship between water-absorbility and antithrombogenicity of these PVA-type polyionic complexes have not yet been reported in detail. In our previous paper^[8], the preparation of polyionic complexes of PVA derivatives and the investigation of the solvation behaviour of these hydrogels have been reported. These PVA derivatives were synthesized by the acetalization reaction of PVA with aldehyde compounds such as glyoxalic acid, *p*-formylbenzoic acid, *p*-formylbenzenesulfonic acid, *p*-formylpyridine, and *p*-dimethylaminobenzaldehyde. In this article, the effect of structure of substituents and degree of substitution on the water-absorbility and antithrombogenicity of these PVA-type PIC have been studied. It was found that the water-absorbility and antithrombogenicity of PIC were improved with increasing substitution degree of polyions.

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EXPERIMENTAL

The preparation of PVA-type polyionic complexes and their chemical structures are described in our previous paper^[8].

Determination of the water-content of PIC: PIC membranes was immersed in distilled water for 48 hours and the water-content of the complex is calculated according to the following equation:

$$\text{Water content \%} = \frac{W - W_0}{W} \times 100$$

where W_0 and W are the weight of dried and wet membrane, respectively.

Determination of antithrombogenicity: Polycation and polyanion were dissolved in H_2O -DMF-NaBr ($\text{H}_2\text{O}/\text{DMF}/\text{NaBr}=60/25/15$) ternary solvent system as 4% solution. After polycation and polyanion solution were mixed thoroughly, 0.5 ml of the mixture was added into a test tube with $\phi 8.5 \times 75$ mm. The test tube was rotated slowly and heated with an infrared heat lamp at the same time to remove the solvent. When the polymer was adhered onto the inner-surface and some NaBr crystal were just emerged, the test tube was impregnated with distilled water for 5 minutes and then, pouring out the water, the test tube was dried again. With another impregnating for 20 minutes to remove the residue organic solvent and microsalt, a test tube with homogenous transparent PIC coated inner surface which was used for antithrombogenicity determination was obtained.

0.1 ml dog plasma which contained anticoagulating reagent was added into the PIC coated test tube and kept for 3 minutes in a thermostat of $37.0 \pm 0.1^\circ\text{C}$. As soon as CaCl_2 solution was added, the antithrombogenicity of PIC was determined by observing the coagulating time of fibrin.

RESULTS AND DISCUSSION

1. Water-absorbility of PVA-type polyionic complexes

Polyvinyl alcohol derived PIC are hydrogels with high water-absorbility. The chemical structure of substituents and degree of substitution of polyions have a significant effect on the water-content of formed complexes, as showed in Table 1. It can be seen that the water-content of all these PVA-type PIC were higher than 250%, but P (HEMA), a typical hydrogel, was only 150%^[9]. The water-absorbility of PIC obtained by the reaction of p-formylbenzenesulfonic acid substituted PVA polyanion with a quaternary ammonium polycation was higher than that of PIC obtained by the reaction of p-formylbenzoic acid substituted PVA polyanion with the same polycation. This may be due to the stronger hygroscopic property of sulfonic acid group compared with carboxy group. For complexes of carboxy group carried polyanions, glyoxalic acid substituted PVA derivative exhibited higher water-absorbility than p-formylbenzoic acid substituted PVA derivative did. Furthermore, the mechanical strength of the former PIC nearly lost over and was jelly-like when immersed in water for 48 hours. This shows that the hydrophobic aromatic ring in PIC structure might make a contribution to the mechanical strength of the formed product.

Table 1 Water-content of polyvinyl alcohol derived PIC

PIC, PC-PA		II ₄ -I ₂	II ₄ -II ₂	II ₄ -III	I ₂ -I ₂	I ₂ -II ₂	I ₂ -III	P(HEMA)
D.S. (mol%)	PC	50	50	50	46	46	46	
	PA	47	31	34	47	31	34	
Water-content (%)		298	343	jelly	250	960	jelly	150 ^[9]

Table 2 Effect of substitution degree of polycations on the water-absorbility of formed polyionic complexes*

D.S. (mol%)	27	36	48	64
Water-content (%)	170	268	264	1270

* Polycation: PC-II

Polyanion: PA-I₁, D.S. 35%

Because the water-absorbility of PIC are related to their ionic bonds, the effect of substitution degree of polyions on the water-content of formed PIC are appreciable. Table 2 shows the relationship between the substitution degree of polycations and the water-content of the corresponding complexes. It can be seen that when substitution degree of polycation increased from 27% to 64%, that is, increased by 1.5 times, the water-content of the corresponding complexes increased from 170% to 1270%, that is, increased by more than 6 times. The PIC with water-content of 1270% behaved as water ultra-absorbing resin. In general, the higher the water-absorbility of hydrogel is, the better the biocompatibility and the greater the permeability to water and oxygen.

Fig. 1 illustrates the relationship between substitution degree of polyions and the water-content or antithrombogenicity of the corresponding PIC. This demonstrates that the higher the substitution degree of polyion, the greater the water-content and the better the antithrombogenicity of the formed complexes.

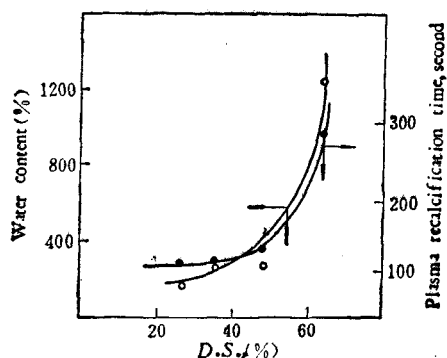


Fig. 1 Water-content and plasma recalcification time of polyionic complexes plotted against degree of substitution of polycation

2. Antithrombogenicity of PVA-type polyionic complexes

Table 3 summarizes the antithrombogenicity, determined by recalcification method, of several PIC derived from PVA. It can be seen that the antithrombogenicity of PIC coated test tube were improved in comparing with the contrast and those PIC with higher substitution degree of polyions were superior to the common poly(ether-urethane), poly(acrylamide), poly(2-hydroxyethylmethacrylate), etc.

Table 3 Plasma recalcification time of polyvinyl alcohol derived polyionic complexes

Sample	D.S. (mol%)		Plasma recalcification time (s)	T_S/T_G
	PC	PA		
PCI ₁ -PAII ₂	35	31	131	1.07
PCI ₁ -PAIII	35	34	125	1.02
PCII ₂ -PAII ₂	36	31	137	1.12
PCII ₂ -PAIII	36	34	141	1.16
PCII ₅ -PAII ₂	64	31	287	2.50
PCII ₅ -PAII ₂	64	41	225	1.80
Glass			122	1.00
P(HEMA)				1.12*
P(AAm)				1.03*
PEU				1.20**
PEU-g-AAm				2.33**
PEU-g-HEMA				1.98**

* [9], ** [10]

Hoffman et al.^[2] have reported the effect of net charge on the antithrombogenicity of PIC derived from polystyrene. For PVA-type PIC, it was found that the negatively-charged PIC was superior to the neutral and positively-charged PIC. From Fig. 2 and Table 4, it

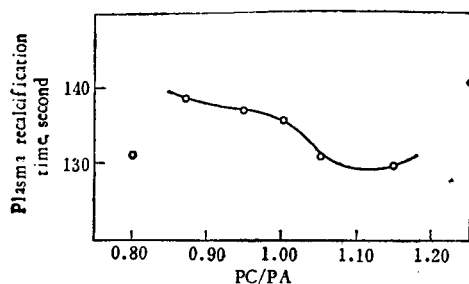


Fig. 2 Plasma recalcification time plotted against PC/PA
Polycation: PC-I₂; Polyanion: PA-I₂.

Table 4 Effect of net charge of PVA-type polyionic complexes on the antithrombogenicity*

PC/PA	1.15	1.05	1.00	0.95	0.87	Glass
Recalcification time(s)	130	131	136	137	139	115

* Polycation: PC-I₂, D.S. 35%; Polyanion: PA-I₂, D.S. 47%

can be seen that all these complexes were superior to the glass reference and within a certain range, the PIC with PC/PA > 1, i.e. positively-charged materials, were inferior to the neutral one. This is in accordance with the results reported by Hoffman about polystyrene derived PIC.

However, for PVA derived PIC, the effect of substitution degree of polyions on antithrombogenicity of formed PIC is more important than that of the net charge of PIC. Table 5

Table 5 Effect of substitution degree of polycations on the antithrombogenicity of the corresponding PIC*

D.S. (mol%)	Glass	27	36	48	64
Coagulation time(s)	115	119	117	134	287

* Polycation: PC-II; Polyanion: PA-II₂, D.S. 31%

shows the plasma coagulation time of PIC formed from polyions with various substitution degree. When the substitution degree were below 50%, there was some improvement in antithrombogenicity with increasing degree of substitution, but the improvement was not significant, whereas the degree of substitution of polycation reached 64%, there was remarkable improvement in the concerned property. The relationship between water-absorbility of PIC and degree of substitution of polyions was similar to that between antithrombogenicity and degree of substitution, as showed in Fig. 1. This demonstrates that the antithrombogenicity would be related to the water-absorbility of PIC.

Other properties of PVA derived PIC, such as mechanical property, permeation property, etc., will be published elsewhere.

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