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Permeability Control of Polyelectrolyte Complex Membrane Including Chitosan Derivative as a Component

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The properties of polyelectrolyte complexes (PEC) and PEC membranes were investigated in the systems of glycol chitosan (GC)-poly(vinyl sulfate) (PVSK) and methyl glycol chitosan (MGC)-(carboxymethyl)dextran (CMD). The degree of dissociation and the conformation of GC and CMD depend upon pH, because GC and CMD are weak polybase and weak polyacid, respectively. On the basis of this knowledge, a research into the pH dependence of dissociation and viscosity of GC and CMD was carried out. PEC including chitosan derivative as a constituent was synthesized at the adequate pH, pH 3.0 in the GC-PVSK system and pH 7.0 in the MGC-CMD system. PEC membranes were prepared, and the permeability of KCl, urea, and sucrose through the GC-PVSK membrane was determined under various pH. It was revealed that the permeability of KCl, urea, and sucrose varies with the solution pH. The permeability in the neutral region was 2—10 times as high as that in acidic region. The increase of permeability in neutral region was considered from IR spectra of membranes to be due to swelling caused by a conformational change.

Polyelectrolyte complexes (PEC) are expected to find a great many applications because of diversity of their structures and properties.[1-3] In particular, membrane application was widely developed, and there have been many studies on the permeability of ions and low-molecular-weight solutes through PEC membranes.[1-5] The investigation on PEC membrane, however, is confined mostly to synthetic polymers, and only a few works on PEC membranes made up of polysaccharide are available.[6,7]

On the other hand, a large amount of chitin is biosynthesized every year and chitin and chitosan derivatives have aroused great interest in recent years.[8] Many-sided applications of them have been proposed as to occupy a field of functional materials. We have already reported about the transport of alkali metal ions through PEC membranes which consist of chitosan derivatives and/or dextran derivatives, methyl glycol chitosan (MGC)-glycol chitosan (GC)-poly(vinyl sulfate) (PVSK),[9] MGC-(carboxymethyl)dextran (CMD)-PVSK,[10] and [2-(diethylamino)ethyl]-dextran (EA)-CMD-PVSK[11] systems.

The present article describes the characterization of GC and CMD and the preparation of PEC and PEC membranes in the GC-PVSK and MGC-CMD systems. Further, the permeability of KCl, urea, and sucrose was determined under various pH conditions in the GC-PVSK membrane, and it is exhibited that the permeation is controlled by pH change. This investigation will support the drug delivery system, the release control capsule, and so on.

Experimental

GC (D.P. 400; nitrogen content 5.51 wt%), PVSK (D.P. 1500; sulfur content 18.91 wt%), and MGC (D.P. 400; nitrogen content 3.33 wt%) were of reagent grade for the colloidal titration supplied by Wako Pure Chemical Industry, Ltd. CMD (mol wt 3×10^7; sodium content 7.38 wt%) was provided by Meito Sangyo Co., Ltd. Deionized water (0.3 $\mu S\,cm^{-1}$) which was degassed with boiling was used for all reagents.

Deionization of GC and CMD solution (0.02 base mol dm^{-3}) was performed by use of a mixture of cation and anion exchangers. After adding NaCl up to 0.1 mol dm^{-3}, 50 cm^3 of GC solution was neutralized by HCl, followed by the back titration with 0.5 mol dm^{-3} NaOH at 25 °C in nitrogen atmosphere. In the case of CMD, 50 cm^3 of CMD solution was directly titrated with 0.5 mol dm^{-3} NaOH after addition of NaCl. In order to estimate the degree of dissociation, hydrogen ion concentration was corrected by back titration of polyelectrolyte-free blank solution.[12] All titrations were carried out with a Hiranuma UCB-7 autoburet and a Horiba M-8 pH meter.

Intrinsic viscosity of GC, PVSK, MGC, and CMD was measured with an Ostwald viscometer in the presence of 1 mol dm^{-3} NaCl in a water bath controlled at 25±0.02 °C.

The preparation of PEC was achieved as described in the previous paper.[9] By the results of potentiometric titrations, GC solution was added dropwise to 100 cm^3 of PVSK solution at pH 3.0, and CMD solution was added dropwise to 100 cm^3 of MGC solution at pH 7.0. In the GC-PVSK system, the resulting precipitate of PEC was dried at 30 °C on a Petri dish. In the MGC-CMD system, the precipitate was interposed between silicone rubbers (50×50×0.5 mm), pressed with PMMA plates (50×50×5 mm) and dried at 30 °C. Thus the PEC membranes about 75 μm in thickness were obtained. The membranes were washed with methanol to remove micro ions prior to the permeation experiment. The measurement of permeability of KCl, urea, and sucrose was carried out with a diaphragm type cell which has 4.0 cm^2 of effective area. In the left-hand chamber of the cell 25 cm^3 of pH 3.0 solution was introduced, and 25 cm^3 of 0.05 mol dm^{-3} KCl, 0.01 mol dm^{-3} urea, or 0.02 mol dm^{-3} sucrose in the

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right-hand chamber, of which pH value was adjusted as the same as that of the left-hand chamber. Similarly the measurement of permeability was performed under proper pH from 3.5 to 7.0. Each pH was adjusted by the citrate or 2-amino-2-hydroxymethyl-1,3-propanediol buffer solution. The cell was then placed in a thermostat controlled at 30 °C, and 0.1 cm^3 of samples were withdrawn from both sides of the membrane every 2 h. KCl was determined by measuring K^+ ion with a Shimadzu AA-640 atomic absorption spectrophotometer. Urea and sucrose were determined with a Hitachi 100-10 spectrophotometer by the biacetyl monoxime method and the phenol-sulfuric acid method, respectively. IR spectra of GC-PVSK membranes previously immersed for 4 h in the pH 3.0, 4.0, 5.0, 6.0, and 7.0 solutions were taken with a Hitachi 270-50 IR spectrophotometer.

Results and Discussion

The applications of chitin and chitosan derivatives have been energetically investigated recently, because they have been produced in a comparable amount to cellulose and have the specific structure of amino polysaccharide. GC is also a chitosan derivative which is hydroxyethylated at the 6-position. Water-insoluble chitosan results in a water-soluble chitosan derivative by this etherification to make GC a very useful reagent for the colloidal titration.[13] However, the degree of dissociation (protonation) varies with pH of the solution, because GC has a primary amino group at the 2-position.[14] The pH dependence of the degree of dissociation, α, of glycol chitosan hydrochloride (GCH) was examined by the potentiometric titration, and is shown in Fig. 1. Free primary amino group was dominant in the pH region above 6.63, and primary ammonium ion was dominant in the region below 6.63. Therefore, pH has to be kept below pH 6.63 in order to prepare the ion-bonded PEC which includes GC as a component.[15] Figure 1 also indicates the pH dependence of the degree of dissociation of CMD by the potentiometric titration. Free carboxyl group was preferential in the pH region below 3.64, and the carboxylate ion was preferential in the region above 3.64. Consequently, pH has to be kept above pH 3.64 for the purpose of preparing the ion-bonded PEC which contains CMD as a component.

Furthermore, $pK=pH-\log\{\alpha/(1-\alpha)\}$ vs. α plots are shown in Fig. 2. It is exhibited that intrinsic and apparent pK of GCH in 0.1 mol dm^{-3} NaCl solution are 6.35 and 6.63, respectively. It was already known that a break is observed in the pK-α curve when the conformational change of macromolecular chain occurs like a helix↔coil transition of poly(L-glutamic acid).[16] No conformational change seems to occur in the main chain of GC, as pK-α curve is linear. We could not observe the conformational change in GC by the potentiometric titration, while Rha et al. have reported that the conformational change occurs in chitosan by the measurement of intrinsic viscosity.[17] They have obtained the result that as the pH of solution was increased, the intrinsic viscosity or the hydrodynamic volume of chitosan was decreased. Our measurement of the intrinsic viscosity, $[\eta]$, of GC showed that the intrinsic viscosity at high pH is larger than that at low pH, on the contrary. These results are shown in Fig. 3. This effect seems to be due to the 2-hydroxyethyl group, but it is indefinite in detail. Further investigation should be performed on this point. Figure 2 also gives the pK-α plots of CMD. It is exhibited that intrinsic and apparent pK of

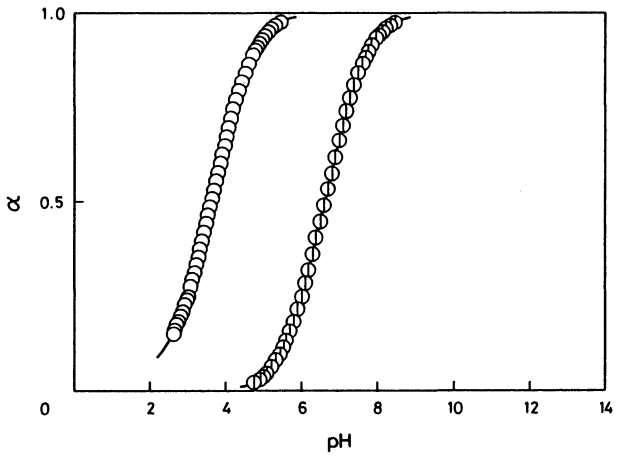

Fig. 1. pH dependence of the degree of dissociation of glycol chitosan hydrochloride and (carboxymethyl)dextran in the presence of 0.1 mol dm^{-3} NaCl at 25 °C. Polymer concentrations are 0.02 base mol dm^{-3}. ⦶: Glycol chitosan hydrochloride, ○: (carboxymethyl)dextran.

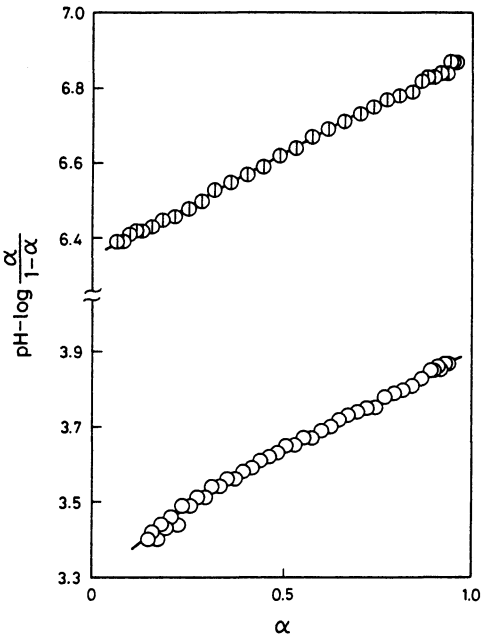

Fig. 2. pK vs. α plots of glycol chitosan hydrochloride and (carboxymethyl)dextran in the presence of 0.1 mol dm^{-3} NaCl at 25 °C. Polymer concentrations are 0.02 base mol dm^{-3}. ⦶: Glycol chitosan hydrochloride, ○: (carboxymethyl)dextran.

CMD in 0.1 mol dm^{-3} NaCl solution are 3.2 and 3.64, respectively. It appears that there is no conformational change in main chain of CMD similarly to GC, for the pK-α curve is continuous. These results of potentiometric titration of CMD were consistent with Gekko's results.[18] The pH dependence of [η] of CMD is shown in Fig. 3. The [η] of CMD changed at about pH 3, and this pH value was same as the inflection point in the α-pH curve in Fig. 1 which indicates the conditions of dissociation of CMD. The [η] of CMD is supposed to increase on account of a more bulky conformation caused by the inter- and intramolecular electrostatic repulsions between dissociable groups, -OCH_2COOH, in the pH region above 3.64.

In addition, Fig. 3 shows the relationship between [η] and pH of MGC and PVSK dealt in this paper, which are strong polybase and strong polyacid, respectively. Linear curves were obtained with respect to the [η]-pH plots of MGC and PVSK. It is apparent that [η] of these two polyelectrolytes is not influenced by pH, because the degree of dissociation of strong polyelectrolytes is constant over wide range of pH.

On the above conclusion, PEC was prepared. In the system of GC-PVSK, i.e., weak polybase-strong polyacid system, GC solution was added dropwise to PVSK solution at pH 3.0. In the system of MGC-CMD, i.e., strong polybase-weak polyacid system, CMD solution was added dropwise to MGC solution at pH 7.0. These synthetic conditions are summarized in Table 1 with the properties of membranes. It was thought that PEC has a ladder-like structure of ionic bond between ammonio groups in GC or MGC and -OSO_3^- group in PVSK or -OCH_2COO^- group in CMD, respectively. Further, inter- and intramolecular hydrogen bond seems to take place, because polysaccharides which are constituents of these PEC have many hydroxyl groups.

Transparent PEC membranes of 75 μm in thickness were obtained from both of the PEC. GC-PVSK membrane was very sturdy and similar to a cellophan membrane. MGC-CMD membrane was moisture-sensitive and extremely swollen in water. It has been reported that once PEC is prepared containing at least one strong polyelectrolyte component, ionic bond of PEC is maintained throughout wide pH range.[19] This concept, however, was not suitable for the MGC-CMD membrane. On the other hand, GC-PVSK membrane was stable over wide range of pH, and the stability of GC-PVSK seems to be due not only to the above reason but also to packing of GC. This fact manifests that PEC consisting of GC and PVSK is

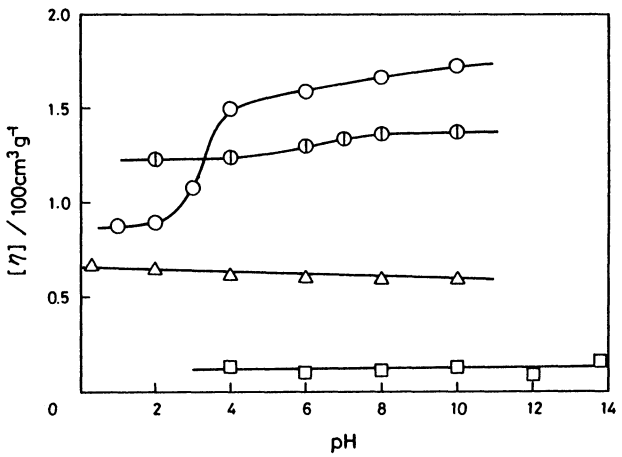

Fig. 3. pH dependence of the intrinsic viscosity of polyelectrolytes in the presence of 1 mol dm^{-3} NaCl at 25 °C. ⦶: Glycol chitosan, △: poly(vinyl sulfate), □: methyl glycol chitosan, ○: (carboxymethyl)-dextran.

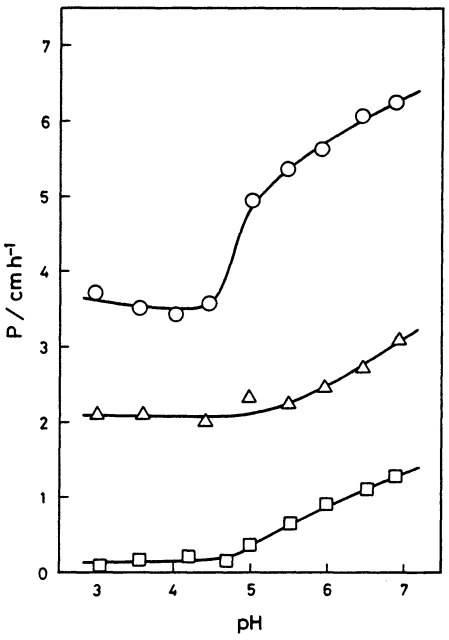

Fig. 4. Effect of pH on the permeability of solutes through polyelectrolyte complex membrane consisting of glycol chitosan and poly(vinyl sulfate) at 30 °C. ○: 0.05 mol dm^{-3} KCl, △: 0.01 mol dm^{-3} urea, □: 0.02 mol dm^{-3} sucrose.

Table 1. Synthetic Conditions for Polyelectrolyte Complexes and Stability of Membranes in Water

Sample	Polycation	Polyanion	pH	Volume of polycation /cm^3	Volume of polyanion /cm^3	Molar ratio of cation site to anion site in the reaction mixture	Membrane
1	GC	⟶ PVSK	3.0	150	100	1.00	Stable
2	MGC	⟵ CMD	7.0	100	74	1.00	Swollen

Concentrations of polyelectrolytes were 2.0 g dm^{-3} each. Arrows represent the titration order.

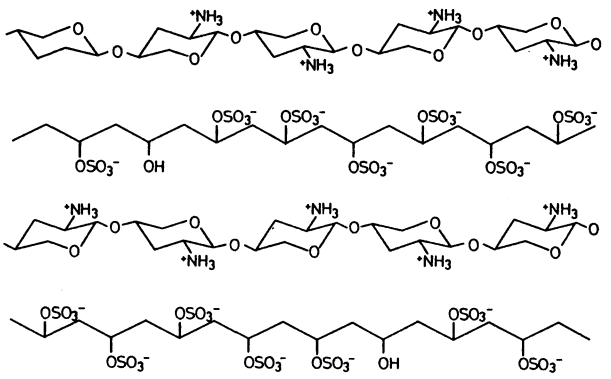

Fig. 5. Schematic model of polyelectrolyte complex in the system of glycol chitosan-poly(vinyl sulfate).

favorable for a membrane material.

Thus the permeability of KCl, urea, and sucrose through this membrane was investigated, and the results are shown in Fig. 4. Permeability, P, was evaluated by the following equation, which derived from the Fick's law of diffusion:[3]

$$Pt = -\frac{V}{2A} \ln \frac{\Delta C}{C_0},$$

where t is the time, V is the volume of each chamber of the cell, A is the area of membrane, C_0 is the initial concentration of solutes in the right-hand chamber, and ΔC is the difference of concentrations in the right- and left-hand chambers. Figure 4 shows that the permeability of KCl, urea, and sucrose depends on the molecular weight and pH. Each permeability decreased proportionally to the molecular weight in the order of KCl>urea>sucrose. GC-PVSK membrane has a cation-exchange ability, because GC is a rigid molecule and the density of cation site of GC is lower than that of anion site of PVSK, as described previously.[15] Schematic model of PEC consisting of GC and PVSK is represented in Fig. 5. Therefore, the electric potential on the left-hand chamber must be higher than that on the right-hand chamber when salt such as KCl was permeated. The electric potential difference between both sides of the membrane was actually 7—8 mV at pH 3.0 after 10 h. Furthermore, permeability increased at about pH 5 where the degree of dissociation and intrinsic viscosity change as shown in Figs. 1 and 3. IR spectra of the GC-PVSK membranes treated for 4 h with the buffer solutions of pH 3.0, 4.0, 5.0, 6.0, and 7.0 are shown in Fig. 6. The absorption band at 1530 cm^{-1} assigned to primary ammonium ion was present in all membranes, whereas 1600 cm^{-1} assigned to primary amino group of GC was absent. That is to say, the dissociation of GC in the membrane was not observed at pH from 3.0 to 7.0. It is clear that breaking of ionic bonds is not responsible for the increase in permeability. Considering that GC has a conformation swelling

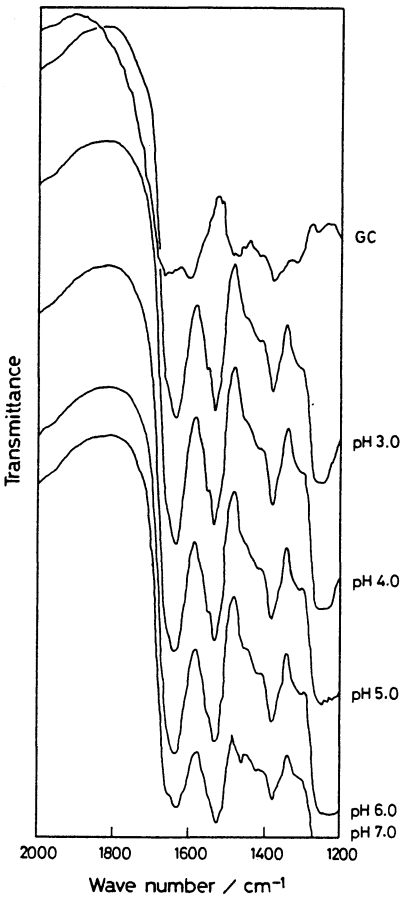

Fig. 6. IR spectra of glycol chitosan and treated polyelectrolyte complex membranes consisting of glycol chitosan and poly(vinyl sulfate).

as pH increases and PVSK has a flexible polymer chain, it is thought that GC-PVSK membrane becomes rather swollen to form a bulky conformation, and hence the permeability increases. Rha et al. have prepared micro capsule whose diffusion rate for γ-globulin and BSA was decreased by decrease in pH, where chitosan was gelified with alginate.[17] PEC membrane in the system of GC-PVSK has controllable permeability for KCl, urea, and sucrose to some extent, even though PEC is previously prepared at a constant pH value.

These investigations suggest a possibility of permeation control of PEC membrane consisting of GC, which is a amino polysaccharide, and PVSK, which has a flexible polymer chain, because it is possible to control the permeability by pH which controls the conformation and packing of PEC.

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