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Spectrophotometric Studies on Accelerated Hydrolysis of Iodine In the Presence of Polyvinylpyrrolidone[1]

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The spectra of iodine in the presence of iodide, iodic acid, and polyvinylpyrrolidone (PVP) were obtained. Large effects of PVP concentrations on the spectra were observed. Changes in iodine spectra in the presence of N-methyl-2-pyrrolidone and N,N-diethylpropionamide in various solvents indicated charge-transfer type interaction in less polar solvents. The spectra of the aqueous iodine solution were more affected by the addition of PVP with a smaller degree of polymerization. Kinetic studies of hydrolysis of iodine in the absence and presence of PVP indicated that PVP accelerates hydrolysis of iodine except for the initial period. The possible mechanism of accelerated hydrolysis of iodine in the presence of PVP is complexation of triiodide ion with PVP and subsequent shifts in the hydrolysis equilibrium of iodine.

Keywords——iodine; polyvinylpyrrolidone; N-methyl-2-pyrrolidone; polyvinylpyrrolidone·triiodide complex; charge-transfer complex; hydrolysis; hydrolytic rate; accelerated reaction; absorption spectrum; degree of polymerization

Polyvinylpyrrolidone-iodine has been used for many years as a topical antimicrobial.[3] During the course of studies on permeability of iodine through partition membranes in the presence of polyvinylpyrrolidone (PVP), it was observed that apparent permeability of iodine decreased with time.[4]

A decrease in apparent permeability of iodine was attributed to a decrease in concentration of molecular iodine due to sequenses of reactions 1,2, and 4 shown in Chart 1;[5]

$$I_2 + H_2O \rightleftharpoons I^- + H^+ + HIO \qquad (1)$$

$$I_2 + I^- \rightleftharpoons I_3^- \qquad (2)$$

$$5I^- + IO_3^- + 6H^+ \rightleftharpoons 3I_2 + 3H_2O \qquad (3)$$

$$PVP + I_3^- \rightleftharpoons PVP \cdot I_3^- \qquad (4)$$

$$PVP + I_2 \rightleftharpoons PVP \cdot I_2 \qquad (5)$$

Chart

It was proposed that PVP interacts according to reaction 4 with triiodide ion, which is formed according to reaction 2 from iodine and iodide ion, which in turn is produced by hydrolysis of iodine according to reaction 1. In order to confirm the above proposition, spectrophotometric studies on changes in absorption spectra of iodine were undertaken.

As to the interaction of iodine with PVP, as early as 1954 Oster and Immergut[6] observed an increase in absorbance of iodine by the addition of PVP. Barkin, *et al.*[7] reported a strong

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[1] Pharmaceutical Studies on Iodine, Part 2; Preceding paper, Part 1, K. Takizawa, M. Nakano, and T. Arita, *Chem. Pharm. Bull.* (Tokyo), **26**, 874 (1978).

[2] Location: *Kita-12, Nishi-6, Kita-ku, Sapporo, 060, Japan.*

[3] H.A. Shelanski and M.V. Shelanski, *J. Int. Coll. Surg.*, **25**, 727 (1956).

[4] Part 1 of this series.

[5] T.L. Allen and R.M. Keefer, *J. Am. Chem. Soc.*, **77**, 2957 (1955).

[6] G. Oster and E.H. Immergut, *J. Am. Chem. Soc.*, **76**, 1393 (1954).

[7] S.M. Barkin, H.P. Frank, and F.R. Eirich, *Ricerca Sci.*, **25**, *Suppl. Simposio Intern. Chim. Macromol.*, Milan-Turin, 844 (1954).

temperature dependence in distribution equilibrium in the interaction of iodine with PVP. Siggia[8] noted that some chemical reactions took place during the preparation of PVP·iodine in solid state and that only about two-thirds of the original amount of iodine remained as available iodine.

Later Moriguchi *et al.*[9] studied the nature of complexation of PVP with iodine spectrophotometrically. More recently, Kaneniwa and Ikekawa[10] reported on a spectral change of iodine in organic solvents by the addition of PVP and α-pyrrolidone, while Cournoyer and Siggia[11] stated that a stable PVP·iodine complex is formed following iodine hydrolysis and subsequent association of ionic iodine with molecular iodine.

Experimental

Materials——Iodine, sodium iodide, iodic acid, cyclohexane, 1,4-dioxane, and dichloromethane (all of reagent grade) were purchased from Wako Pure Chemical Industries, while N-methyl-2-pyrrolidone and N,N-diethylpropionamide from Tokyo Kasei Kogyo Co., and polyvinylpyrrolidone (PVP) K-15, K-30, and K-90 (labeled average molecular weights of 10000, 40000, and 360000, respectively) from Daiichi Pure Chemical Co. They were used without further purification.

Measurements of Absorption Spectra——Because of much temperature dependence of the spectra of iodine in the presence of PVP, all spectra were obtained with a 1 cm-cell (with a Teflon-cap) placed in 198157 Thermoregulated Rectangular Cell Holder (30°) of Beckman ACTA M-VI spectrophotometer except for spectra shown in Fig. 1, which were obtained with Shimadzu UV-300 spectrophotometer at ambient temperature.

Kinetic Studies——In order to investigate the kinetics of hydrolysis of iodine, a concentrated solution of iodine in dioxane was employed as a stock solution. The stock solution was diluted with prewarmed distilled water (resultant solvent, dioxane: water=1: 30) in a cell placed in the thermoregulated cell holder (30°) and the absorption spectra were obtained at suitable time intervals employing 574060 Rep. Scan Timer Accessory for Beckman ACTA M-series spectrophotometer. The kinetics of hydrolysis of iodine in the presence of PVP was investigated in the similar manner.

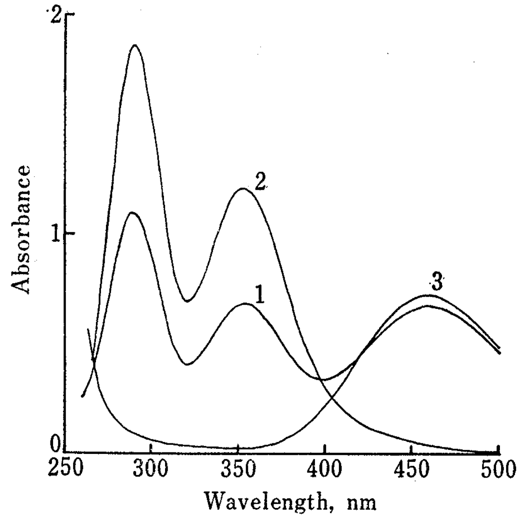

Fig. 1. Absorption Spectra of 1×10^{-3} M Iodine in Water (1), 5×10^{-5} M Iodine in 2% NaI Solution (2), and 1×10^{-3} M Iodine in 0.01 M HIO_3 Solution (3)

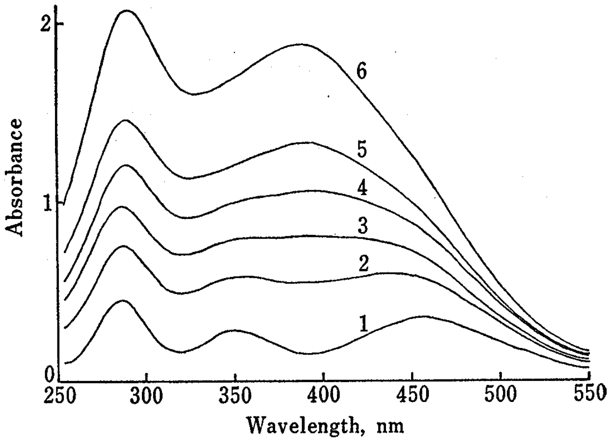

Fig. 2. Absorption Spectra of 5×10^{-4} M Iodine in 0% (1), 0.01% (2), 0.02% (3), 0.03% (4), 0.05% (5), and 0.1% (6) PVP K-15 Solutions in Water

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[8] S. Siggia, *J. Am. Pharm. Assoc., Sci. Ed.*, **46**, 201 (1957).

[9] I. Moriguchi, Y. Araki, and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **17**, 2088 (1969).

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[11] R.F. Cournoyer and S. Siggia, *J. Polymer Sci., Polymer Chem. Ed.*, **12**, 603 (1974).

Results and Discussion

Spectra of Iodine in the Presence of Iodide, Iodic Acid, and PVP

The absorption maxima of an aqueous iodine solution were observed at 288, 352, and 460 nm (curve 1, Fig. 1). In the presence of sodium iodide, the two peaks at 288 and 352 nm originated from triiodide ion, I_3^-, formed according to reaction 2 were observed (curve 2, Fig. 1). In the presence of iodic acid, on the other hand, only one peak at 460 nm originated from iodine, I_2, was observed (curve 3, Fig. 1) since iodide ion reacts with iodic acid to form iodine according to reaction 3. These observations are in agreement with published reports.[5,9]

By the addition of PVP to an aqueous iodine solution, the peaks originated from triiodide ion were red-shifted[9] while the peak originated from iodine was blue-shifted (compare curve 2 with curve 1, Fig. 2). These shifts may be attributed to the appearance of a strong absorption band between the two peaks. In the aqueous iodine solution containing sodium iodide, the peaks originated from triiodide ion were also red-shifted by the addition of PVP (not shown), whereas in the aqueous iodine solution containing iodic acid, little change was observed by the addition of PVP (not shown). Little interaction of iodine with PVP may represent either weak interacting tendency of PVP with molecular iodine in a highly polar solvent such as water or changes in the PVP structure in the presence of highly acidic iodic acid (resultant pH, 2.0) and a resultant decrease in an interacting tendency.

Effect of Concentration of PVP on the Spectra

The absorption spectra of an aqueous iodine solution were found to be extremely dependent on the concentrations of PVP (Fig. 2). The peaks possibly originated from PVP·triiodide ion complex formed according to reaction 4 were observed at around 290 and 380—390 nm when concentrations of PVP were high. When concentrations of free triiodide ion were high *i.e.* when sodium iodide was added or when the ratio of PVP to iodine was very large (greater amounts of iodide are formed by reaction of iodine with terminal double bonds of PVP; refer to discussion on "effect of degree of polymerization of PVP" for the explanation), the peak in the region of 380—390 nm was blue-shifted (not shown) because of large molar absorptivity of triiodide ion at 352 nm.

Interaction of Iodine with Amides

In order to investigate the interaction of molecular iodine with PVP, four solvents with different polarity; cyclohexane, dichloromethane, dioxane, and water (in the increasing order of polarity), were employed. Since PVP is practically insoluble in nonpolar organic solvents,

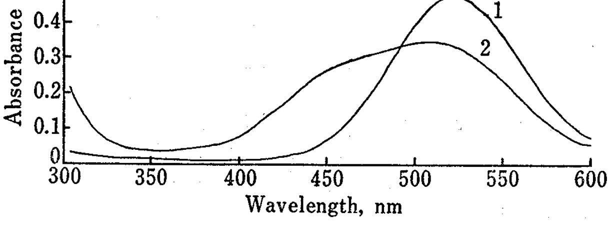

Fig. 3. Absorption Spectra of 5×10^{-4} M Iodine in the Absence (1) and in the Presence (2) of 2.5×10^{-2} M N-Methyl-2-pyrrolidone in Cyclohexane

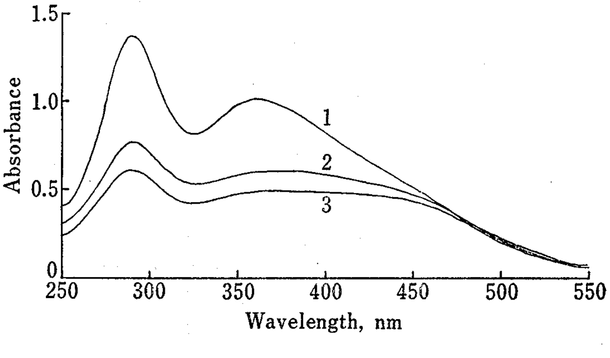

Fig. 4. Absorption Spectra of 3×10^{-4} M Iodine in 0.05% Aqueous Solutions of PVP K-15 (1), PVP K-30 (2), and PVP K-90 (3) All Stored for 24 hr at 30° Prior to Measurement after Preparation

two amides, N-methyl-2-pyrrolidone and N,N-diethylpropionamide, were employed as electron donors instead of PVP. The absorption maximum of iodine in cyclohexane at 525 nm was blue-shifted in the presence of N-methyl-2-pyrrolidone as shown in Fig. 3, similar shifts being also noted by the addition of the amides to the solution of iodine in the organic solvents. Little shift was however observed by the addition of the amides to the aqueous iodine solution. Based on the observation that the interaction of N-methyl-2-pyrrolidone with iodine appears to be more pronounced when the solvent with lower polarity was employed and not observed when water, a highly polar solvent, was used, the interaction of iodine with amides in less polar solvents may be attributed to a charge-transfer interaction.⁹⁾ The fact that the interaction was observed in N,N-diethylpionamide as well as in N-methyl-2-pyrrolidone indicates that the interaction is not characteristic of a lactam ring only but of amide groups in general.

Effect of Degree of Polymerization of PVP on the Spectra

When the w/v% concentrations of PVP were the same, the absorption spectra of the aqueous iodine solution were more affected by the addition of PVP with a smaller degree of polymerization (Fig. 4). If there are two unsaturated terminal groups (double bonds) per PVP molecule, 0.05% PVP (Fig. 4) is equivalent to 1×10^{-4} M, 2.5×10^{-5} M, and 1.8×10^{-6} M with respect to unsaturated groups for PVP K-15, K-30, and K-90, respectively. The absorbance due to PVP·triiodide ion complex increased in the following order, PVP K-90, K-30, K-15, namely in the order of the "concentration" of unsaturated groups.

The above observations may be rationalized in the following way. Since iodine is expected to react with terminal unsaturated groups in PVP to form iodide ion,⁸⁾ triiodide ion is formed according to reaction 2. Triiodide ion in turn interacts with PVP according reaction 4, resulting in the appearance of strong absorption due to PVP·triiodide ion complex.

Kinetics of Hydrolysis

Change in the absorption spectra of iodine in water with time are shown in Fig. 5. The absorbance of triiodide ion increased while that of iodine decreased with time. Spectral changes are in accordance with hydrolysis of iodine according to reaction 1. Changes in absorption spectra of iodine with time in the presence of PVP are shown in Fig. 6. The absorbance in all wavelength regions increased with time. Because of strong absorption bands due to PVP·triiodide ion complex, a possible decrease in absorbance due to a decrease in molecular iodine is overwhelmed by an increase in absorbance of broad absorption band of PVP·triiodide ion complex. The roughly estimated reaction rate constants were 3.3 hr⁻¹ without PVP and 1.6 hr⁻¹ with PVP (0.03%) during the first 30 min, whereas they were 0.1 hr⁻¹ without PVP and 0.2 hr⁻¹ with PVP (0.03%) during 6 hr period from 1 to 7 hr. They

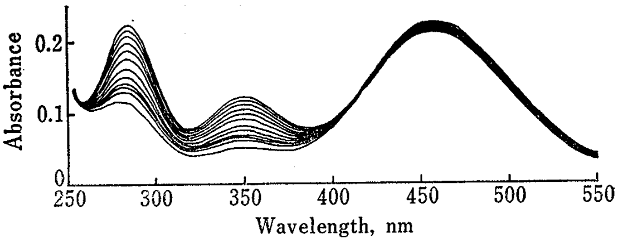

Fig. 5. Change in Absorption Spectra of 3.2×10^{-4} M Iodine in Water at 30° with Time (0, 10, 20, 30 min, 1, 2, 4, 6, 8, 10, 12 and 14 hr, from Bottom in Short Wave Length Region)

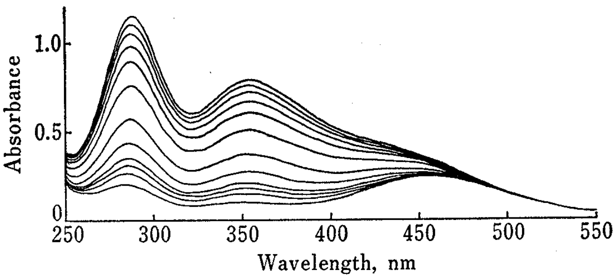

Fig. 6. Change in Absorption Spectra of 3.2×10^{-4} M Iodine in 0.03% Aquepus PVP K-15 Solution at 30° with Time (0, 10, 20, 30 min, 1, 2, 4, 6, 8, 10, 12 and 14 hr, from Bottom)

were estimated employing Guggenheim method[12] under the following assumptions; (1) since reactions 2 and 3 (Chart 1) may be considered to be rapid, reaction 1 be rate determining, (2) in the absence of PVP, the change of the absorbance of triiodide ion be proportional to the cumulative amount of iodide ion produced, (3) in the presence of PVP, the change of the absorbance of PVP·triiodide ion complex be proportional to the cumulative amount of iodide ion produced, (4) uncomplexed iodine be the only species which is susceptible to hydrolysis, and (5) during the initial hours of the reaction, a decrease in uncomplexed iodine according to reaction 2 be negligible compared to the total amount of uncomplexed iodine present. The wavelengths chosen for absorbance reading in the estimation of the reaction rate constants were 350 nm without PVP and 353 nm with PVP. Thus the reaction rate constant in the presence of PVP was larger than that in its absence except for the initial period of hydrolysis, when it was smaller in the presence of PVP than that in its absence. The difference in the rate constants in the presence and absence of PVP may be rationalized in the following fashion. Since at the beginning of hydrolysis only a small amount of iodide ion is formed and the concentration of molecular iodine is much greater than that of triiodide ion, in the presence of PVP, iodine may form a weak complex with it (Chart 1, reaction 5) and is less available for hydrolysis than in the absence of PVP. An alternative explanation is a possible change in activity of water in the presence of PVP, resulting in retarding the hydrolysis of iodine in the presence of PVP. As the time elapses, the concentration of triiodide ion formed according to reaction 2 increases and in the presence of PVP triiodide ion forms complex with it. Therefore effective concentrations of triiodide and iodide ions tend to decrease. Under this condition, equilibrium hydrolytic reaction according to reaction 1 proceeds to the right to maintain this equilibrium and therefore hydrolysis rate in the presence of PVP is greater than that in its absence.

Conclusion

Spectroscopic evidence indicated interaction of polyvinylpyrrolidone with triiodide ion. Since triiodide ion is formed by reaction of iodine and iodide, which in turn is formed by hydrolysis of iodine, hydrolysis of iodine can be accelerated by PVP. This proposition is in agreement with the observation that an amount of permeable iodine decreased with time as reported in the preceeding paper on changes in apparent permeability of iodine in the presence of PVP.

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