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Influence of Molecular Weight of Polyethylene Glycol on Interaction between Polyethylene Glycol and Iodine

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Interaction of iodine with ethylene glycol, diethylene glycol, triethylene glycol and polyethyleneglycols (PEGs) of molecular weight between 2×10^2 and 1.1×10^4 in ethanol and in carbon tetrachloride was investigated.

Absorbance of an ethanol solution of iodine at 360 nm increased by the addition of PEGs. A new peak was observed at 380 nm by the addition of PEGs of molecular weight above 3×10^2 to the carbon tetrachloride solution of iodine. These findings were considered to be due to formation of iodine in the diatomic state whose interatomic distance was a little prolonged by the interaction between iodine and PEGs. Formation of iodine in the diatomic state whose interatomic distance was a little prolonged was remarkable when the molecular weight of PEG was high and the concentration of PEG was large. It was considered that the interaction force was a very weak "short-range force."

From the results of the measurement of solubility of PEGs in carbon tetrachloride, optical rotatory dispersion spectra and viscosities of the solutions of PEGs, it was suggested that a PEG molecule was in spherical conformation in ethanol and that formation of iodine in the diatomic state whose interatomic distance was a little prolonged might be remarkable in the presence of PEG molecules in spherical conformation.

Mueh measured the number-average molecular weights of various polyethylene glycols (PEGs) of molecular weights between 2×10^2 and 3.5×10^4 by various methods. The ebulliometric method and the end-group method gave values which agreed within five percent for molecular weights below 2×10^3. But the ebulliometric method in the molecular weight region above 2×10^3 gave lower values than the osmotic pressure method and the end-group method, and the difference increased with an increase of molecular weight of PEG.[2] Calleja, *et al.* reported that the crystallinity of PEG of molecular weight below 2×10^3 increased with increasing molecular weight and that the crystallinity of PEG of molecular weight above 2×10^3 was not influenced by molecular weight of PEG.[3] The above findings show that physical and chemical properties of PEG are influenced by molecular weight of PEG. Hiskey, *et al.* found that filterable precipitates were obtained by the addition of PEGs to an aqueous solution of potassium iodide and iodine. They made a qualitative comparison between the interaction of KI_3 with PEGs of various molecular weights, using PEG 400, PEG 1000 and PEG 4000, and showed that the amount of KI_3 needed to obtain the precipitates decreased as the molecular weight of the PEG increased.[4]

In this work, interaction between iodine and PEGs in ethanol and in carbon tetrachloride was studied and influence of molecular weight of PEG on the interaction was investigated in detail.

Experimental

The materials used were ethylene glycol of guaranteed grade of Wako Junyaku Kogyo Co., diethylene glycol and triethylene glycol of guaranteed grade of Koso Yakuhin Co., and polyethylene glycols (PEGs)

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[1] Location: *Hatanodai, 1–5–8, Shinagawa-ku, Tokyo.*

[2] G. Mueh, *Makromol. Chem.*, **77**, 64 (1964).

[3] F.J.B. Calleja and S. Garcia-Blanco, *Rev. Plasticos Mod.* (Madrid), **15**, (91) 1, 15 (1964).

[4] C.F. Hiskey and F.F. Cantwell, *J. Pharm. Sci.*, **55**, 166 (1966).

Table I. Average Molecular Weights of PEGs Determined by End-Group Method and Molecular Weights of the Other Materials

Material	Molecular weight	Average molecular weight
Ethylene glycol	6.21×10	
Diethylene glycol	1.06×10^2	
Triethylene glycol	1.50×10^2	
PEG 200		2.02×10^2
PEG 300		3.04×10^2
PEG 400		3.99×10^2
PEG 600		6.05×10^2
PEG 1000		1.02×10^3
PEG 1540		1.49×10^3
PEG 2000		2.00×10^3
PEG 4000		3.11×10^3
PEG 6000		7.50×10^3
PEG 10000		1.10×10^4

purchased from Nihon Yushi Co. Ethylene glycol, diethylene glycol and triethylene glycol were dried and distilled. In Table I are shown the values of molecular weights of PEGs obtained by the end-group method. These samples were kept in a desiccator containing calcium chloride. In this paper, these materials are generically named PEG. Iodine, potassium iodide, ethanol and carbon tetrachloride were of guaranteed grade.

Absorption, nuclear magnetic resonance (NMR) and optical rotatory dispersion (ORD) spectra of ethanol solutions and carbon tetrachloride solutions of various concentrations of PEG and iodine were measured after keeping the solutions at 30° for 24 hours from the time of the preparation. Absorption spectra were measured with a Hitachi recording spectrophotometer (Model EPS-2), NMR spectra were measured with a Hitachi high resolution NMR spectrometer (Model R-20) and ORD spectra were measured with a JASCO optical rotatory dispersion spectrometer (Model ORD/UV-5). Absorbance of the absorption maximum of the solutions around 360 nm were measured with a Hitachi-Perkin Elmer spectrophotometer (Model 139).

The mixture of one gram of PEG and 2 ml of carbon tetrachloride was kept at 30° for a week, occasionally shaken intensely. The weight of PEG dissolved in one gram of a carbon tetrachloride solution was measured after drying the solution in vacuum. Viscosities of the ethanol solutions and carbon tetrachloride solutions of PEGs were measured with a Ubelohde type viscometer at 30°.

Results and Discussion

1) Interaction between PEG and Iodine

A brown solution is obtained when iodine is dissolved in the solution of potassium iodide and in this case, it is considered that iodine exists as triiodide anions. On the other hand, it has been known that brown solutions are also obtained when iodine is dissolved in alcohols, ethers, ketons, organic acids and basic nitrogeneous solvents. Then, a spectroscopic study was made in order to clarify whether iodine existed as triiodide anions or not in ethanol.

As shown in Fig. 1, three peaks were found at 292 nm, 360 nm and 445 nm in the absorption spectra of the ethanol solutions of iodine. It has been known that absorption maximum is observed around 450 nm in the absorption spectra of alcohol solutions and ether solutions of iodine,[4] and Mulliken and Hildebrand, *et al.* showed that the peak was due to iodine binding to oxygen.[5] In the absorption spectrum of an ethanol solution of iodine and potassium iodide, the peak at 445 nm was not observed and absorbance at 292 nm and 360 nm were much larger than that in the spectra of ethanol solutions of iodine. On the other hand, absorbance of an ethanol solution of iodine at 360 nm increased remarkably by cooling in a dry ice-ethanol bath (Fig. 2), and decreased gradually and reverted to the original value by leaving the solution alone

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[5] J.H. Hildebrand and B.H. Glascock, *J. Am. Chem. Soc.*, **31**, 26 (1909); R.S. Mulliken, *ibid.*, **72**, 600 (1950).

at room temperature. This phenomenon was not observed by cooling an ethanol solution of iodine and potassium iodide. It has been known that iodine solutions in pure solvents are either violet or brown. Violet solutions are formed in such solvents as carbon disulfide, carbon tetrachloride and simple aliphatic hydrocarbons. In these solvents iodine has an absorption spectrum similar to that which it has in the gaseous state with an absorption maximum around 519 nm. It is a well known phenomenon that the brown solutions of iodine in polar solvents tend to become violet when heated, reverting to the original color on cooling. Also it has been observed that the violet color of the carbon disulfide solution may be changed to the brown color as the solution is cooled in a dry ice-ether bath.[4] Beckman by means of precise molecular weight determinations in both the violet and the brown solutions established that iodine was present in the diatomic state in both instances.[6] Hiskey, *et al.* made interesting qualitative observations concerning the filterable precipitates obtained by the addition of PEG to the aqueous solution of iodine and potassium iodide. When the mole ratio of $-CH_2-OCH_2-$ of PEG to iodine was small, the precipitates were dark black with a submetallic lustre resembling that of iodine itself. On the other hand, when the ratio was large, that is, 10 and higher, the precipitates were light reddish brown in color, becoming lighter as the ratio increased. By washing with distilled water, these light reddish-brown precipitates immediately became much darker in color and their appearance changed to that of the precipitates with the I_2: $-CH_2OCH_2-$ ratio of approximately 1.0.[4] It is considered from the above facts that the peak at 360 nm is attributed not only to triiodide anions but to the iodine which is in the diatomic state and whose interatomic distance is a little prolonged by the interaction with solvent molecules and so on. It is also considered that iodine is in the diatomic state in ethanol.

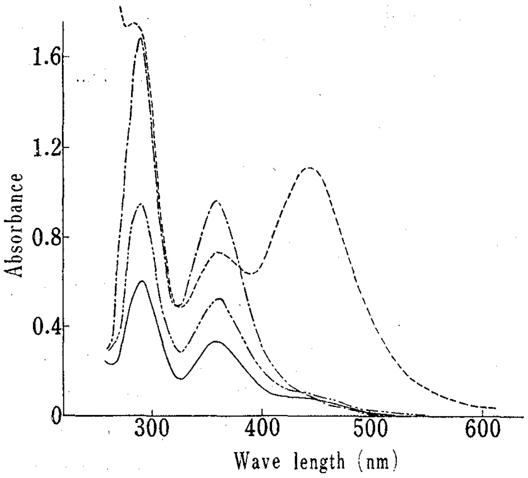

Fig. 1. Influence of Addition of Potassium Iodide or PEG on Absorption Spectra of the Ethanol Solutions of Iodine

————: 1.00×10^{-4}M of iodine
— — —: 9.85×10^{-4}M of iodine
—·—·—: 3.62×10^{-5}M of iodine and 2.60×10^{-4}M of potassium iodide
- - - - -: 1.00×10^{-4}M of iodine and 8.90×10^{-2}M of PEG 6000 (monomer unit)

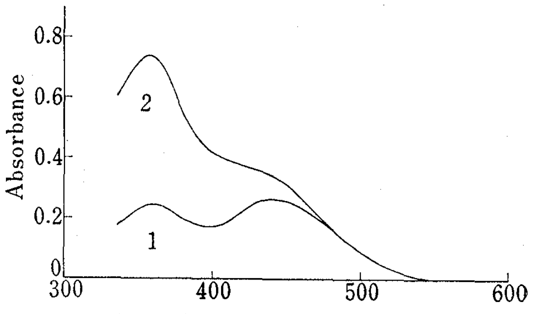

Fig. 2. Influence of Cooling on an Absorption Spectrum of an Ethanol Solution of Iodine

1 3.1×10^{-4}M of iodine
2 3.1×10^{-4}M of iodine, immediately after cooling in a dry ice-ethanol bath

Intensity of the optical absorption at 292 nm and 360 nm for an ethanol solution of iodine increased by the addition of PEG (Fig. 1). An apparent decrease of absorbance of the ethanol solution of 3.9×10^{-5}M of iodine and 3.3×10^{-3}M of potassium iodide at 360 nm by the addition of 8.5×10^{-2}M of PEG 4000 (monomer unit) was not observed even after keeping

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[6] E. Beckman, *Z. Physik. Chem.*, **58**, 543 (1907); *idem, ibid.*, **17**, 107 (1895).

the solution at 30° for a week. The violet solution of iodine in carbon tetrachloride changed into brown by the addition of PEG. As shown in Fig. 3, the peak at 518 nm in the absorption spectrum of a carbon tetrachloride solution of iodine shifted to 513 nm and a new peak appeared at 386 nm by the addition of PEG. The peak at 513 nm decreased and the new peak at 386 nm increased with an increase of the concentration of PEG, and an isosbestic point was observed at 495 nm. The brown solution of a carbon tetrachloride solution of iodine and PEG became violet by heating and reverted to brown by keeping the solution at room temperature. It is considered from the above findings that the interatomic distance of iodine in the diatomic state is a little prolonged by the interaction between PEG and iodine.

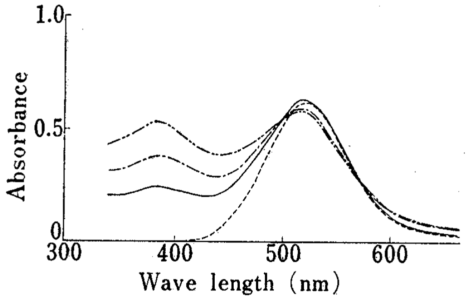

Fig. 3. Influence of Addition of PEG 4000 on Absorption Spectra of the Carbon Tetrachloride Solutions of Iodine

- - - - - -: 6.5×10⁻⁴M of iodine

————: 6.5×10⁻⁴M of iodine and 1.3×10⁻¹M of PEG 4000 (monomer unit)

—·—·—: 6.5×10⁻⁴M of iodine and 2.6×10⁻¹M of PEG 4000 (monomer unit)

—··—··—: 6.5×10⁻⁴M of iodine and 3.9×10⁻¹M of PEG 4000 (monomer unit)

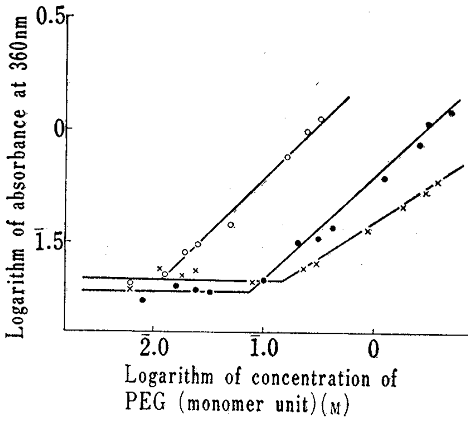

Fig. 4. Influence of Concentration of PEG on Absorbance of PEG–Iodine–Ethanol Solutions at 360 nm

concentration of iodine; 9.92×10^{-5}M

The value of logarithm of absorbance of an iodine-ethanol solution at 360 nm was $\bar{1}.32$.

×: triethylene glycol

●: PEG 400

○: PEG 6000

Fig. 4 shows the influence of the concentration of PEG on absorbance of the ethanol solutions of PEG and iodine at 360 nm. It is shown in Fig. 4 that interatomic distance of iodine in the diatomic state is a little prolonged only when the concentration of PEG is larger than the limiting concentration, C_l. This fact may suggest that the interaction force between iodine and PEG is a very weak "short-range force." As shown in Fig. 5, C_l decreased with an increase of the molecular weight of PEG in case of PEG of molecular weight below 3×10^2 and C_l was influenced little by the molecular weight in case of PEG of molecular weight between 3×10^2 and 2×10^3. The values of C_l for PEG of molecular weight above 2×10^3 were smaller than those for PEG of molecular weight between 3×10^2 and 2×10^3.

As shown in Fig. 6, the difference of the absorbance of an ethanol solution of iodine at 360 nm in the presence of PEG of molecular weight below 2×10^3 to that in the absence of PEG was small. On the contrary, the difference for PEG of molecular weight above 2×10^3 was large and increased with an increase of molecular weight of PEG.

Fig. 7 shows the absorption spectra of the carbon tetrachloride solutions of PEG and iodine. PEG of molecular weight below 2×10^2 was slightly soluble in carbon tetrachloride, and by shaking the mixture of a carbon tetrachloride solution of iodine and small amount of PEG of molecular weight below 2×10^2, iodine dissolved in PEG completely. But the peak around 380 nm was not observed in the absorption spectra of the PEG solutions of iodine. When molecular weight of PEG was between 3×10^2 and 1.5×10^3, a small peak was observed around 380 nm only when the concentration of PEG was large enough. The peak around 380 nm was observed by the addition of small amount of PEG of molecular weight above

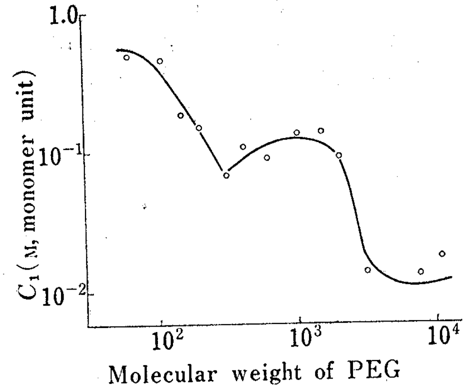

Fig. 5. Influence of Molecular Weight of PEG on C_1

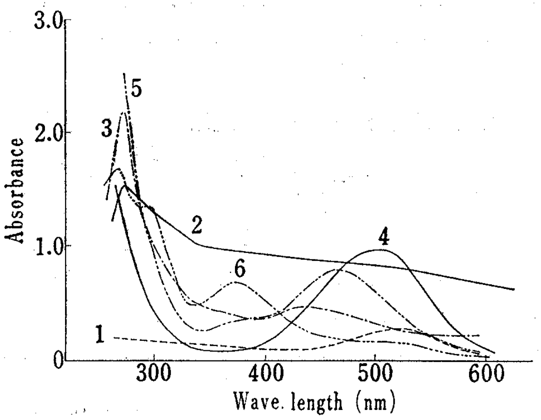

Fig. 7. Influence of the Addition of PEGs of Various Molecular Weights on Absorption Spectra of the Carbon Tetrachloride Solutions of Iodine

1: 2.43×10^{-4}M of iodine
2: ethylene glycol and iodine
3: triethylene glycol and iodine
4: 9.30×10^{-1}M of PEG 600 (monomer unit) and 1.22×10^{-3}M of iodine
5: the mixture of 0.82 g of PEG 1540 and 3 ml of 1.22×10^{-3}M of iodine
6: 7.35×10^{-1}M of PEG 10000 (monomer unit) and 2.43×10^{-4}M of iodine

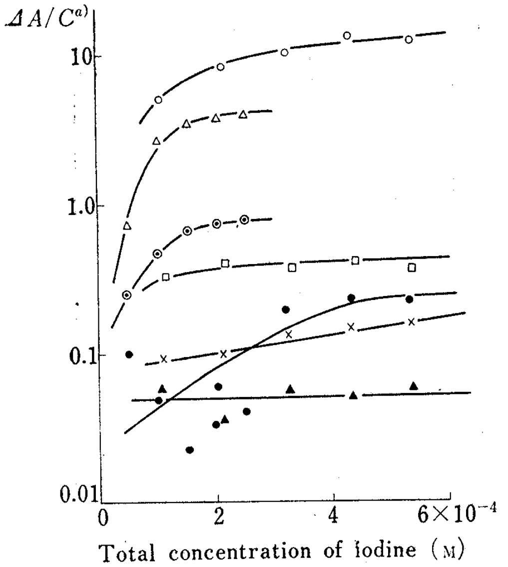

Fig. 6. Variation of the Absorbance of the Ethanol Solutions of PEG at 360 nm with Varying Concentration of Iodine

●: 1.4 M of ethylene glycol
×: 2.0 M of PEG 200 (monomer unit)
▲: 1.7 M of PEG 2000 (monomer unit)
⊙: 2.6×10^{-1}M of PEG 4000 (monomer unit)
□: 7.0×10^{-2}M of PEG 6000 (monomer unit)
△: 2.7×10^{-1}M of PEG 6000 (monomer unit)
○: 4.2×10^{-2}M of PEG 10000 (monomer unit)
a) ΔA: difference of the absorbance of an ethanol solution of iodine in the presence of PEG at 360 nm to the absorbance in the absence of PEG
C: molar concentration of PEG (monomer unit)

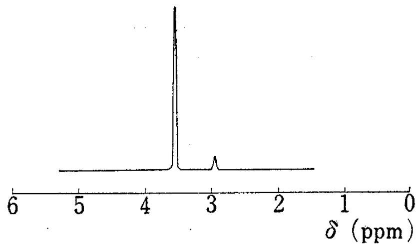

Fig. 8. A NMR Spectrum of A PEG 400–Iodine–Carbon Tetrachloride Solution

0.90M of PEG 400 (monomer unit) and 8.6×10^{-4}M of iodine

2×10^3. The peak around 380 nm shifted slightly with variation of the concentration of PEG, but the peak shifted from 370 nm to 390 nm with an increase of the concentration of iodine from 2×10^{-4}M to 2×10^{-3}M.

As shown in Fig. 8, a signal was observed at 3.55 ppm of δ in the NMR spectrum of a carbon tetrachloride solution of PEG. The NMR spectrum of PEG of molecular weight below 3×10^2 was not influenced by the addition of iodine, but a new signal appeared at the magnetic field of δ smaller than 3.55 ppm by the addition of iodine to the solution of PEG of molecular weight above 3×10^2. The new signal was observed at a higher magnetic field by adding iodine to the solution of PEG of molecular weight above 2×10^3 than by adding iodine to the solution of PEG of molecular weight between 3×10^2 and 2×10^3 (Fig. 9). Apparent change was not obtained in the IR spectra of the chloroform solution of PEG by the addition of iodine.

2) Examination in Conformation of a PEG Molecule

As shown in Fig. 10, PEG of molecular weight below 3×10^2 was freely soluble in distilled water and slightly soluble in carbon tetrachloride. PEGs of molecular weight between 4×10^2 and 1.5×10^3 were soluble both in distilled water and in carbon tetrachloride. One gram of PEG of molecular weight between 4×10^2 and 1.5×10^3 was dissolved in 2 ml of carbon tetrachloride completely. PEGs of molecular weight above 2×10^3 were slightly soluble both in distilled water and in carbon tetrachloride.

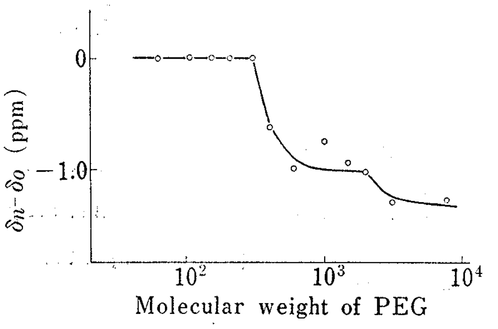

Fig. 9. Relation between Molecular Weight of PEG and the Difference of the Value of δ for the Original Signal in a NMR Spectrum of a Carbon Tetrachloride Solution of PEG, δ_o, to the Value for the New Signal Observed by the Addition of Iodine, δ_n

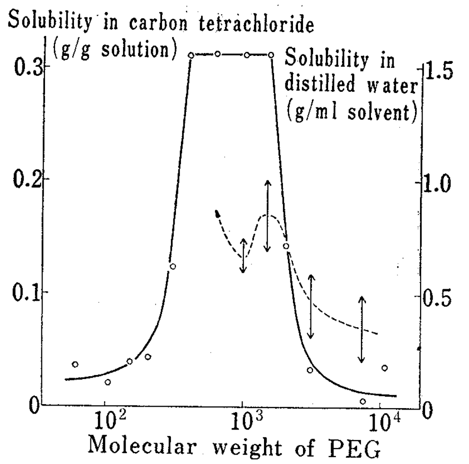

Fig. 10. Influence of Molecular Weight of PEG on Solubility in Carbon Tetrachloride and in Distilled Water

—○—: in carbon tetrachloride at 30°
--- ↕ ---: in distilled water at 20°
The data in "Daishichikaisei Nihon Yakkyokuho Daiichibu Kaisetsusho, C-1300 (1965), Hirokawa Shoten" were plotted for solubility of PEG in distilled water.

When molecular weight of PEG was between 6×10^2 and 4×10^3, a broad signal was observed in an ORD spectrum of a carbon tetrachloride solution of PEG and iodine (Fig. 11), though the similar phenomenon has not been reported yet. This finding shows that a PEG molecule of molecular weight between 6×10^2 and 4×10^3 is in loosely spiral conformation in carbon tetrachloride. High solubility of PEG of molecular weight between 4×10^2 and 1.5×10^3 in carbon tetrachloride is probably attributed to the spiral conformation of the PEG molecules. Recently, it was clarified by the study of X-ray, IR and Raman spectra of PEGs that a PEG molecule in solid state was in spiral conformation consisting of seven monomer units in which methylene groups were outside the spiral and oxygen atoms were inside the spiral.7) The signal disappeared gradually with the lapse of the time after 24 hours from the time of the preparation. Probably, the spiral conformation of a PEG molecule is destroyed by the interaction with iodine.

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7) H. Tadokoro, Y. Chaya, M. Kobayashi, T. Yoshihara, S. Murahashi, and K. Imada, *Repts. Progr. Polymer Physics Japan*, **6**, 303 (1963); H. Tadokoro, Y. Chaya, T. Yoshihara, S. Tahara, and S. Murahashi, *Makromol. Chem.*, **73**, 109 (1964); Y. Murai, T. Tsubota, H. Tadokoro, and T. Yoshihara, *J. Polymer Sci.*, **A**, **3**, 2275 (1965).

The relation between intrinsic viscosity, $[\eta]$, and molecular weight, M, was represented by equation (1) for PEGs of molecular weight above 2×10^2.

$$[\eta] = KM^{\alpha} \qquad (1)$$

K,α; Parameters dependent on physical and chemical properties of the polymers and so on

Kuhn showed that α was 0.5 for a polymer molecule in spherical conformation[8] and Debye showed that α was 1.0 for a polymer molecule in neckless-like conformation.[9] As shown in Fig. 12, α was 0.55 for the ethanol solutions of PEGs of molecular weight above 2×10^2 and 0.68 for the carbon tetrachloride solutions. Formation of iodine in the diatomic state and whose interatomic distance is a little prolonged by the interaction with PEG may be remarkable when PEG molecules are in spherical conformation. PEGs of molecular weight above 2×10^3 may be in more spherical conformation than the molecules of molecular weight below 2×10^3.

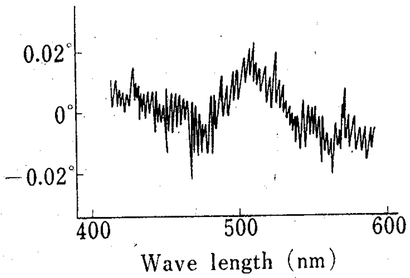

Fig. 11. An ORD Spectrum of a PEG 2000–Iodine–Carbon Tetrachloride Solution

9.0×10^{-1}M of PEG 2000 (monomer unit) and 2.4×10^{-4}M of iodine

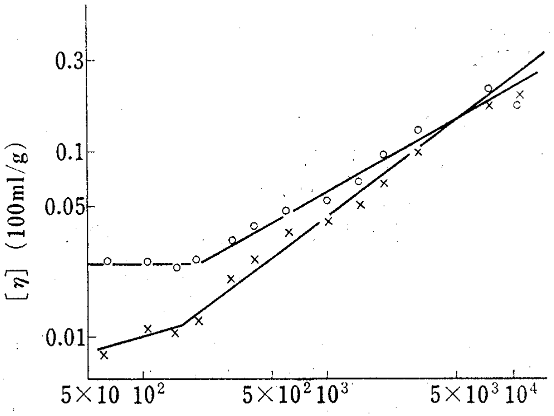

Fig. 12. Relation between Molecular Weights of PEGs and Intrinsic Viscosities of the Ethanol Solutions and the Carbon Tetrachloride Solutions

○: in ethanol
×: in carbon tetrachloride

Acknowledgement The authors express their gratitude to Mrs Mayumi Tobe, one of the members of Analytical Center of School of Pharmaceutical Sciences, Showa University, for measurement of IR and NMR spectra.

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[8] W. Kuhn, *Helv. Chim. Acta*, **26**, 1394 (1943).
[9] P. Debye, *J. Chem. Phys.*, **14**, 636 (1946).