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Change in Apparent Permeability of Iodine in the Presence of Polyvinylpyrrolidone[1]

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The permeation patterns of iodine through a dimethylpolysiloxane membrane were studied using an all-glass permeation cell. The permeability of iodine was greater from solvents in which iodine is less soluble. In the presence of polyvinylpyrrolidone (PVP), the permeability decreased with storage period and with increasing amount of PVP. The permeability of iodine from a solution containing PVP decreased with increasing storage temperature prior to permeation studies. When iodide ions were added to the PVP-iodine system, the permeability of iodine became less than that in the absence of iodide ions. Further, the storage-time dependent decrease in permeability of iodine was much less in the presence of iodide ions. These observations suggest the decrease in the amount of permeable iodine in the system with time. This phenomenon is attributed to the acceleration of the hydrolysis of iodine in the presence of PVP.

Keywords——iodine; polyvinylpyrrolidone; polyvinylpyrrolidone-iodine; silicone membrane; permeability; storage temperature; storage period; permeable species; complexation; sustained release

Iodine has been used as a disinfectant for many years. Its high subliming tendency due to the high vapor pressure, staining property, and irritant action have been listed to be the disadvantages of iodine as a topical disinfectant.[3] In order to overcome these shortcomings, many iodophores have been prepared. Iodophores are carriers of iodine and are usually complexes of iodine with certain types of surfactants and water-soluble polymers.[4] In spite of extensive use of iodophores as disinfectants, the exact nature of iodine in iodophores has not been fully established.

Synthetic polymer membranes have been examined as a rate-limiting barrier to drug release in an attempt to sustain the action of drugs.[5] Silicone, ethylene-vinyl acetate copolymer, and other synthetic membranes have been explored in this respect.

In the present study, polymer membranes have been employed to examine the possible utility of these membranes in sustaining the release of iodine and facilitate the determination of free iodine in aqueous solutions containing iodine and a polymer from the measurement of permeation rates of iodine. The property of partition membranes through which only unionized and uncomplexed species in the polymer complex permeate constitutes the basis of the present study.[6,7] Polyvinylpyrrolidone has been employed as a water-soluble polymer because there has been still controversy as to the nature of iodine in polyvinylpyrrolidone-iodine system.[8-11]

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Experimental

Materials——The medical grade dimethylpolysiloxane sheeting (Silastic, non-reinforced, Lot HH1207, Dow Corning Corporation) in a labeled thickness of 5 mil (127 μm) and a polyethylene membrane (Sumikasen, Lot A1108, Sumitomo Chemical Industries Co.) in a labeled thickness of 20 μm were used.

Iodine, sodium iodide, and propylene glycol (all of reagent grade) were purchased from Wako Pure Chemical Industries, while macrogol 400 from Koso Chemical Co. and polyvinylpyrrolidone (PVP) K-15 and K-90 (labeled average molecular weights of 10000 and 360000, respectively) from Daiichi Pure Chemicals Co. They were used without further purification.

Permeation Studies——For measurement of permeability of iodine through silicone and polyethylene membranes, a permeation cell similar to that reported elsewhere[12] was employed. In short, the permeation cell consisted of 2 compartments, one on top of the other, with a membrane between them. The donor compartment was agitated by a magnetic stirring bar while the receptor compartment was agitated by a glass propeller. Thirty milliliter of a test solution and 25 ml of 10% sodium iodide solution (added to maintain a sink condition), which has been prewarmed, were placed in the donor and the receptor compartments, respectively. The permeation cell was immersed in a water bath maintained at 30.0°. The area available for permeation was 12.56 cm^2. At suitable time intervals, 5 ml of samples was pipetted from the receptor solution, appropriately diluted with 2% sodium iodide solution and assayed for total iodine spectrophotometrically at 352 nm employing Hitachi 200-20 digital spectrophotometer. A cumulative correction was made for the previously removed samples.

Determination of Solubility——An excess amount of iodine was placed into each solvent in a test tube with a glass-stopper. The suspension was equilibrated in a water bath maintained at 30.0° for about 24 hr by stirring it with a magnetic bar (10 mm long). A portion of the equilibrated mixture was filtered quickly through a sintered-glass disk. An aliquot of the filtrate was assayed for iodine in the same manner as in the permeation studies.

Results and Discussion

Effect of Solvents on Permeability[13]

The permeation patterns of iodine through the silicone membrane from four media are shown in Fig. 1. When the initial concentration of iodine was the same, the permeability was greater from the solvent in which solubility of iodine (Table I) was smaller. This indicates that the permeability depends on the activity of iodine in each medium.[14] Thus iodine in water has much greater tendency to partition into membrane (permeate) than that in propylene glycol or macrogol 400. The permeability of iodine through the silicone membrane calculated from the permeation rate from its suspension in water was 2.8×10^{-5} cm^2/sec at 30°. The initial permeation rate of iodine through the 127 μm silicone membrane from 2% sodium iodide solution was 19 times as great as that through the 20 μm polyethylene membrane (not shown) although the silicone membrane was thicker than the polyethylene membrane. Thus the permeability of iodine through the polyethylene membrane was estimated to be about

Table I. Solubility of Iodine at 30°

Solvent	Solubility (M)
Water	1.5×10^{-3}
2% NaI	7.0×10^{-2}
Propylene glycol	5.4×10^{-1}
Macrogol 400	>2.4

12) M. Nakano, N. Kohri, Y. Arakawa, and T. Arita, to be published.
13) When iodine permeates through a partition membrane from the donor compartment to the sink, the permeation rate is expressed by $ADKfC/l$, where A = area for permeation, D = diffusivity in the membrane, K = (membrane/donor solution) partition coefficient, f = fraction of permeable species, C = total concentration of iodine, l = thickness of membrane; and permeability and apparent (app.) permeability are defined by DK and DKf, respectively.
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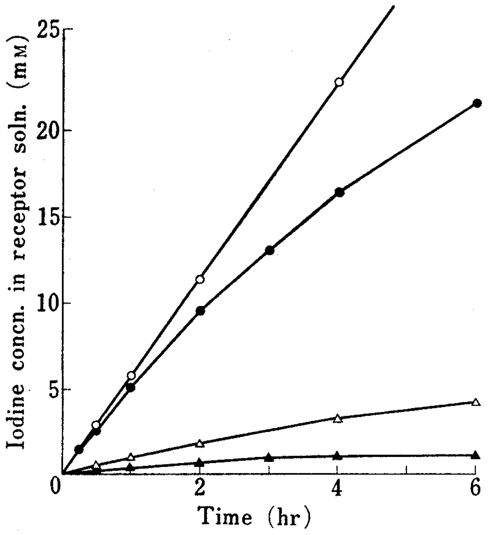

Fig. 1. Permeation Patterns of Iodine through the Silicone Membrane at 30° from Iodine Suspension in Water (○), 1% Iodine in 2% NaI (●), 1% Iodine in Propylene Glycol (△), and 1% Iodine in Macrogol 400 (▲)

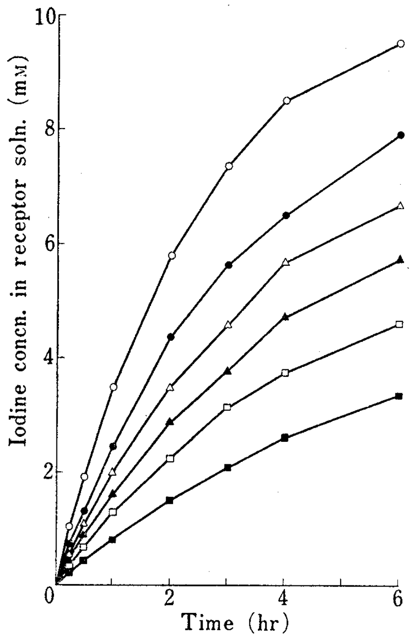

Fig. 2. Permeation Patterns of Iodine (Initial concn., 1%) through the Silicone Membrane from 2% PVP K-15 Solution at 30° Following Storage at 30° for 1 (○), 3 (●), 5 (△), 8 (▲), 12 (□), and 21 (■) Days prior to Permeation Studies after Preparation

2.3×10^{-7} cm^2/sec at 30°. Thus in order to obtain the sustained release of iodine, choice of membranes and solvents as well as thickness of the membrane must be considered.[6)]

Effect of Storage Period on App. Permeability[13)]

As shown in Fig. 2, the app. permeability of iodine through the silicone membrane from PVP K-15 solution decreased with an increase in the storage period of the PVP-iodine solution prior to the permeation experiment. Solubility studies undertaken separately (not shown) indicated that the apparent solubility of iodine in PVP K-15 solution increased with time over 40 day period examined. Such a decrease in the app. permeability with the storage period was observed also with a high molecular weight PVP (PVP K-90), with different concentrations of PVP K-15 (5% and 9%), with another partition membrane (polyethylene membrane), with reagents from other sources (PVP K-15 from Tokyo Kasei Kogyo Co. and iodine from E. Merck A.G.) and with carefully redistilled water from an all-glass distillation apparatus. On the other hand, little change was observed in the app. permeability of iodine with storage time when iodine was dissolved in sodium iodide solution. Based on these observations, except for a possible catalytic effect of some impurities present in all PVP or iodine samples, other factors may be essentially ruled out.

Effect of PVP Concentrations on App. Permeability

The permeation patterns of iodine through the silicone membrane from iodine solution with varying PVP K-15 concentrations are shown in Fig. 3. The higher PVP K-15 concentration, the smaller became the app. permeability. This indicates that the amount of iodine in the membrane-permeable form in the donor solution decreases with increasing PVP K-15 concentration. The decrease in the amount of iodine in the membrane-permeable form may be attributed either to reversible interaction (complexation) of iodine with PVP or to direct or indirect reaction of iodine in the presence of PVP.

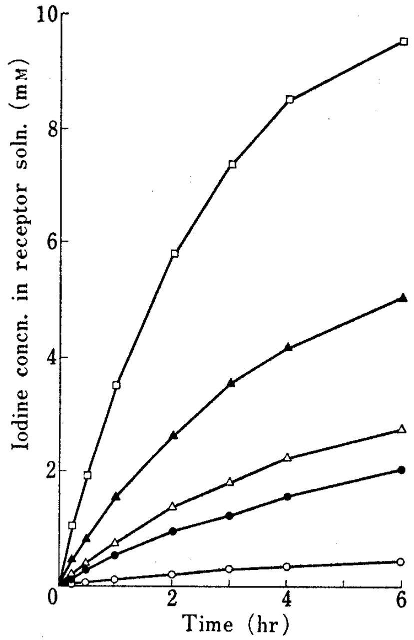

Fig. 3. Permeation Patterns of Iodine (Initial concn., 1%) through the Silicone Membrane at 30° from 2% (□), 3% (▲), 4% (△), 5% (●), and 9% (○) PVP K-15 Solutions All Stored at 30° for 24 hr prior to Permeation Studies after Preparation

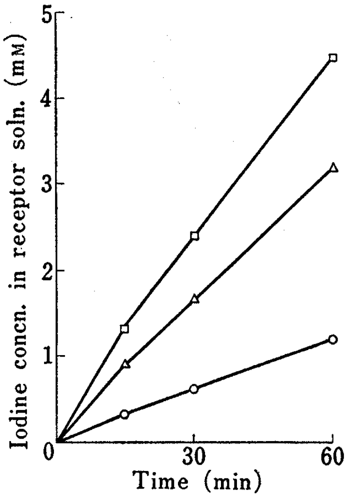

Fig. 4. Permeation Patterns of Iodine (Initial concn., 1%) through the Silicone Membrane at 30° from 2% PVP K-15 Solution Following Storage for 1 Day at 6° (□), 30° (△), and 50° (○) prior to Permeation Studies after Preparation

Effect of Storage Temperature on App. Permeability

The permeation patterns of iodine through the silicone membrane from iodine solutions stored at three different temperatures are shown in Fig. 4. Since the total amount of both iodine and PVP are the same in all cases and the permeation studies were carried out at 30°, the difference in app. permeability cannot be attributed to complexation of iodine with PVP. Thus reaction of iodine in the presence of PVP has to be taken into consideration.

Effect of Addition of Both PVP and Iodide on App. Permeability

The app. permeability of iodine through the silicone membrane from iodine solution containing both PVP K-15 and sodium iodide was much smaller than that from iodine solutions containing either one of these additives (Fig. 5). The decrease in the app. permeability of iodine from PVP-iodide system over 22 hr period of storage was much smaller (10%) than that from PVP K-15 solution over the same period of storage (40%). In the absence of PVP, the app. permeability of iodine from sodium iodide solution did not significantly change with storage time (not shown). This indicates that interaction of iodine with iodide is a rapid process and the amount of permeable species does not change significantly with time over the period. The decrease in the amount of permeable species with time in the presence of PVP, must therefore be rationalized from the standpoint of possible reaction of iodine in the presence of PVP.

General Discussion

The rate of reaction of iodine in the presence of PVP seems to be slow at 30° (Fig. 2) but increases with an increase in temperature (Fig. 4). The cause for the decrease in concentration of permeable species with PVP concentration (Fig. 3) may be attributed partly to an accelerated reaction of iodine with an increase in PVP concentration, although a large amount

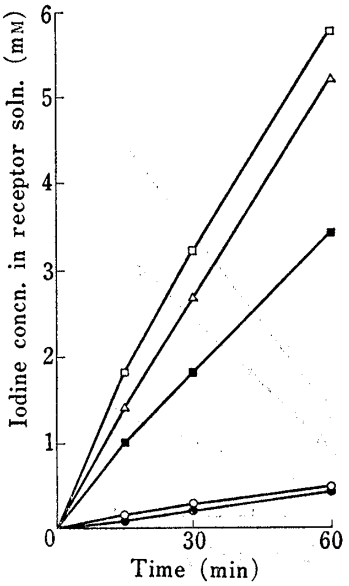

Fig. 5. Permeation Patterns of Iodine (Initial concn., 1%) through the Silicone Membrane at 30° from 2% PVP K-15 Stored for 2 hr (□), 2% PVP K-15 Stored for 24 hr (■), 2% NaI (△), 2% NaI+2% PVP K-15 Stored for 2 hr (○), and 2% NaI+2% PVP K-15 Stored for 24 hr (●) All Stored at 30° prior to Permeation Studies after Preparation

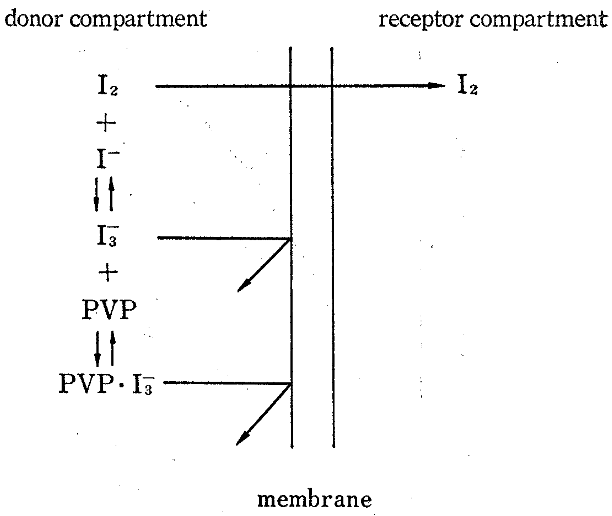

Chart 1. Proposed Model for Interaction of Iodine with Iodide Ion and PVP and Permeation of Free Iodine

of PVP tends to increase the proportion of iodine in the complexed form and thereby to decrease the concentration of the permeable species. Only slight changes in permeable species with time in the presence of both PVP and iodine (Fig. 5) may be rationalized from the proposition that most of iodine be in the complexed form in the presence of both PVP and iodide and only a small portion of iodine is uncomplexed and therefore reactive. Possible reaction of iodine in the presence of PVP has been studied spectrophotometically, the results of which will be published separately.[15] The spectrophotometric study essentially supports the present proposition that reaction of iodine be accelerated by PVP. In short, accerelated reaction of iodine in the presence of PVP may be rationalized in the following fashion (Chart 1). In aqueous solution, iodine is hydrolyzed to form iodide ion, which in turn is bound to iodine to form triiodide ion. In the absence of PVP, the above two processes are in equilibrium and hydrolysis of iodine is limited. In the presence of PVP, on the other hand, triiodide ion formed in the second process complexes with PVP and is removed from the initial equilibrium reaction. Thus hydrolysis proceeds further with a resultant decrease in free iodine concentration with time.

PVP has been known to interact with many drugs.[16,17] Since complexes are often less reactive, the addition of complexing agents is sometime used to depress the reaction.[18] According to the above proposition, on the contrary, the interactive property of PVP becomes the driving force of accelerated reaction.

Since only iodine in an uncomplexes and unreacted form is permeable to partition membranes (Chart 1), determination of permeability through such membranes may serve to be a convenient method of assay of free iodine in systems where iodine interacts with another component. The chemical method of dertermination of iodine, on the other hand, gives the total amount of iodine present in the system.[3,9]

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Conclusion

Although PVP has been known to interact with many drugs, PVP tends to accelerate hydrolysis of iodine and the amount of iodine in an uncomplexed form decreases with time in the presence of PVP.

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