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PROPERTIES AND PERMEABILITIES OF POLYVINYL ALCOHOL MEMBRANES CONTAINING OXYSTARCH*

Enteric coated tablets are made by coating with various materials on a core tablet, whose materials have specific properties being soluble in alkaline condition thus allowing the drug (in tablet form) to elute easily in the body. In order for the drug to release its agents continuously, it is preferable to directly coat the tablet with polymer film materials on granules or on particles of drug, and to endow a permeation varied with pH change for the materials.

On the basis of these points of view, polyvinyl alcohol (PVA) membranes containing oxystarch likely to be soluble in alkaline solution were prepared. The permeations and properties of the membranes are discussed herewith.

Experiments

Oxystarch used here was prepared by oxidizing a defatted corn starch with periodic acid, according to the manner described by Jackson (1). The degree of oxidation was determined by reductions with sodium borohydride solution, as was made by Rankin (2). More than 75% of pyranose ring in starch was converted to two aldehyde groups. Commercially obtained PVA (Koso chemical Co. Ltd., degree of polymerization being 2000) were used without further treatments.

PVA membranes containing various amounts of the oxystarch were prepared by casting the solution mixture of PVA and oxystarch in water on a flat glass surface at room temperature. After drying, these membranes were annealed at 80, 100, 120, and 150°C for 1 hour.

Permeability measurements of the membrane (thickness 1×10^{-1} mm) for polyethylene glycohol (PEG) 200 were carried out at 36°C for 3 hours, using the dialysis cell (12 ml) on which the pre-swollen membrane was mounted.

A concentration of PEG was determined by Abbe 3-L type refractometer (Shimazu Ltd.). An initial concentration of PEG equals 3.0 gr/100 ml.

Tensile strength of membranes was measured at room temperature with Shimazu outograph P-100 type testing instruments.

X-ray diffraction patterns were recorded with nickel filtered copper K_α radiation by the JEOL JDX-5P type apparatus. The crystallite size of PVA was roughly estimated from a half width of the diffraction peak at $2\theta = 19.6°$.

Differential scanning calorimetric (DSC) measurements were made by a heating rate of 16°C/min from room temperatures to 350°C, using the Perkin-Elmer DSC-1B type apparatus.

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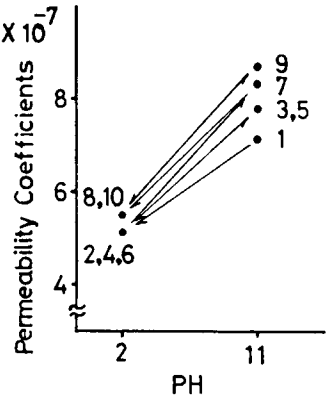


Fig. 1. Permeabilities of PVA-oxystarch membranes at pH 2 and pH 11, annealed at 120°C for 1 hr, oxystarch contents 33 wt-%.

	pH 11		pH 2
1*	7.1×10^{-7} (cm^2/sec)	2	5.2×10^{-7} (cm^2/sec)
3	7.8	4	5.2
5	7.8	6	5.2
7	8.3	8	5.5
9	8.7	10	5.5

*Numbers represent the order of measurements.

Results and Discussion

The permeabilities of the membrane containing oxystarch 33 wt-%, which was annealed at 120°C for 1 hour, increased prominently in the alkaline region compared to that in the acidic region (3). As shown in Figure 1, the permeability coefficients at pH 2 are $5.2 - 5.5 \times 10^{-7}$ (cm^2/sec), while these at pH 11 increase gradually from 7.1×10^{-7} (cm^2/sec) to 8.7×10^{-7} (cm^2/sec) during the repeating operation. In the PVA membrane no such change in permeation was observed (4).

It is well known that oxystarch are solubilized through decomposition of aldehyde in alkaline solution (5). A part of oxystarch, however, reacted with hydroxy group of PVA to form cross-links. Such a reaction of oxystarch with alcohol was shown by Goldstain et al. (6). Therefore, it is expected that the membrane becomes insoluble in water.

This seems to be caused by the dissolution of only small amounts of oxystarch in the membrane that gradually increase permeation during the repeating operation and the higher value at pH 11 than that at pH 2. However, the marked difference in permeability between pH 2 and pH 11 in Figure 1 cannot be explained in terms of only the cross-linkage structure and the partial dissolution of the oxystarch. The phenomena are probably related to a reversible change of swelling of the membrane in both the alkaline and acidic condition.

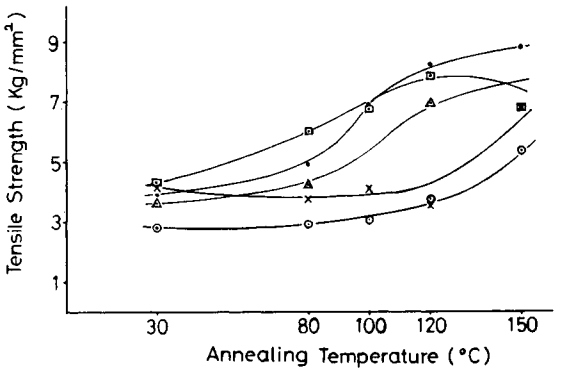


Fig. 2. Relation between tensile strength and annealing temperature for the membranes, —●— PVA, ✳ 14 wt-%, —⊙— 33 wt-%, —⊡— 44 wt-%, —Δ— 69 wt-% oxystarch contents.

The relationship between the tensile strength of membranes and annealing temperatures is shown in Figure 2. The tensile strength of membranes, except for contents of 14 wt-% and 33 wt-% oxystarch, tends to increase with an increase of the annealing temperature. For the two membranes (14 wt-% and 33 wt-% oxystarch contents), the tensile strength did not vary with the treatments up to 120°C but did slightly increase at 150°C. Furthermore, the tensile strength of the membranes containing oxystarch of 44 wt-% and 69 wt-% were restored to that of the PVA membrane.

As will be shown herewith by the x-ray diffraction and DSC studies, the crystallinity and crystal perfection of the PVA in the membrane increase, above room temperature, by annealing. Thus, enhancement of the film strength with annealing can be considered a consequence of the increase in crystallinity of the PVA phase. On the other hand, the recovery of the strength with decreasing PVA contents in membranes is considered to be caused mainly by the interaction between PVA and oxystarch, such as cross-linking, even though it may be influenced by the properties of oxystarch itself.

The relation between the crystallite size estimated from the x-ray diffraction peak and annealing temperature for the membranes containing oxystarch is shown in Figure 3. For the membranes of PVA and oxystarch contents of 14 wt-% and 33 wt-%, the crystallite size of PVA in membranes gradually developed with the increasing of the annealing temperature. However, in the membrane containing 69 wt-% oxystarch the crystallite size remained unaltered with the annealing. This suggests that the crystal growth of PVA was inhibited due to the cross-linkage occurred by the reaction between the hydroxyl groups of PVA and aldehyde groups of oxystarch present in the membranes. It may be expected that the cross-linkage structure is also slightly produced in the membrane of less oxystarch contents.

DSC thermograms of the membranes annealed at 80°C are shown in Figure 4. Comparing the blank test curve, broad and comparatively sharp endothermic peaks appeared at around 120 and 200°C, respectively. The former peak cor-

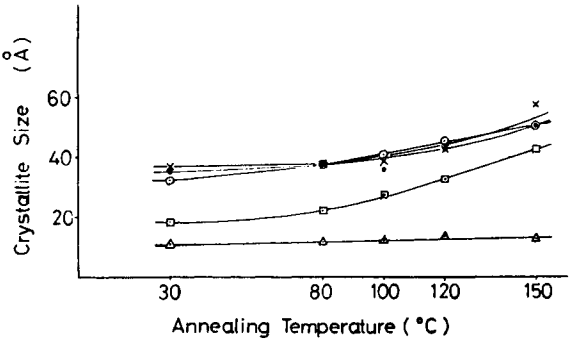


Fig. 3. Relation between annealing temperature and crystallite size of PVA in the membranes, —●— PVA, ⁎ 14 wt-%, —⊙— 33 wt-%, —⊡— 44 wt-%, —Δ— 69 wt-% oxystarch contents.

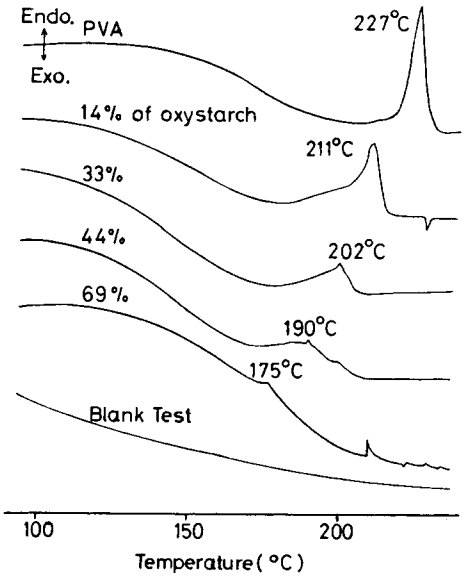


Fig. 4. DSC thermograms of PVA-oxystarch membrane annealed at 80°C.

responded to the desorption of water from the membrane and the latter to the fusion of PVA crystals. The melting peak (200°C) decreased in the area and shifted toward lower temperature with increasing oxystarch contents. This indicates a decrease in the crystallite size or crystal perfection of PVA. These facts, also suggest an existence of cross-linking in the membranes–which is consistent with previous findings in the x-ray studies.

The permeation of PVA membranes containing 70 wt-% of polyacrylic acid (PAA) is shown in Figure 5. Although a marked histerisis was observed between pH 2 and pH 11, the constant values for the permeability coefficients at pH 2 and pH 11 were obtained during a few cycles of the operation. The

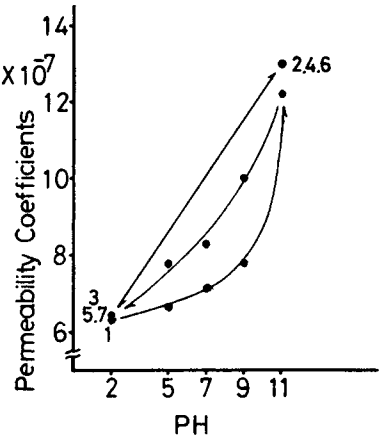


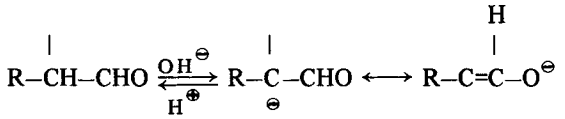
Fig. 5. Permeabilities of PVA-PAA membrane between pH 2 and pH 11, annealed at 100°C for 1 hr, PAA contents 70 wt-%.

behavior was similar to that of PVA containing oxystarch; however, in this case the reversibility between pH 2 and pH 11 was decidedly better.

According to Kuhn et al. (7) filaments containing PAA and polyvalent alcohol brought about dilation and contraction by pH change. The phenomena were explained with the arguments concerning the electrostatic energy of the ionized system.

From the results obtained herewith, in PVA membranes containing oxystarch the existence of the cross-linkage structure was almost confirmed. Hence, it is assumed that cross-links in the membrane prevent its dissolution but they will hardly enhance swelling by themselves. As described in the previous section, the small but gradual increase in the permeability at pH 11 suggests that a small amount of the oxystarch in the membrane dissolved during the cycles of the measurements. This suggests that the cross-linking density in the membrane is not so high. When the cross-linking density is fairly low, parts of the oxystarch molecules apart from the cross-linkage can swell in a solution.

The marked difference observed here in the permeability between pH 2 and pH 11 is concerned with a variation in swelling of the membrane due mainly to that of the unsolubilized oxystarch by rather small numbers of cross-linkings with PVA. Furthermore, the increase of swelling, hence the increase in permeability, in alkaline condition is thought to be caused by the electrostatic interaction among the negative charge, which is attributed to the dissociation in aldehyde of the oxystarch, such as



It is required for the practical view points that an appreciable change in permeation of drugs for membranes occur within the range of pH 2 to 8. As one attempts to meet these requirements, the introducing of sulfonyl groups to polymer molecules must be considered, which groups are liable to dissociate in a more acidic region compared to the aldehyde groups.

Further descriptions of these studies will be published at a later date.

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Yasuo Nozawa
Fukuji Higashide

Shizuoka College of Pharmacy
Oshika 2-2-1, Shizuoka
Japan

Tetsuo Kanakoto

Department of Chemistry
Faculty of Science
Science University of Tokyo
Kagurazaka 1-3, shinjuku-ku
Tokyo, Japan

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