DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 20(6), 1007-1020 (1994)

THE EFFECT OF PLASTICIZERS ON THE PROPERTIES OF POLYVINYL ALCOHOL FILMS

L. Y. Lim and Lucy S. C. Wan

Department of Pharmacy, National University of Singapore
10, Kent Ridge Crescent, Singapore 0511

ABSTRACT

The effect of water-soluble plasticizers *viz* propylene glycol (PG), glycerol and polyethylene glycol 600 (PEG) on the morphology and water resistance of polyvinyl alcohol (PVA) films was investigated. Polyvinyl alcohol films were cast from aqueous solutions, and their morphology studied using differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). Water resistance was characterized by the extent of film dissolution and the water uptake capacity of remnant films after immersion of the films in distilled water for 3 days at 37°C. DSC thermograms showed that crystallite formation in the PVA films was affected to different extent by addition of the three plasticizers. The plasticizers not only reduced the degree of crystallinity in the films, but also lowered the crystalline melting temperatures probably by introducing defects into the crystal lattice. This factor, coupled with leaching of the water-soluble plasticizers from the films when immersed in distilled water, lowered the water resistance of the plasticized PVA films. The influence of plasticizers on the properties of PVA films was further related to the degree of compatibility between the plasticizers and PVA.

INTRODUCTION

In some drug delivery systems, the release of incorporated drug from the system is controlled by the rate of diffusion of drug molecules across a polymer membrane. For the polymer membrane to act as an effective barrier to drug release, it must remain intact during the course of drug delivery. The membrane must be tough, resilient and be resistant to dissolution in an aqueous medium. At the same time, it should have adequate hydrophilicity to allow the penetration of water molecules into, and the diffusion of dissolved drug molecules out of the system.

Polyvinyl alcohol (PVA) has potential for use in these membrane-controlled drug delivery systems[1]. PVA films are easily prepared by evaporating to dryness an aqueous solution of the polymer. As PVA is water soluble, PVA films can be formed without the use of noxious solvents. The resultant films are resistant to tear, have a high degree of clarity and gloss, and do not irritate the skin[2]. One limitation which may however, impede the ability of PVA films to effect a controlled release of drug from a delivery system is the water solubility of the films. This situation may be remedied by heat treating the films before use. An earlier study has shown that heat treatment effectively enhanced the water resistance of PVA films leading to a slower rate of release of sulphathiazole from the films[3]. The water resistance of a PVA film is therefore a critical factor to its performance as a rate-limiting membrane in controlled release drug delivery systems.

Although heat treatment improves the water resistance of PVA films, it also renders the films brittle and difficult to handle. Film flexibility can be enhanced by the incorporation of plasticizers into the film[4]. The presence of plasticizers, especially those that are water-soluble, may however, weaken the water resistance of PVA films. This paper examines the effect of three water-soluble plasticizers namely glycerol, propylene glycol and polyethylene glycol 600, on the water resistance of PVA films. The results were correlated to plasticizer-induced changes in the morphology of the films.

MATERIALS

Polyvinyl alcohol (>98% hydrolysed, mw 14,000), propylene glycol (USP), glycerol (BP) from Sino Chemical Company Pte. Ltd. and polyethylene glycol 600 from BDH Chemicals Ltd. were used as supplied.

METHODS

Preparation of Films

Polyvinyl alcohol (PVA) films were cast from solutions containing 7.5% w/w of PVA, or of a mixture of PVA and plasticizer, in distilled water. The amount of plasticizer used was 5%, 10% or 20% of the total weight of solids in solution. Twenty grams of casting solution were weighed onto a disposable plastic petri dish having a diameter of 85mm, and the solvent evaporated off in an oven at 60°C over a period of 17 hours. The formed films detached readily from the petri dishes and were cut into discs measuring 30mm in diameter. The films were stored in desiccators at ambient temperatures for at least 24 hours before they were studied.

Characterization of Films

Film thickness was measured using a thickness gauge (Mitutoyo #7305) and recorded as the mean of five measurements. The films were dried to constant weight (W_1) in a desiccator at ambient temperatures before they were immersed for 3 days in 100ml of distilled water at 37°C. Excess water present on the swollen films were then removed by careful blotching of the films with filter paper. The films were weighed (W_2), returned to the desiccator and dried to constant weight, and reweighed (W_3). The amount of water imbibed per unit weight of PVA films was measured as a swelling index ($SI = (W_2 - W_3)/W_3$). The percent dissolution of the films was determined by calculating the difference in dry film weight before and after immersion of the films in distilled water (percent dissolution = $100(W_1 - W_3)/W_1$). All experiments were performed in triplicates.

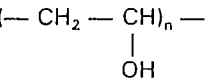
Surface morphology of the films was studied under a scanning electron microscope (Joel JSM 5200). Samples were mounted on studs and coated for 120s with a layer of gold using a sputter coater (Bio-Rad Microscience Division SC502). Scanning was performed at 20°C using a low beam voltage of 10kV.

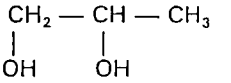
The films were further characterized using differential scanning calorimetry (Perkin Elmer DSC 4). Five-mg samples were weighed into standard aluminium pans and scanned at a rate of 20°C/min over a temperature range of 50°C to 250°C. Samples were scanned in triplicates.

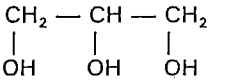
RESULTS AND DISCUSSION

Propylene glycol (PG), glycerol and polyethylene glycol 600 (PEG) were effective plasticizers of PVA molecules in that they reduced the brittleness of dry PVA films. Films containing 20% of the plasticizers were sufficiently flexible to be bent in the dried state without breaking. The incorporation of plasticizers up to 20% of polymer weight did not change significantly the thickness of PVA films. The mean thickness of PVA films was 224 ± 34 μm whilst films containing between 5 to 20% of PG, glycerol or PEG had thicknesses ranging from 201 to 240 μm.

To impart flexibility to a polymer, the plasticizer molecules have to interact with the polymer molecules[5]. Both glycerol and PG are polyols while PEG contains several ethylene oxide groups (Figure 1). The plasticizer molecules are therefore capable of forming hydrogen bonds with the PVA molecules. Polyethylene glycol 600 was, however, relatively incompatible with PVA. This incompatibility was evident during film preparation. While glycerol and PG were miscible with PVA solution when mixed to form the casting solution, the liquid PEG precipitated out of the polymer solution and had to be redissolved with mild heating. Although PEG then remained miscible with the polymer solution upon cooling, some of it may have precipitated separately from PVA during the subsequent process of solvent evaporation. As a result, PVA films

Polyvinyl Alcohol 

Propylene glycol 

Glycerol 

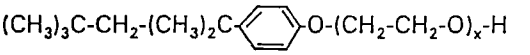
Polyethylene glycol 600 

FIGURE 1

Molecular formula of PVA and the plasticizers.

plasticized with increasing amounts of PEG exhibited increasing degrees of translucency and "bleeding". SEM micrographs of the films showed heterogeneity (Figure 2) on the surface which was in contact with the petri dish during film formation. There were irregular patches of darker regions interspersed amongst a lighter background. The other surface of the films was homogeneous when viewed under the SEM. In contrast, PVA films containing up to 20% of PG or glycerol were clear and glossy like the unplasticized PVA films. Both surfaces of these films had a homogeneous morphology when viewed under the SEM (Figure 2).

DSC thermograms of unplasticized PVA films showed a single endotherm having a peak temperature (T_m) of 225.95 ± 1.65°C and an enthalpy (ΔH) of 78.95 ± 2.84 J/g (Figure 3). The addition of plasticizers reduced to different extents both the values of T_m

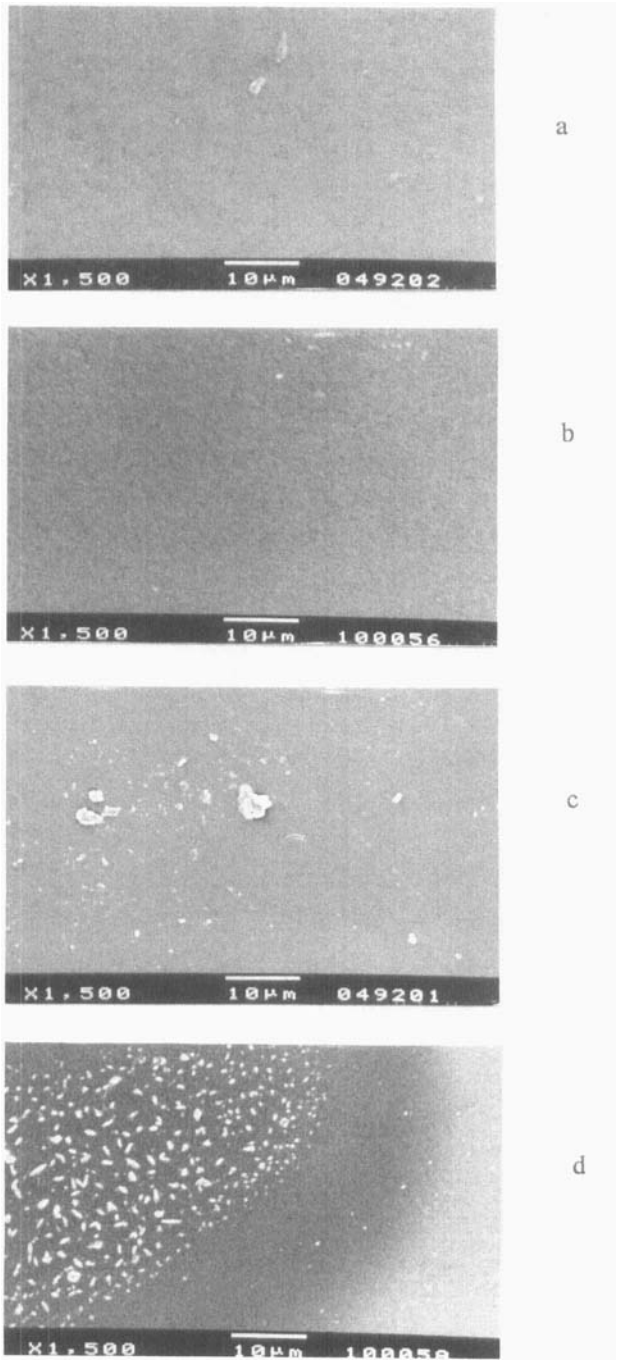


FIGURE 2

SEM micrographs of unplasticized PVA films (a) and of PVA films plasticized with 20% w/w propylene glycol (b), glycerol (c) and polyethylene glycol 600 (d).

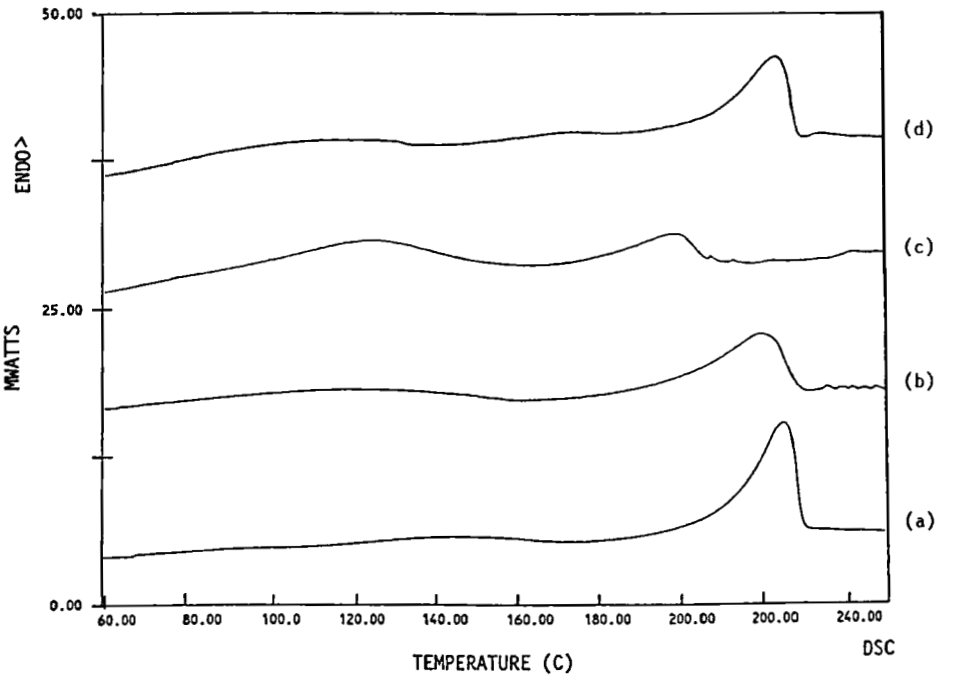


FIGURE 3

DSC thermograms of unplasticized PVA films (a) and of PVA films plasticized with 20% w/w propylene glycol (b), glycerol (c) and polyethylene glycol 600 (d).

and ΔH (Table 1). Crystallites are formed in a polymer when the polymer molecules align themselves into a lamellar lattice. This alignment is facilitated when the polymer molecules are linear in structure[6]. In the plasticized films, crosslinking of PVA molecules can occur via hydrogen bonding with the plasticizer molecules. Such structural modifications may hinder the formation of PVA crystallites in the plasticized films[7], the extent of hindrance being influenced by the size of the plasticizer molecule.

The molecular weights of PG, glycerol and PEG were 76, 92 and 646 (average) respectively. Small molecules like PG prevented to a small extent the formation of PVA crystallites in the films.

TABLE 1
Effect of Plasticizer on the T_m and ΔH values of PVA Films.

Plasticizer	T_m (°C)	ΔH (J/g)
-	225.95 ± 1.65	78.95 ± 2.84
Propylene glycol		
5%	222.86 ± 0.60	76.70 ± 2.51
10%	219.50 ± 1.78	70.97 ± 3.89
20%	214.54 ± 1.81	66.68 ± 5.29
Glycerol		
5%	219.53 ± 1.53	74.01 ± 4.30
10%	212.35 ± 0.68	60.13 ± 2.05
20%	195.95 ± 1.47	19.66 ± 3.56
Polyethylene glycol		
5%	224.58 ± 0.65	73.82 ± 1.02
10%	224.16 ± 0.24	69.21 ± 2.44
20%	223.77 ± 1.98	61.12 ± 5.41

Their presence lowered also the melting temperatures of PVA crystallites, possibly by introducing defects into the crystal lattice. Both the T_m and ΔH values decreased with increasing glycerol content in the PVA films (Table 1). DSC thermograms showed the emergence of a second endotherm at about 120°C, signifying the preferred formation of another type of crystallites in these films (Figure 3). Glycerol molecules, being larger in size than PG molecules, are not as easily accommodated in the crystal lattice of PVA films. As a result, much smaller and probably more defective crystallites of lower melting temperatures were formed in the PVA films plasticized with glycerol. Nevertheless, the overall degree of crystallinity in these films, as measured by the summation of enthalpies in the two endotherms, was similar to that of the unplasticized PVA film. The incorporation of PEG into PVA films did not affect significantly the T_m values, indicating that PEG did not cause

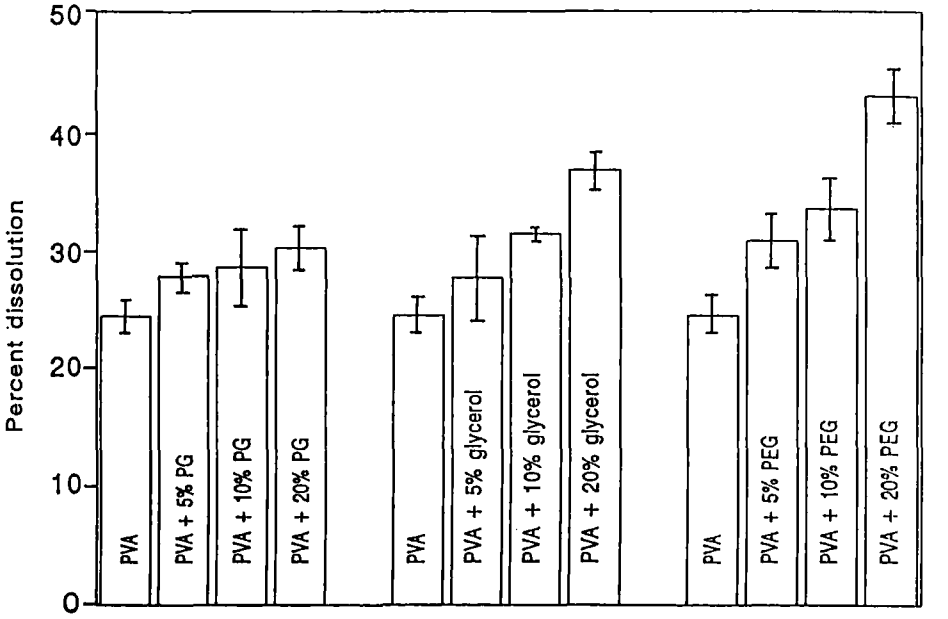


FIGURE 4

The influence of plasticizers on the aqueous solubility of PVA films.

defects to be formed in the crystal lattice. One reason could be that the PEG molecules, being seven times larger in size than glycerol molecules, were rejected from the crystal lattice of PVA films. This rejection was characterized by the observed "bleeding" of PVA films plasticized with PEG. However, the presence of PEG molecules in the amorphous regions of the polymer may physically obstruct the alignment of PVA molecules to form crystallites, thereby lowering the ΔH values.

Unplasticized PVA films had weak water resistance. Upon immersion in distilled water for three days, almost 25% of the film had dissolved away, and the remnant film absorbed up to two times its own weight of water. The presence of plasticizers in the PVA film further weakened its resistance to solubility in distilled water (Figure 4). Present at a concentration of 20%

w/w, PG, glycerol and PEG increased the dissolution of PVA films by 5.87%, 12.46% and 18.72% respectively. Of the three plasticizers, PEG was therefore most effective in reducing the water resistance of PVA films. Film dissolution was observed to increase almost proportionally with plasticizer concentrations. In the case of films plasticized with PG, this increase was insignificant.

Two factors may account for the observed difference in aqueous solubility between the plasticized and unplasticized PVA films. Being hygroscopic liquids which are miscible with water, the incorporated plasticizers could leach out from PVA films immersed in distilled water. The loss of plasticizers from the films will then contribute towards the calculated percent dissolution of the films. The second factor is that the aqueous solubility of PVA films *per se* was raised in the presence of the plasticizers. Plasticizer molecules can increase the flexibility of PVA molecules and render the PVA films more penetrable to water molecules. In addition, the presence of plasticizer molecules decreased the amount and/or quality of crystallites formed in the PVA films, thereby enhancing the susceptibility of the films to dissolution in distilled water.

For PVA films plasticized with PEG, the first factor was probably more predominant than the second factor in raising the aqueous solubility of the films. The reason is that the high aqueous solubility of such films cannot be accounted for by the small decrease in PVA film crystallinity brought about by the addition of PEG. Moreover, the incompatibility between PEG and PVA should encourage leaching of PEG from the films into the dissolution medium.

DSC thermograms of film remnants retrieved after dissolution studies of unplasticized PVA films showed an endotherm whose magnitude and position were similar to those obtained for film remnants of plasticized PVA films (Figure 5). The implication is that PVA molecules in the plasticized films were able to rearrange themselves to form more stable crystallites when immersed in distilled water at 37°C. As a

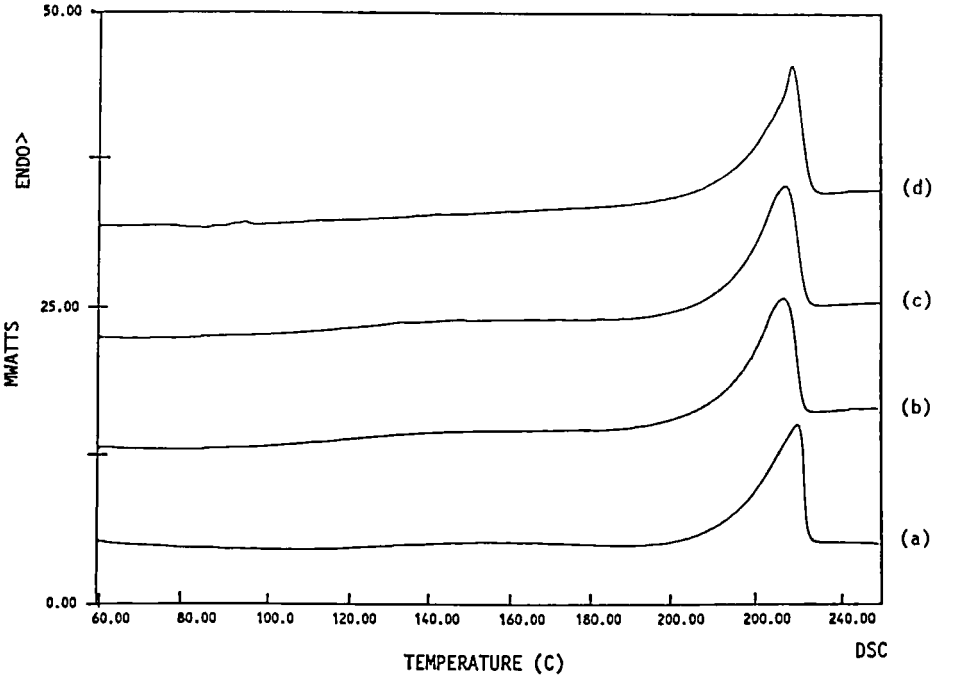


FIGURE 5

DSC thermograms of film remnants retrieved after dissolution studies of unplasticized PVA films (a), and of PVA films plasticized with 20% w/w propylene glycol (b), glycerol (c) and polyethylene glycol 600 (d).

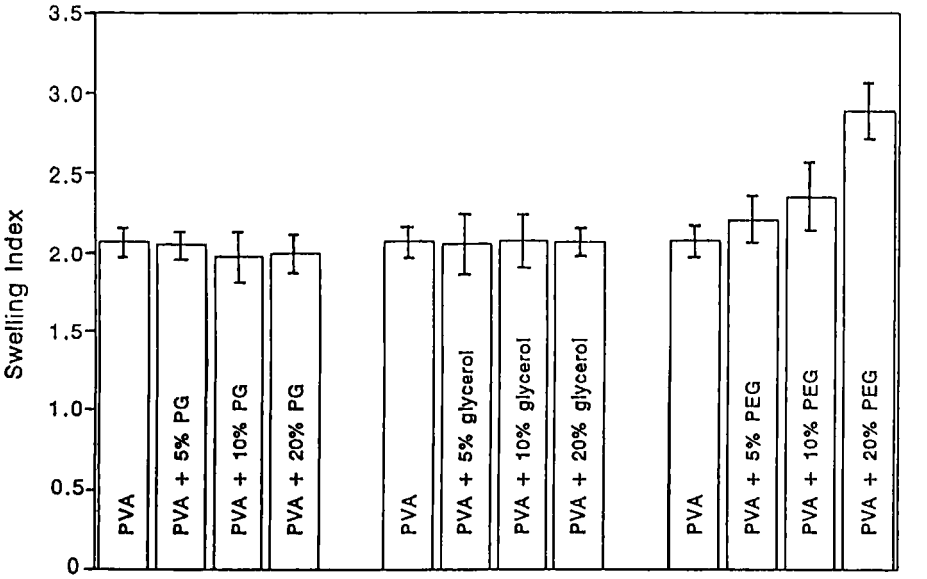


FIGURE 6

The influence of plasticizers on the swelling index of PVA films.

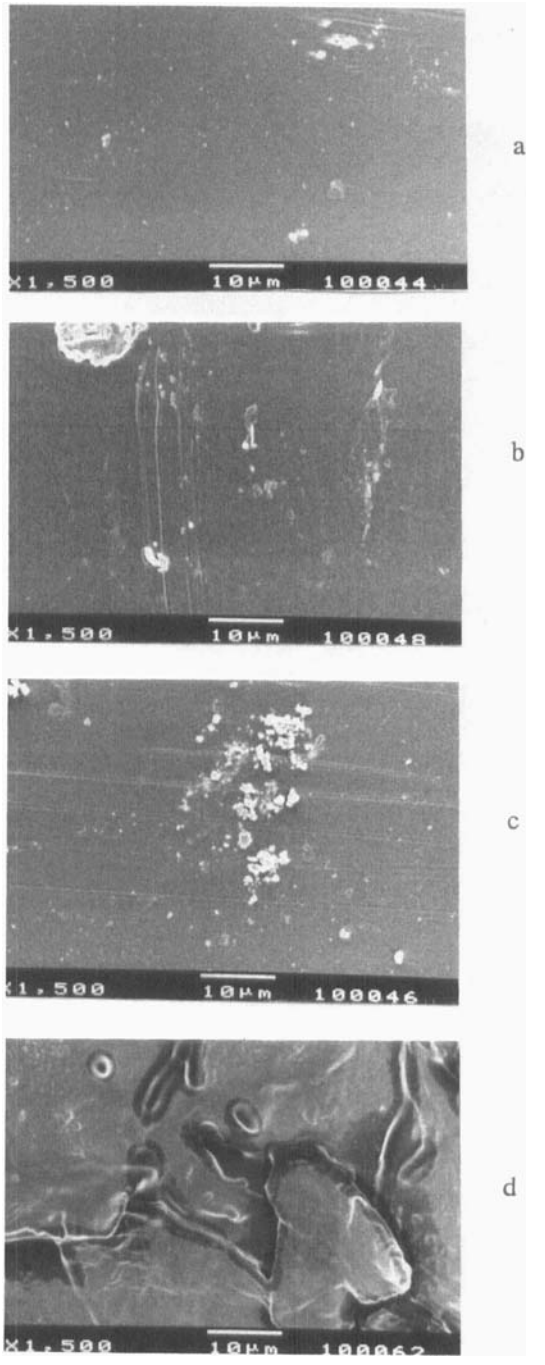


FIGURE 7

SEM micrographs after film dissolution of unplasticized PVA films (a) and of films plasticized with 20% w/w propylene glycol (b), glycerol (c) and polyethylene glycol 600 (d).

result, the remnants of plasticized films appear to have similar amounts and types of crystallites as those of the unplasticized films.

The capacity for water uptake by the film remnants is measured by the swelling index. The swelling indices of unplasticized PVA films and of films plasticized with up to 20% PG or glycerol were not significantly different (Figure 6), being 2.09 ± 0.09, 2.01 ± 0.12 and 2.08 ± 0.09 respectively. These results are in agreement with the observations from DSC analyses that the film remnants had similar degrees of crystallinity and hence similar water uptake capacities. However, PVA films plasticized with increasing amounts of PEG had higher values of swelling index compared to the unplasticized PVA films (Figure 6). SEM micrographs of remnants of PVA films plasticized with PEG showed crevices and pores which were not seen in the remnants of unplasticized films or of films plasticized with PG or glycerol (Figure 7). The presence of these crevices and pores allowed more water to be imbibed by remnants of films plasticized with PEG, thereby raising the values of their swelling indices.

CONCLUSION

The incorporation of propylene glycol, glycerol or polyethylene glycol into PVA films increase film flexibility, thereby lowering the water resistance of the films and enhancing their aqueous solubility. The morphology of the plasticized films depends on the extent of interaction between the plasticizer and PVA molecules, which in turn is influenced by the structure of the plasticizer molecule.

REFERENCES

1. Morimoto, K., Nagayasu, A., Fukanoki, S., Morisaka, K., Hyon, S. H. and Ikada, Y., Drug Dev. Ind. Pharm., 16(1), 13, (1990).

2. Modi, T. W., in "Handbook of Water-Soluble Gums and Resins", R. L. Davidson ed, MaGraw-Hill Book Co., p 20-1, (1980).
3. Wan, L. S. C. and Lim, L. Y., Drug Dev. Ind. Pharm., 18 (17), 1895, (1992).
4. Toyoshima, K., in "Polyvinyl Alcohol - Properties and Applications", Finch, C. A. ed, John Wiley and Sons Ltd., p 339, (1973).
5. Billmeyer, F. W. Jr., "Textbook of Polymer Science", 3rd edn, Wiley-Interscience Pub., (1984).
6. Peterlin, A., J. Polym. Sci., Part C, 9, 61, (1965).
7. Peppas, N. A., in "Hydrogels in Medicine and Pharmacy", Vol. II, Peppas, N. A. ed, CRC Press, p 1, (1987).