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Evaluation of the Rheological Properties of Various Kinds of Carboxyvinylpolymer Gels

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The rheological properties of carboxyvinylpolymer (CVP) hydrogels were evaluated using various methodologies. As CVPs, the series of Hiviswako (HVW) 103, 104, and 105 (denoted as H_{103}, H_{104}, H_{105}, respectively), and Carbopol (CP) 934, 940, and 941 (denoted as C_{934}, C_{940}, C_{941}, respectively) were used. The rheological measurements were carried out by the capillary tube method, oscillation method, and continuous shear method (Ferranti–Shirley viscometer). These measurements were mainly performed on the HVW series because their properties are not as well established as those of CPs.

In the HVW series, the order of magnitude of intrinsic viscosities obtained by the capillary tube method was $H_{105} > H_{104} > H_{103}$ at all pH values examined. This order agreed with that of the viscoelastic parameters obtained by the oscillation method and that of the viscosity obtained by the continuous shear method when the gels were in a non-neutralized state. However, the orders were reversed when they were partially neutralized by adding alkali.

From these results, the gel structure of each polymer was presumed to be as follows. In the case of H_{103}, the polymer is rich in side chains or cross-links and takes a compact form in the non-neutralized state. When alkali is added to H_{103}, side chains are extruded into the water phase by the electric repulsive forces between carboxyl groups, and the polymer molecules become entangled with each other, so that the gel shows larger viscoelastic values. On the other hand, in the case of H_{105}, the polymer is poor in side chains and the addition of alkali has less effect on the viscoelastic properties than in the case of H_{103} or H_{104}, due to the lack of entanglement of side chains. The viscoelastic properties measured in glycol solutions and the swelling rate for the HVWs supported the above hypothesis.

As regards CP, C_{941} showed almost the same properties as H_{105}. C_{934} and C_{940} showed similar properties to H_{103} and H_{104} respectively, although some differences were observed among them.

Keywords——carboxyvinylpolymer; Carbopol; Hiviswako; hydrogel; rheology; oscillation method; capillary tube method; continuous shear method; gel structure

Hydrogels prepared by the use of carboxyvinyl polymer (CVP) have been widely used as vehicles for ointments,[1)] buccals,[2)] or suppositories,[3)] because of the following advantages: 1) high consistency even at low CVP concentrations, 2) high dissolving capacity for the active ingredients, and 3) excellent appearance and subjective acceptability.

CVPs are polymers mainly composed of acrylic acid. Since B. F. Goodrich Chemical Co. began to supply these polymers under the brand name of Carbopol (CP), their use for topical pharmaceuticals or cosmetics has expanded considerably. This company has developed many kinds of polymers, and among them, CP 934, 940 and 941 (denoted as C_{934}, C_{940} and C_{941}) have been widely used.

In Japan, Wako Pure Chemical Industries, Ltd. has developed analogous polymers under the trade name of Hiviswako (denoted as HVW). Among them, HVW 103, 104, and 105 (denoted as H_{103}, H_{104}, and H_{105}) are widely used and are considered to be analogous in physicochemical properties to the C_{934}, C_{940} and C_{941} series.

Since these 6 brands have been used in Japan as thickening agents for pharmaceutical dosage forms or cosmetic vehicles, some of their rheological properties relevant to practical use have been presented in various papers and catalogues.[4] However, few detailed studies have been presented from fundamental physicochemical viewpoints, especially for HVWs.

Barry and Mayer carried out rheological evaluations by the creep and oscillation methods for neutralized and non-neutralized gels of C_{940} and C_{941},[5,6] and observed some interesting phenomena. However, their studies seem insufficient to establish the relationship between the polymer gel structures and the rheological properties, because few kinds of CVPs were used and only limited numbers of physicochemical measurements were made.

Thus, to examine this relation in more detail, rheological measurements were performed by several methods on the above 6 products in this study. HVWs were mainly used and the results were compared with those for CPs.

First, intrinsic viscosity ($[\eta]$) was measured by the capillary tube method for each polymer in a diluted state, because $[\eta]$ reflects the rheological characteristic of the isolated polymer free from interaction with other polymer molecules. Then the following measurements were performed for the gels; 1) evaluation of viscoelastic properties by the oscillation method applying the nonlinear analysis developed in the previous paper,[7] 2) continuous shear experiments using a Ferranti–Shirley cone-and-plate viscometer, and 3) measurement of swelling rates. From these data, possible structures of the gel networks are proposed.

Experimental

Materials——CVP; C_{934}, C_{940} and C_{941} (B. F. Goodrich Chemical Co.) and H_{103}, H_{104}, and H_{105} (Wako Pure Chemical Industries, Ltd.) were used as received. These polymers were stored over phosphorus pentoxide and the weights of polymers were determined after correction for the water content measured by the Karl–Fischer titration method. The water contents were always less than 3%.

The amount (w/w%) of carboxyl groups in dried CVPs was determined by potentiometric titration with 0.1 N KOH ethanol in 30% dimethylformamide solution according to The Japanese Standards of Cosmetic Ingredients, Second Edition (JSCI-II)[8] and the results are shown in Table I. All of them met JSCI-II specifications.

Purified water was prepared by distillation before use. A 0.1 N NaOH solution was used as the neutralizing agent. Ethylene glycol (EG) (Katayama Chemical Industries Co., Ltd.), propylene glycol (PG) (Katayama Chemical Industries Co., Ltd.), and 1,3-butylene glycol (BG) (Daicel Chemical Industries, Ltd.) were used as received.

Gel Preparation——One gram of CVP was weighed rapidly in a 100 ml beaker, and wetted well by adding 30 ml of purified water. A definite amount of 0.1 N NaOH and the remaining amount of purified water were added under agitation. The obtained gels were degassed well by centrifugation (1000—2000 rpm). These gels were stored at 25 ± 1 °C until measurements.

Rheological Measurements——All of the following measurements were performed at 25 ± 0.1 °C.

Capillary-Tube Method: Portions of about 1 g of gels containing about 1% CVPs were weighed exactly in 100 ml volumetric flasks and purified water was added to make 100 ml. These solutions were diluted with the purified water to appropriate CVP concentrations. By the use of a Cannon–Fenske viscometer #50, the falling time, t, was measured. Intrinsic viscosities $[\eta]$ were obtained by extrapolation of η_{sp}/c to zero concentration.

$$\eta_{sp}=(\eta-\eta_0)/\eta_0=(t-t_0)/t_0 \tag{1}$$

where t and t_0 are falling times of CVP solution and purified water, respectively, and c is the CVP concentration (g/100 ml purified water).

Oscillation Measurement: A Shimadzu RM-1 rheometer was used as described previously[7]; cone angle (ε), 7×10^{-2} rad; strain amplitude (λ), 1.75×10^{-2} rad; radius of cone-and-plate (R), 2.5 cm; torsion constant of wire (K), 2.22×10^{6} dyn cm/rad.

The strain is applied sinusoidally, $\gamma(t)=\gamma_0\sin\omega t$, so the stress ($\sigma$) also shows a sinusoidal pattern, $\sigma(t)=\sigma_0\sin(\omega t+\phi)$. The stress signals were amplified and sent to a personal computer (HP-85, Hewlett Packard Co.) through an A/D converter (3456A digital voltmeter, Hewlett Packard Co.). As rheological parameters, storage elasticity (G'), storage viscosity (G''), and loss tangent ($\tan\delta$), were calculated by means of the following equations[7];

$$G'=(3Ka/2R^3)/(\varepsilon/\lambda) \tag{2}$$

$$G''=(3Kb/2R^3)/(\varepsilon/\lambda) \tag{3}$$

$$tan\ \delta=G''/G' \tag{4}$$

where a and b are the first coefficients of the constituent wave in the Fourier series. Nonlinearity parameter Dnl was calculated by the use of Eq. 5.

$$Dnl=\left(\int_0^{2\pi}|\sigma_{\text{obs}}-\sigma_{1\text{st}}|\,d\theta\right)\Big/\left(\int_0^{2\pi}|\sigma_{\text{obs}}|\,d\theta\right) \tag{5}$$

where σ_{obs} and $\sigma_{1\text{st}}$ are the observed wave and calculated one, respectively. $\sigma_{1\text{st}}$ was calculated by means of Eq. 6.[7)]

$$\sigma_{1\text{st}}=(a\ \sin\theta+b\ \sin\theta)\times 3\,K/2R^3 \tag{6}$$

Measurements were performed at $\omega=4.7\times10^{-1}$ rad/s except for the investigation of frequency (ω) dependency.

Continuous Shear Method: By use of the Ferranti–Shirley cone-and-plate viscometer, the relationship between shear rate and shear stress was determined. The operating conditions were as follows: sweep time, 60 s; shear rate, 0—625 s^{-1}.

Swelling Rate Measurements: About 10 g of gel containing 1% CVP was placed gently in visking tubing (Visking No. 1 18/32″), and immersed in purified water at 25±0.1 °C. At an appropriate period, the Visking tubing was removed from the water and weighed after light swabbing with tissue paper. The swelling percent S was calculated as follows.

$$S=[(W-W_0)/W_0]\times100 \tag{7}$$

where W and W_0 are the weights of gel at the measuring time and at the initial time, respectively.

Results and Discussion

Dissociation of H^+ Ions from Carboxyl Groups of Each CVP

CPs and HVWs have many carboxyl groups, and the degree of dissociation of a polymer can vary depending on the molecular conformation. Thus, 0.1 N NaOH were added step by step to gels containing 1% polymer and the pH values were measured. In Fig. 1, the pH values of H_{103}, H_{104}, and H_{105} gels are plotted against neutralizing degree (Nd), defined by Eq. 8.

$$Nd=\frac{\text{alkali amount added to gels}}{\text{alkali amount necessary to neutralize CVPs in gels}} \tag{8}$$

The alkali amount necessary to neutralize each CVP was estimated from the values presented in Table I. As shown in Fig. 1, when Nd values were below 1, the order of pH values of gels was $H_{103}>H_{104}>H_{105}$. In the case of CPs, the order was $C_{934}>C_{940}>C_{941}$ (data not shown). Thus, H^+ ions dissociate more easily from C_{941} or H_{105} than from other CVs or HVWs.

Viscosity Measurement in Diluted Solutions

From the rheological properties of diluted polymer solutions, information about the conformation of a single polymer molecule can be obtained, because each molecule of

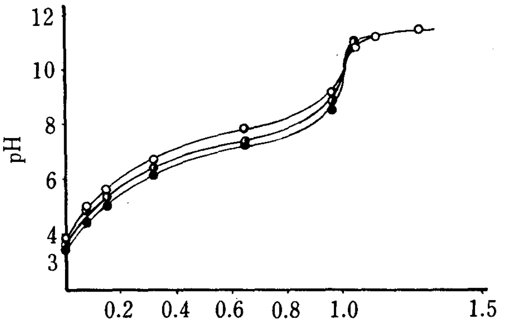

Fig. 1. pH Values of Each Gel against Degree of Neutralization (Nd) Calculated by Eq. 8

○, H_{103}; ◑, H_{104}; ●, H_{105}.

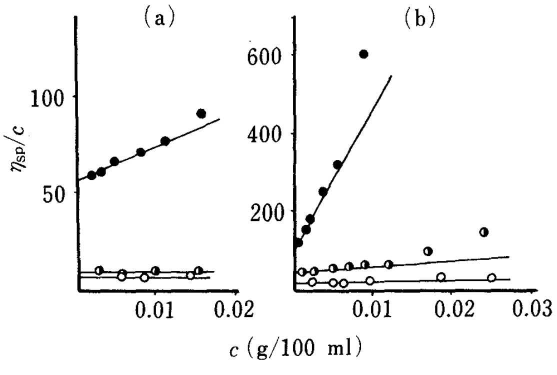

Fig. 2. Relationship between CVP Concentration (c) and Reduced Viscosity (η_{sp}/c) Measured by the Capillary Tube Method

a) Non-neutralized gels of HVW. b) Partially neutralized (pH 6) gels of HVW. Symbols are as in Fig. 1.

Table I. Assayed Values of Carboxyl Groups in Each CVP (w/w% in Dried CVPs) Used in This Experiment

CVP	C_{934}	C_{940}	C_{941}	H_{103}	H_{104}	H_{105}
Carboxyl group (%)	62.6	63.0	60.0	60.6	61.4	58.2

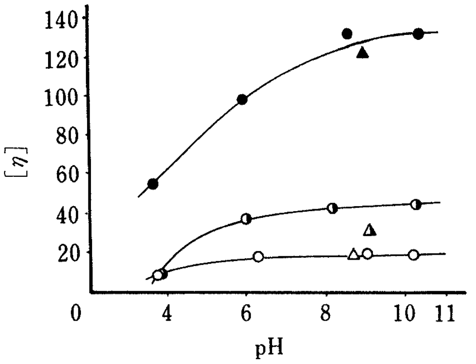

Fig. 3. Intrinsic Viscosity of CVPs Plotted against pH

○, H_{103}; ◑, H_{104}; ●, H_{105}; △, C_{934}; ◭, C_{940}; ▲, C_{941}.

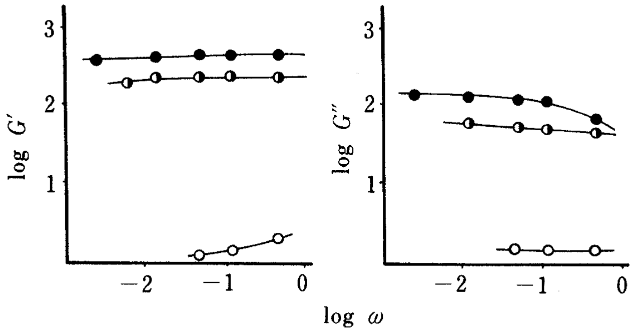

Fig. 4. ω Dependency of Storage Elasticity (G') and Storage Viscosity (G'') of Non-neutralized CVP Gels (1%)

Symbols are as in Fig. 1.

polymer should be isolated in the diluted solution. These data should be useful in considering the gel networks of CVPs, but no such measurements have been reported for CPs or HVWs as far as we know. Thus, the viscosity was measured by the capillary tube method for each polymer solution. Figure 2 shows examples of the measurement for HVW solutions whose *Nd* values were 0 (pH; about 3) and 0.25 (pH; about 6). A fairly good linearity was observed between η_{sp}/c and c in both solutions at lower CVP concentrations.

Generally, the shape of the plot of η_{sp}/c *vs.* c with solutions of polyelectrolytes does not give a straight line but a concave curve unless salts are added. That is, η_{sp}/c gives higher values as the polymer concentration is decreased. This depends on the ionization and resulting expansion of polyelectrolytes due to the repulsive electrostatic interactions between charged groups. This tendency was slightly observed in H_{103} and H_{104} (Fig. 2a) when they were not neutralized. However, in most cases of a partially neutralized polymer, the η_{sp}/c values decreased linearly as the concentration decreased (Fig. 2b). Thus, intrinsic viscosity $[\eta]$ was estimated by linear extrapolation to zero concentration of the plot of η_{sp}/c *vs.* c. The value of $[\eta]$ obtained for the original 1% gels is plotted against pH in Fig. 3. As shown in Fig. 3, $[\eta]$ of each HVW gel increased until pH 6 and remained almost constant at pH values over 8. Throughout the pH range, the order of $[\eta]$ was the $H_{105} > H_{104} > H_{103}$ for HVWs. In CP, $[\eta]$s were measured at around the neutralizing point, and the values were in the order of $C_{941} > C_{940} > C_{934}$.

Generally, intrinsic viscosity $[\eta]$ is related to the molecular weight (Mw) of a polymer as follows.

$$[\eta] = K\, Mw^{\alpha} \qquad (9)$$

However, as far as we know, none of these parameters, K and α, have been reported for CVPs. As regards the molecular weight of CPs, some values have been presented. For example, Bardet *et al.* reported a value of $(2.4 \pm 0.24) \times 10^6$ for C_{940},⁹⁾ and Bloemer and van der Horst reported 3×10^6 for C_{934}.¹⁰⁾ The supplier claims 3×10^6, 4×10^6, and 1.25×10^6 for C_{934}, C_{940}, and C_{941}, respectively.⁴ᵇ⁾ JSCI-II gives $(2—3) \times 10^6$, $(2—3) \times 10^6$, and 1.5×10^6 for C_{934}, C_{940}, and C_{941}, respectively.[8] As to HVWs, no molecular weights have been reported as far as we know, but according to the supplier, the molecular weights of H_{103}, H_{104}, and H_{105} are similar to those of C_{934}, C_{940}, and C_{941}, respectively.

As shown in Fig. 3, the order of $[\eta]$s were $H_{105}>H_{104}>H_{103}$ for HVWs and $C_{941}>C_{940}>C_{934}$ for CPs. However, according to JSCI-II, the molecular weight of C_{941} is the smallest among the CPs. As the molecular weights of the polymers would not be affected by the pH of the gels, the change of $[\eta]$ with pH (Fig. 3) is presumed to reflect the change in K and α in Eq. 9. This suggests that the struture of the polymer molecule itself changes with pH. Therefore, in this paper, $[\eta]$ is regarded as an index which reflects polymer conformation in diluted solutions, rather than molecular weight.

The $[\eta]$ values should depend on many factors including numbers of side chains in a polymer, degree of cross-linking, hydration number, and so on. H_{105} and C_{941}, which gave the largest $[\eta]$ values among the brands in spite of having the smallest molecular weights, are presumed to have larger molecular volumes than other CVPs. Therefore, in H_{105} and C_{941}, many hydrophilic groups are presumed to be exposed directly to the aqueous phase. Molecular forms having fewer side chains or less cross-linking may show such expanded conformations, because steric hindrance of side chains or cross-links should prevent the hydrophilic groups from contacting water molecules. Thus, it is presumed that H_{105} and C_{941} are rich in linear chains, whereas H_{103} and C_{934} have more side chains or cross-links.

This presumption was also supported by the pH titration curves (Fig. 1). CVPs having fewer side chains or cross-links, such as H_{105} or C_{941}, should release H^+ ions more easily than H_{103} or C_{934}.

Viscoelastic Evaluations by the Oscillation Method

Usually, CVP gels are prepared at more than 0.5% polymer concentration. In Figs. 4 and 5, storage elasticity (G') and storage viscosity (G'') calculated by the use of Eq. 2 and 3, respectively, are plotted against frequency for 1% HVW gels whose Nd values are 0 and 0.25. As shown in Figs. 4 and 5, the change of G' and G'' values of these gels was small in this ω range. This is a remarkable characteristic of CVP gels compared with other semisolid ointment vahicles. In Fig. 5, the G′ and G″ values of vaseline and Macrogol ointment (containing equal amounts of Macrogol 400 and Macrogol 4000) are shown for comparison.[7] The lower dependency of G' and G'' of CVP gels on ω should reflect that these gels are more resistant to shear than other ointment vehicles. Barry and Mayer considered on the basis of the creep test that C_{940} and C_{941} gels more closely approximate to an elastic solid than other pharmaceutical vehicles such as o/w and w/o creams.[5] The result that the G' values were larger than the G'' values (Figs. 4 and 5) supports their conclusion.

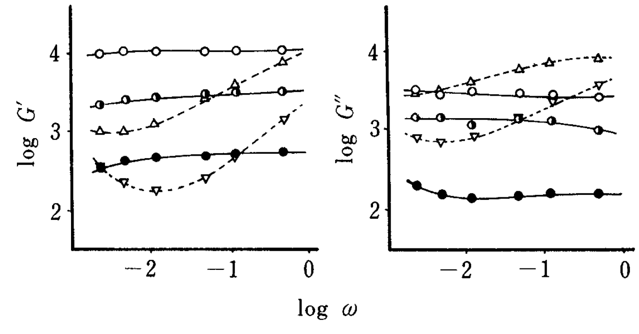

Fig. 5. ω Dependency of G' and G'' of Partially Neutralized CVP Gels (pH 6, 1%)

The data for other ointment vehicles are given in a previous paper.[7] △, macrogol ointment; ▽, vaseline; others are as in Fig. 1.

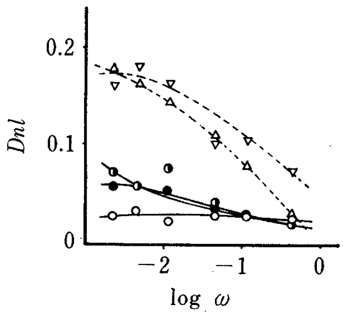

Fig. 6. Nonlinearity Parameter, Dnl, for HVW Gels (pH 6, 1%) and Other Ointment Vehicles

Symbols are as in Fig. 5.

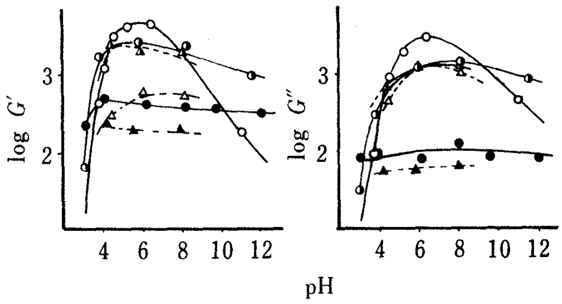

Fig. 7. pH Dependency of G' and G'' Values Measured at $\omega = 0.47$ rad/s for Each Gel

Symbols are as in Fig. 3.

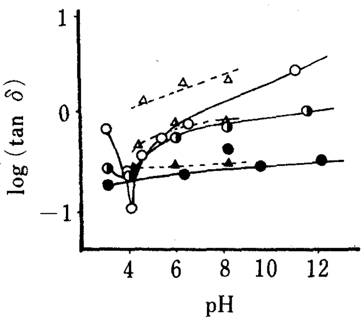

Fig. 8. pH Dependency of Loss Tangent

Symbols are as in Fig. 3.

The nonlinearity parameters *Dnl*s calculated using Eq. 5 are shown in Fig. 6 for HVWs compared with other ointment vehicles. *Dnl* indicates the extent of deviation of a stress curve from an ideal sinusoidal curve, and is regarded as an index reflecting the extent of thixotropic properties.[7)] As shown in Fig. 6, *Dnl* values of CVPs were smaller than those of vaseline of Macrogol ointment, shown as examples. The smaller *Dnl* means that the gels have less thixotropic properties than other ointment vehicles. This seems to support the above presumption that CVP gels are resistant to shear.

The G' and G'' values of non-neutralized gels were in the order of $H_{105} > H_{104} > H_{103}$, in agreement with that of $[\eta]$ (Figs. 2 and 4). However, in partially neutralized gels, the values were in the order of $H_{103} > H_{104} > H_{105}$, opposite to that of $[\eta]$ (Figs. 2 and 5). To investigate this phenomenon in more detail, the viscoelasticities of gels prepared at various pH values were evaluated at $\omega = 0.47$ rad/s (Fig. 7). In the HVW series, G' and G'' increased rapidly when the pH increased from about 3 (non-neutralized gels) to about 4 (*Nd* is less than 0.1) and the degree of increase of G' and G'' depended on the CVP types. The increases of H_{103}, H_{104}, and H_{105} were several hundredfold, several tenfold and only several fold, respectively. The G' and G'' values of H_{103} were the largest among HVWs between pH 4 and 8, although the $[\eta]$ value was the smallest. On the other hand, H_{105}, whose $[\eta]$ was the largest among the HVWs, gave the smallest G' and G'' values.

The G' and G'' values of CP gels are also shown in Fig. 7 by dotted lines in the pH range between 4 and 8. C_{941}, which showed the largest $[\eta]$ among CPs, gave the smallest values of G' and G'' in the same manner as H_{105}. C_{940} also showed almost the same values of G' and G'' as H_{104}. However, C_{934} showed fairly different viscoelastic properties from H_{103} although the $[\eta]$ values were almost the same. The G'' values of C_{934} did not greatly differ from those of H_{103}, but the G' values of C_{934} were very much smaller than those of H_{103} and were intermediate between those of C_{941} and C_{940}.

The loss tangent ($\tan\delta = G''/G'$) was the smallest at around pH 4 in H_{103} and H_{104} and hereafter it increased gradually with pH increase (Fig. 8), while H_{105} gave almost the same $\tan\delta$ value between pH 3 and 12.

A lower $\tan\delta$ means that the contribution of solid-like properties is larger than that of liquid-like properties. Therefore, the results that $\tan\delta$ of H_{103} and H_{104} took the minimum values at around pH 4 mean that the contribution of solid-like properties is the largest at around pH 4. This suggests that most of the gel network is constructed by addition of a small amount of alkali (*Nd* values of less than 0.1). The increase of $\tan\delta$ in the higher pH range could be caused by the increase of Na^+ site binding due to the increase of ionic strength by the addition of alkali. It is presumed that a part of the negative charges of carboxyl groups is neutralized by the site binding with Na^+ ions and the electronic repulsive forces between side chains are decreased. The expansion force on side chains is reduced, and consequently, the polymer entanglement is decreased. The lesser change and the lowest value of tan δ in H_{105} are interesting, and could be caused by the small amount of side chains in this polymer.

Among CPs, C_{940} and C_{941} gave almost the same tan δ as H_{104} and H_{105}, respectively, but C_{934} showed the largest tan δ in the partially neutralized state and it differed somewhat from H_{103}. The result that C_{934} gave the largest tan δ means that C_{934} had the most liquid-like property among the CVPs used. Therefore, C_{934} is presumed to gave some characteristic molecular conformation. Side chain length, branching positions or other factors may account for this, but no information is available at present.

From the $[\eta]$ and pH values, we presumed that the order of side chain numbers in a polymer is $H_{103} > H_{104} > H_{105}$ for HVWs. The viscoelastic data seem to support this order. Namely, in the non-neutralized state, side chains in H_{103} or C_{934} are bound to the polymer skeleton by hydrophobic bonding so that polymers take rigid and compact forms. In this state, greater numbers of carboxyl groups are hidden inside the polymer molecules, so that the degree of ionization of dissociable groups of polymers is less. When alkali is added to CVPs having many side chains, carboxyl groups of the side chains near the surface of the polymer globes are neutralized first and the side chains are extruded into the water phase, because the electric repulsive forces of charged carboxyl groups are much larger than the hydrophobic bonding forces of uncharged side chains. When more alkali is added, the side chains hidden inside the polymer are gradually neutralized. The gel strength should depend greatly on the numbers of side chains near the surface, because these side chains have greater likelihood of entangling with other polymer side chains. Thus the rapid increase in G' and G'' with small amounts of alkali should be caused by the extrusion of side chains from the polymer surface into the water phase (Fig. 9). On the other hand, H_{105} or C_{941} should be fairly expanded even in the non-neutralized state because these polymers are presumed to have fewer side chains and larger numbers of carboxyl groups could contact water molecules in the non-neutralizing state. Therefore, the addition of alkali has less effect on the viscoelasticity because entanglement between polymer molecules should be less in the linear polymers.

The phenomenon that the increases of G' and G'' values of H_{103} or C_{934} are larger than those of H_{105} or C_{941} could be explained by the schema in Fig. 9.

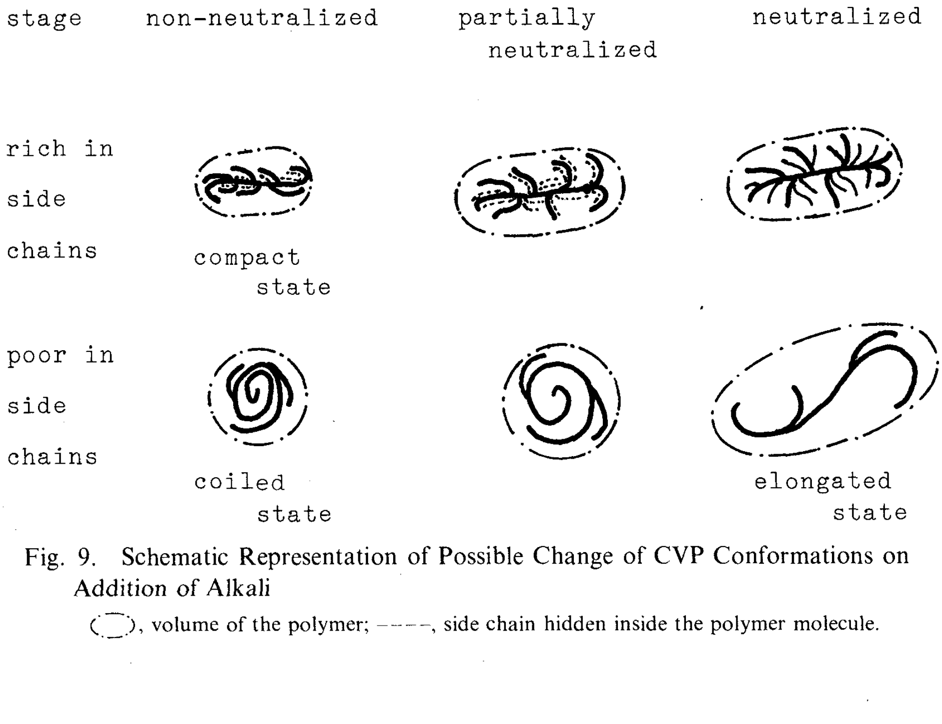

Fig. 9. Schematic Representation of Possible Change of CVP Conformations on Addition of Alkali

(⌒), volume of the polymer; ----, side chain hidden inside the polymer molecule.

Measurement of Swelling Rates

The extent of hydrophilicity of each HVW was evaluated by swelling rate measurement. In Fig. 10, swelling percent calculated from Eq. 6 is plotted against immersion time. As shown, the swelling increased linearly with immersion time within the measurement period. The apparent swelling rates were calculated from the slope and are shown in the figure as *SR* (%/h). The order of *SR* was $H_{105} > H_{104} > H_{103}$ in both non-neutralized and neutralized gels. As the swelling rate seems to reflect the affinity of polymer segments for water molecules, H_{105} should attract water more strongly than H_{103}. Therefore, it is presumed that the phenomena that H_{103} gave larger G' and G'' values in the partially neutralized state is not caused by water attracted around carboxyl groups but mainly by the entanglement of side chains of the polymers. Thus, the results of the swelling rate measurements seemed to support the polymer structure presumed in the preceding section (Fig. 9).

Evaluation by Continuous Shear Methods

In the preceding oscillation method, lower strain is imposed, and the gel is evaluated at the rheological ground state, so that the fundamental properties of gels in the static state can be examined by this method.[11] However, larger shear rates would be imposed on preparations during practical manufacturing processes. Thus, by use of a Ferranti–Shirley viscometer, continuous shear rheograms were obtained at shear rates from 0 to $625\,\mathrm{s}^{-1}$; the results for HVW gels (1%, pH = 6) are shown examples (Fig. 11).

Each gel showed plastic flow, and the hysteresis area between the upward and downward

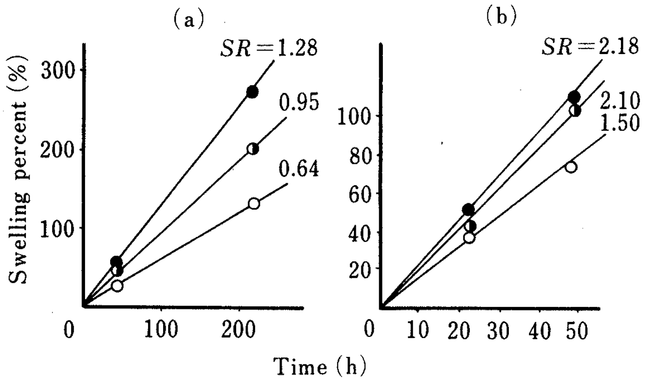

Fig. 10. Swelling Percent of Non-neutralized and Partially Neutralized Gels (1%) Immersed in Water at 25 °C

Symbols are as in Fig. 1.

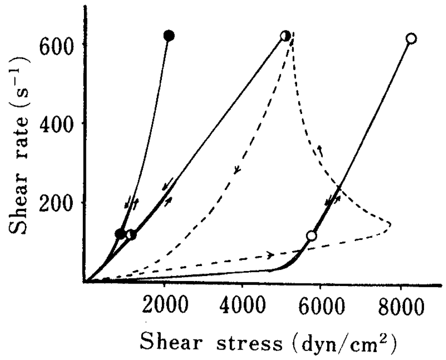

Fig. 11. Rheograms Obtained by the Use of a Ferranti–Shirley Viscometer for Various HVW Gels (pH 6, 1%)

Symbols are as in Fig. 1.

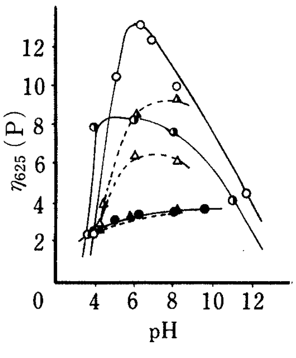

Fig. 12. Dependency of Apparent Viscosity, η_{625}, on pH Value of CVP Gels (1%)

Symbols are as in Fig. 3.

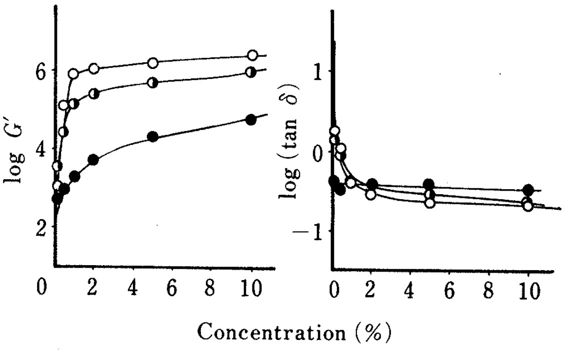

Fig. 13. Dependency of G' (a) and Loss Tangent (b) on CVP Concentration (pH 6)

Symbols are as in Fig. 1.

curves was very small compared with other semisolid ointment vehicles (in Fig. 11, the rheogram of vaseline is shown by a dotted line for comparison). The small hysteresis was common for both HVW and CP gels (data for CP are not shown). This suggests that the structures of CVPs are hardly destroyed by the imposition of shear, or they rapidly recover after the removal of shear.

Barry and Mayer considered for the gels prepared with C_{940} and C_{941} that no structure breakdown occurred under these shearing conditions.[6] The results for HVWs are consistent with this suggestion.

In Fig. 12, the apparent viscosities calculated at the shear rate of $625\,s^{-1}$ (η_{625}) for 1% HVW and CP gels are plotted against pH values. As shown in Fig. 12, η_{625} of HVW gels rapidly increased between pH 4 and 6, and the order of η_{625} of partially neutralized gels was $H_{103} > H_{104} > H_{105}$. The η_{625} values of non-neutralized gels of H_{103}, H_{104}, and H_{105} were 2.3, 2.4, and 2.5 P, respectively, and the order was opposite to that of partially neutralized gels. These tendencies are the same as in the case of the viscoelastic properties (Fig. 7). The η_{625} values of H_{103} and H_{104} were the highest at around pH 6 ($Nd = 0.25$) and decreased over pH 10. H_{105} gave low values but showed less pH-dependent patterns.

Among the CPs, C_{941} showed almost the same values as H_{105}, and C_{934} took intermediate values between C_{941} and C_{940}. The tendency was similar to that of G' (Fig. 7).

Dependency of the Viscoelasticity on the Polymer Concentrations

The effect of polymer concentration on G' and $\tan\delta$ was investigated for HVW gels of pH 6, and the results are shown in Fig. 13.

The G' values of H_{103} and H_{104} increased rapidly until 1%, and thereafter increased moderately. On the other hand, G' of H_{105} gradually increased with concentration. $\tan\delta$ of H_{103} and H_{104} decreased until 1% and thereafter showed almost constant values, whereas H_{105} gave almost the same values irrespective of the concentration. These facts suggest that the gel structure of H_{105} is hardly influenced by pH (Fig. 7) or concentration (Fig. 13), and is stable under various circumstances even though the gel is softer than that of H_{103} or H_{104}.

The rapid decrease of $\tan\delta$ in H_{103} and H_{104} until 1% might suggest that the gel networks are almost constituted at 1% concentration. Barry and Mayer presumed that gel networks in CPs were formed at concentrations of less than 1%, though they did not give any evidence.[5] The results in Fig. 13 might support their presumption.

Viscoelastic Properties of CVPs in Glycol Solutions

For ointment vehicles, many kinds of glycols are used. Therefore, HVWs were dissolved at 1% concentration in EG, PG, and BG, and the oscillation method was applied. The results are shown in Table II in comparison with those for aqueous gels. As shown in Table II, H_{103} gave the largest G' values in glycols, although it gave the smallest values in water among HVWs. Since H_{103} was supposed to have many side chains, it is presumed that H_{103} has the greatest hydrophobicity and has the highest affinity for glycols among HVWs. Thus

TABLE II. Viscoelastic Parameters of CVP Gels Dissolved in Various Solvents

	$\log G'$				$\tan\delta$			
	Water	EG	PG	BG	Water	EG	PG	BG
H_{103}	0.30	2.62	2.38	2.12	0.64	0.16	0.24	0.65
H_{104}	2.36	1.80	2.27	2.12	0.20	0.32	0.40	0.42
H_{105}	2.66	1.98	1.88	1.78	0.15	0.43	0.55	0.69

CVP concentration, 1 w/w%. Measurement frequency, 0.47 rad/s.

expansion of H_{103} polymer is the largest, resulting in the high G' value. The data in Table II also support the hypothesis described in the preceding sections as to the polymer conformation.

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