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EFFECTS OF PLASTICIZERS ON WATER PERMEATION AND MECHANICAL PROPERTIES OF CELLULOSE ACETATE: ANTIPLASTICIZATION IN SLIGHTLY PLASTICIZED POLYMER FILM

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ABSTRACT

The effects of plasticizers, triacetin and three different molecular weights of polyethylene glycol, on the water permeation and mechanical properties of cellulose acetate were investigated. At 37°C, the water permeability of cellulose acetate was found to decrease with increasing plasticizer to a minimum and then to increase with higher concentrations of plasticizer. Low plasticizer concentrations caused a decrease in water permeability by antiplasticization. Antiplasticization arose from an interaction between the polymer and the plasticizer molecules and decreases the molecular mobility of the polymer. This effect was confirmed by mechanical measurements of polymer free films at the same experimental temperature. However, when the temperature was raised above the glass transition temperature, T_g, of the polymer films, the polymer films contain enough energy to overcome the

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interaction between the polymer and plasticizer molecules, and the antiplasticization effect disappeared.

INTRODUCTION

In pharmaceutical controlled release film coatings, plasticizers or low-molecular-weight diluents, are added to polymers to modify their physical properties and to improve their film forming characteristics (1-3). Plasticizers can change the viscoelastic behavior of polymers significantly. In particular, plasticizers can turn a hard, brittle polymer into a softer, more pliable material, and possibly make it more resistant to mechanical stress. These changes in the mechanical properties also affect the permeabilities of polymer films (3-7).

Plasticizers differ in their ability to modify the properties of a polymer. The plasticizing efficiency of the dialkyl phthalates and the polyethylene glycols on ethylcellulose and hydroxypropyl methylcellulose films, for example, have been measured by Rowe et al (8) and Sakellariou et al (9). The plasticizing efficiency of the four phthalates was found to be diethyl > dimethyl > dibutyl > dioctyl. The plasticizing efficiency of the polyethylene glycols decreased with increasing molecular weight, with the high molecular weight solid members exhibiting phase separation.

The effects of plasticizers on the water vapor transmission of cellulose acetate phthalate were studied by Lachman and Drubulis (10). They found that the water vapor transmission of cellulose acetate phthalate plasticized by dimethyl phthalate, or Citroflex-2, first decreased with increasing plasticizer and then increased with higher concentrations of plasticizer. They suggested that at low plasticizer concentration, the plasticizer filled the interstices of the polymer and caused a decrease in water vapor transmission of cellulose acetate phthalate. Further addition of the plasticizer had only a dilution effect on the polymer film, and the water vapor transmission increased.

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The term "antiplasticization" has been ascribed to the mechanical behavior observed on adding certain low-molecular-weight materials to polymers in which there occurs an increase in modulus, or a decrease in compliance and the appearance of brittleness (11). An "unexpected maximum" in the modulus of poly(vinyl chloride) at 10% di-2-ethylhexyl phthalate concentration was reported by Walter (12). A "plasticization threshold" had to be passed before most of the "normal" plasticizer effects were observed on the physical properties of the polymer. The antiplasticization of poly(vinyl chloride) was studied more recently by Kinjo and Nakagawa (13), who found that the modulus vs. plasticizer content curve showed a maximum when poly(vinyl chloride) was plasticized by any of the following: tricresyl phosphate, butyl benzyl phthalate, dioctyl phthalate, dibutyl sebacate, or dioctyl sebacate. Jackson and Caldwell (14) confirmed that antiplasticization was a general phenomenon and that beyond a certain concentration, the antiplasticizer reverted to a plasticizer and thereafter exhibited normal behavior.

By measuring the dynamic mechanical properties and the specific volume of poly(vinyl chloride), the antiplasticization mechanism of dioctyl phthalate on poly(vinyl chloride) was studied by Kim, et al (15). They found that when the measurement temperature was above the glass transition temperature, T_g, a small amount of dioctyl phthalate would plasticize poly(vinyl chloride), but an antiplasticization effect was observed when the temperature was below the T_g. Hence, they supposed that the antiplasticization effect was more pronounced at lower temperatures.

The mechanism for antiplasticization at low plasticizer concentration is not clear yet. One hypothesis is that when a small amount of plasticizer is incorporated into a polymer, the polymer gains free volume, which allows the polymer molecules to move to a more thermodynamically stable state. The result is that the polymer tends to become more ordered and compact as existing "crystallites" grow or new "crystallites" form at the expense of the more fluid parts of the amorphous polymer

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(16). From the study of a number of polymers, Jackson and Caldwell (17-19) found that antiplasticization cannot be explained exclusively by crystallization, because some polymers are noncrystalline. They concluded that the mechanism of antiplasticization was perhaps a combination of several factors: the reduction of the free volume of the polymer; the interaction between the polar groups of the polymer and of the antiplasticizer; and a physical stiffening resulting from the presence of rigid antiplasticizer molecules adjacent to the polar groups of the polymer. The free volume and the annealing and antiplasticizing of bisphenol A polycarbonate were studied by Robertson and Joynson (20). They found that the free volume in the bisphenol A polycarbonate consisted of at least two independent parts, one of which is affected by annealing and the other by antiplasticization.

In this study, the effects of triacetin and three different molecular weights of polyethylene glycols on the water permeation and the mechanical properties of cellulose acetate were investigated.

Preparation of Free Films

Several cellulose acetate solutions were prepared. Cellulose acetate (398-10, FMC Corp., Lot # SA 740, M_w = 177,000, M_n = 58,500, 39% acetyl) and triacetin (glyceryl triacetate, Sigma Chemical Company, St. Louis, Lot # 27E-3407, Anhydrous Mol. Wt. 218.2.) were dissolved in acetone at a concentration of 4% w/v. Cellulose acetate and three different molecular weights of polyethylene glycols (Lot # 28F-0031, Approx. Mol. Wt. 600; Lot # 39F-0678, Approx. Mol. Wt. 3,350; Lot # 78F-0049, Approx. Mol. Wt. 8,000, Sigma Chemical Company, St. Louis) were dissolved in 1:4 v/v acetone/methylene chloride mixtures at a concentration of 4% w/v. The triacetin and polyethylene glycol levels, in the cellulose acetate films, were

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changed from 0 to 50% w/w. Two milliliter of polymer solution were poured into an aluminum evaporating pan and covered with an inverted funnel to prevent solvent removal by convection. After drying, the free films were lifted off the pan and cut into 15 x 2 mm rectangular pieces and 2.0 cm diameter circular pieces. The film samples were stored in a desiccator at room temperature for a minimum of one week.

Permeability Measurements

The water permeability tests of polymer free films were performed in a standard diffusion cell system at 37°C. The system included a MGW Lauda M3 water circulator (Messgerate-Werk Lauda, Lauda-Konigsofen, West Germany) and 3 mL side-by-side diffusion cells (Crown Glass Co., Vineland, NJ). Before each permeability experiment was performed, the thickness of the film was measured with a Mettler TMA40 Thermomechanical Analyzer (Mettler Instruments, Hightstown, NJ) (thickness is 0.0183 ± 0.0009 -mm range). Two 3 mm Silastic gaskets were placed on each side of the circular film and placed between each half of the diffusion cell. The cells were then clamped to prevent leakage. In the receiver side of the system, a saturated sodium chloride solution in the presence of excess NaCl was placed, while distilled water was added to the donor side. In order to reduce boundary layer effects, stirring bars were placed in both cells.

A specially made 2mm ID graduated capillary tube with a 7/25 male fitting was inserted in the sampling port of the receiver side. Silicone grease was added to the surface of the fitting to prevent leakage. Water level readings were taken periodically over a period of 4 hr. These readings can be converted to the volume or weight of water that passes through the polymer film from the donor side to the receiver side, and the water permeability coefficient of the polymer film could be calculated from

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$$P \cdot S \cdot \Delta C = \frac{dM}{dt} \qquad (1)$$

where P is the water permeability coefficient, S is the surface area of the film that contacts with solution, ΔC is the concentration difference of water between the two diffusion cells, and dM/dt is the weight change of the water level in the capillary tube with respect to time.

Mechanical Experiment

Creep compliance tests and the glass transition temperature of polymer film samples were performed and measured with a Mettler TMA40 Thermomechanical Analyzer (Mettler Instruments, Hightstown, NJ). Film samples were fixed between two stainless steel clamps with emery paper placed between the clamp and sample in order to avoid slippage. Following this, the sample was placed in a dry nitrogen environment in the TMA40 and the creep compliance behavior was measured at 37^oC and at other specific temperatures. The glass transition temperatures of film samples were measured at the same analyzing rate in the TMA40.

RESULTS

The water permeability coefficients of cellulose acetate films plasticized by two types of plasticizers, triacetin and three different molecular weights of polyethylene glycol, are presented in *Figure* 1. The water permeability for both was found to decrease with increasing plasticizer levels at the lower concentrations, and then to increase with higher plasticizer concentrations. As seen in *Figure* 1, the minimum water permeability of cellulose acetate films occurred at 5 wt% for each of the different molecular weight polyethylene glycols.

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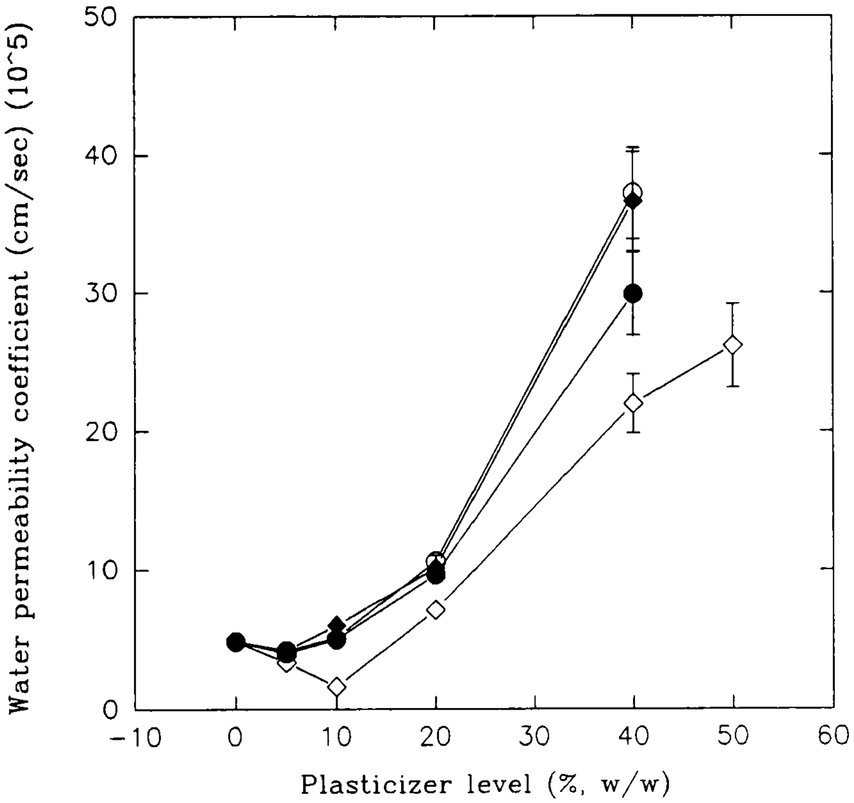

Figure 1 The effect of plasticizers on the water permeability of cellulose acetate free film. (◊) triacetin, (o) PEG600, (♦) PEG4000 and (o)PEG8000.

The effects of the plasticizers on the creep compliance behavior of cellulose acetate free films are illustrated in *Figures* 2 and 3. The 100-second creep compliance of cellulose acetate free films plasticized by triacetin is shown in *Figure* 2, and the 10-second creep compliance for cellulose acetate free films plasticized by the polyethylene glycols is shown in *Figure* 3. Like the water permeability, the creep compliance was seen to decrease with increasing plasticizer at the lower plasticizer concentrations and then to increase with higher plasticizer concentration. The creep compliances of the cellulose acetate films plasticized by polyethylene glycol

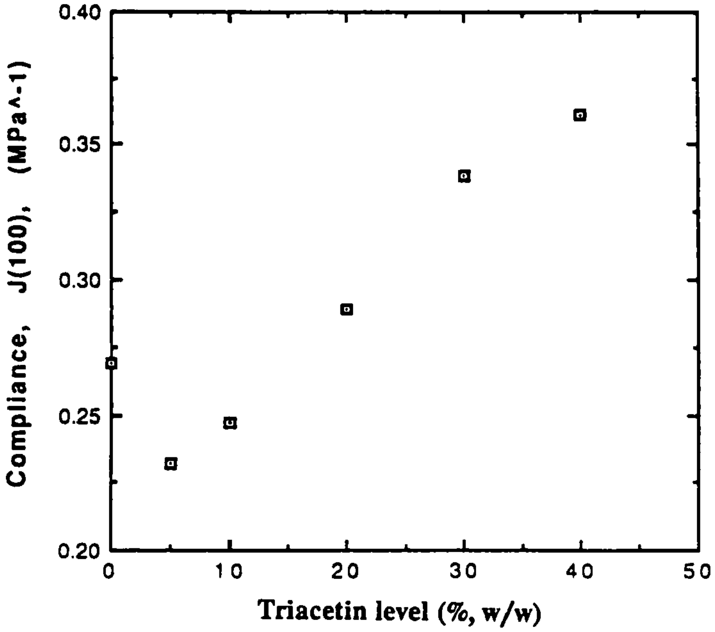

Figure 2 The effect of triacetin on the 100-s second creep compliance of cellulose acetate free films (measured at 37°C).

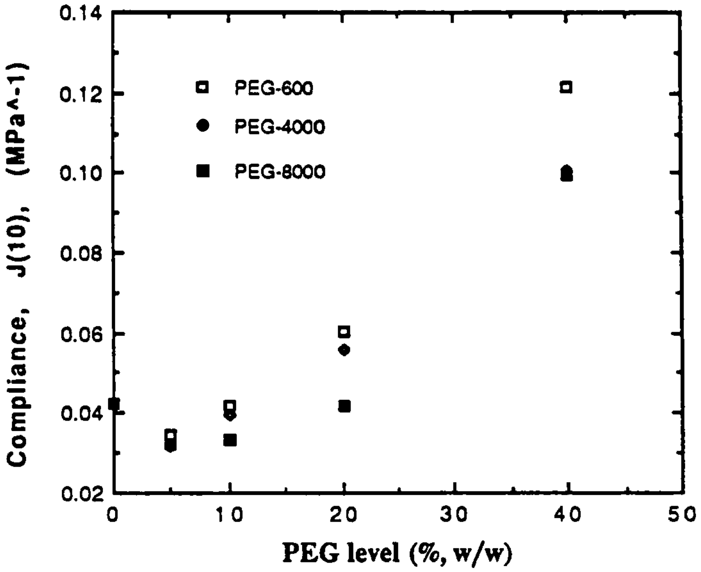

Figure 3 The effect of polyethylene glycols (PEG) on the 10-s second creep compliance of cellulose acetate free films. (□) PEG600, (◇) PEG4000 and (■) PEG8000 (measured at 37°C).

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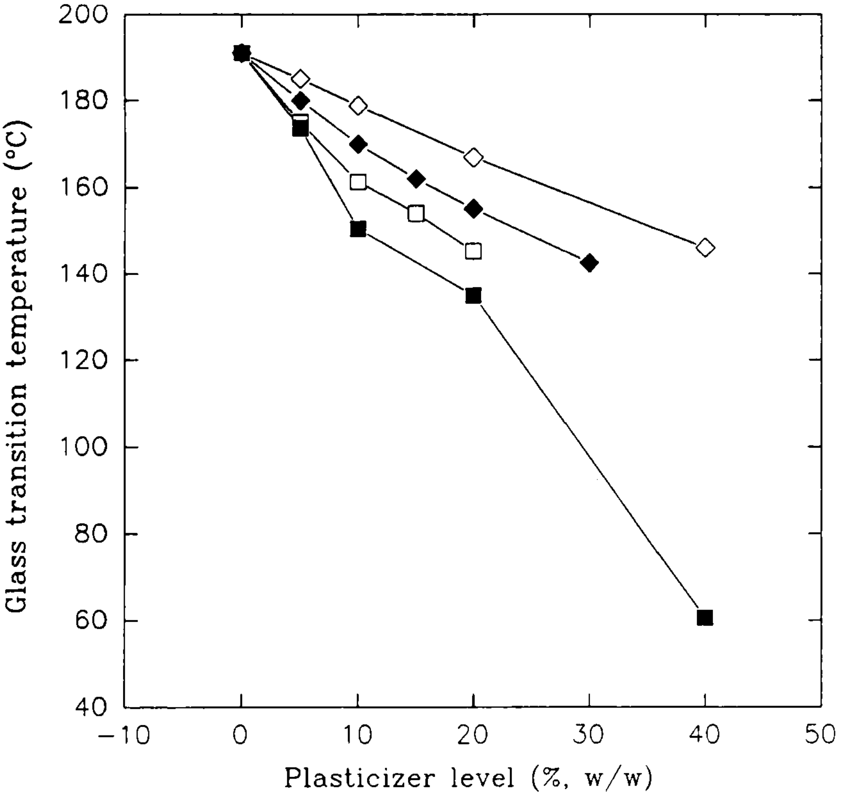

Figure 4 The effects of plasticizers on the glass transition temperature of cellulose acetate free films. (◇) PEG8000, (◆) PEG4000, (□) PEG600 and (■) triacetin.

are seen in *Figure* 3 to increase with increasing polyethylene glycol molecular weight at the same plasticizer level.

The effect of the two types of plasticizers on the glass transition temperature of cellulose acetate films is shown in *Figure* 4. The glass transition temperature of cellulose acetate films was seen to decrease with plasticizer concentration for all concentrations. Moreover, the decrease in T_g was essentially linear, with no apparent break in slope in the vicinity of the concentration where the water permeability and creep compliance reach minima. The glass transition temperature

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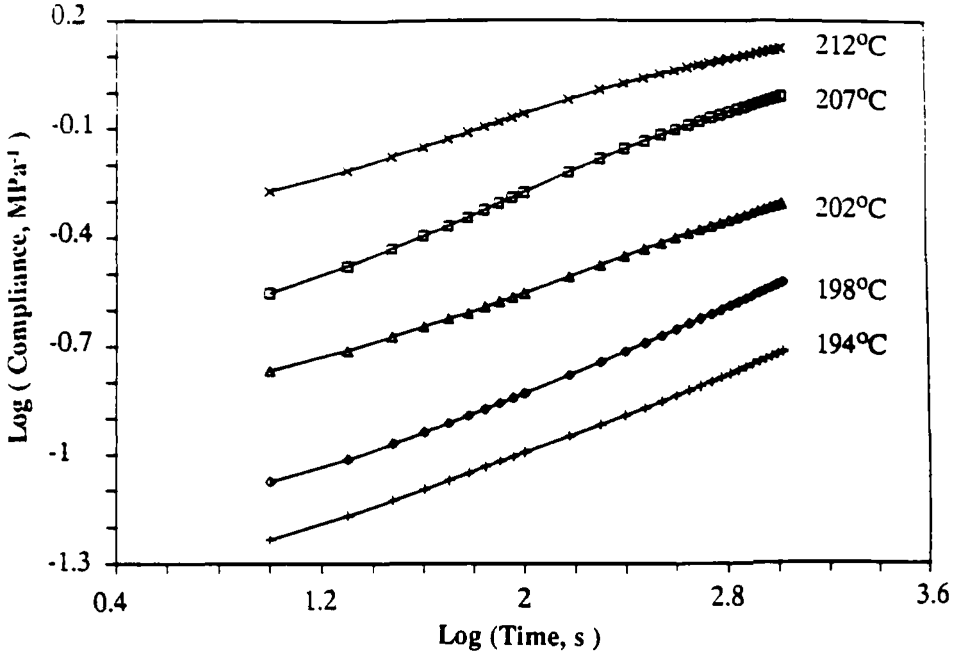

Figure 5 The creep compliance of cellulose acetate free films measured at different temperatures. (x) 212°C, (□) 207°C, (Δ) 202°C, (◇) 198°C and (+) 194°C.

of cellulose acetate film plasticized by polyethylene glycol increased with increasing polyethylene glycol molecular weight at the same plasticizer level.

The creep compliances of unplasticized cellulose acetate films measured at different temperatures are presented in *Figure* 5. By shifting the data in *Figure* 5 horizontally, a superposition of the creep curves or master curve of unplasticized cellulose acetate film at the reference temperature of 194°C was obtained and is shown in *Figure* 6. By using the same method, the master curves for cellulose acetate films plasticized by 5 wt% and 10 wt% polyethylene glycol 600 at the reference temperatures 178°C and 165°C, respectively, were obtained and are presented with the master curve of unplasticized cellulose acetate films in *Figure* 7. The order of the creep compliance data of these films are found to be as follows:

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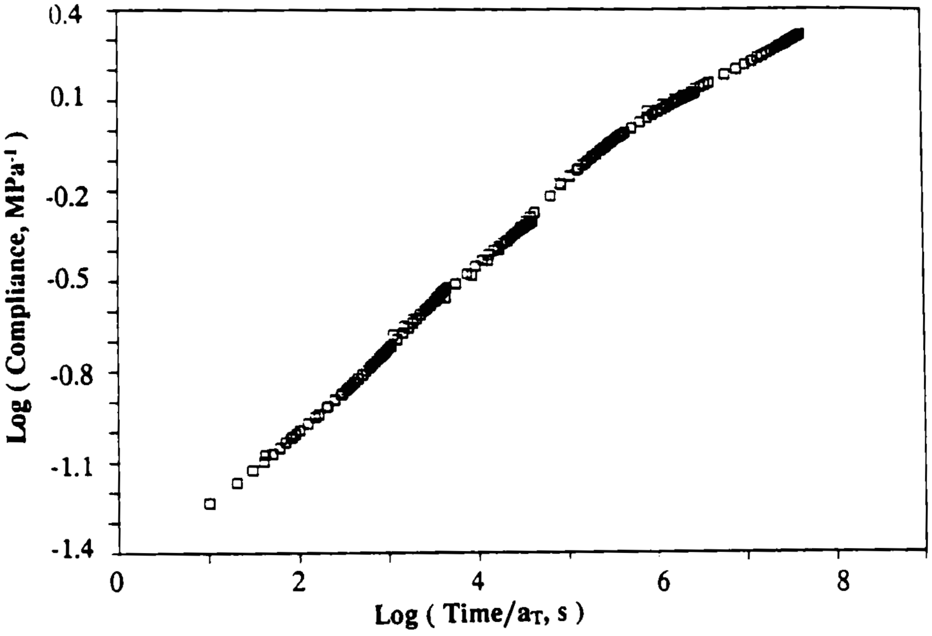

Figure 6 The master curve of the creep compliances of cellulose acetate free film at reference temperature 194°C obtained by shifting the data in *Figure* 5 horizontally.

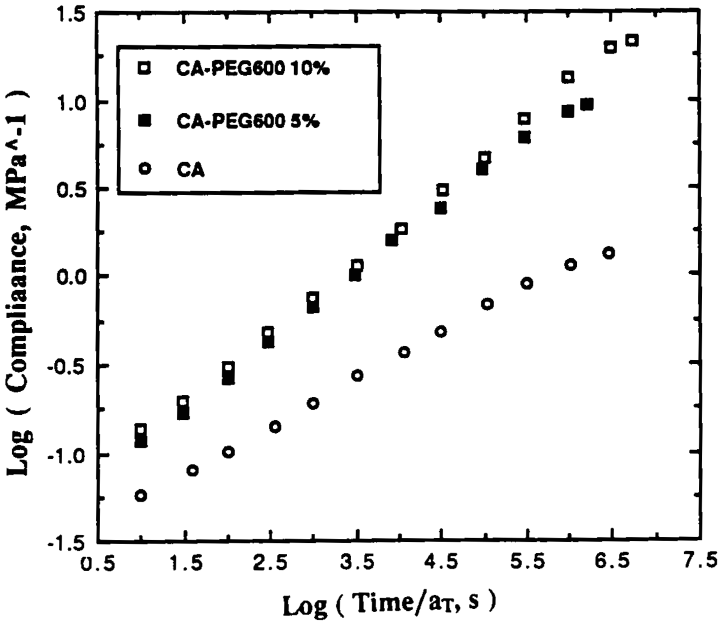

Figure 7 The master curves of cellulose acetate (CA) free films at different polyethylene glycol-600 (PEG600) levels and reference temperatures. (□) CA-10% PEG600 at 165°C, (■) CA-5% PEG600 at 178°C and (○) CA at 194°C.

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(cellulose acetate-10 wt% polyethylene glycol 600) > (cellulose acetate-5 wt% polyethylene glycol 600) > (cellulose acetate). Although the difference between the two films plasticized by polyethylene glycol was small, when the experimental temperature was higher than the glass transition temperature, the creep compliance of more highly plasticized cellulose acetate films was higher than that of less highly plasticized cellulose acetate films.

DISCUSSION

As seen in *Figure* 1 the water permeability of cellulose acetate films decreased to a minimum value at low plasticizer concentration and then increased with the plasticizer level can be interpreted by the antiplasticization effect of low plasticizer concentration. The antiplasticization effect of low plasticizer concentration results from an interaction between the polymer and the plasticizer molecules, which decreases the molecular mobility of polymer. This effect was confirmed with mechanical measurements of polymer free films, shown in *Figures* 2 and 3.

That incorporating a plasticizer into a polymer generally leads to a lowering of the glass transition temperature of the polymer can be explained in terms of the additional free volume introduced with plasticizer. Therefore, as found in *Figure* 4, the glass transition temperature of cellulose acetate decreases with increasing plasticizer level. The relationship of the glass transition temperature between the simple polymer and a second component (plasticizer or polymer) was derived by Couchman and Karasz (21) and Couchman (22-24) and given as

$$T_g = (T_{g1} \cdot M_1) + (T_{g2} \cdot M_2) \qquad (2)$$

where T_g is the glass transition temperature of the plasticized polymer, T_{g1} and T_{g2} are the glass transition temperatures of the respective pure components, and M_1 and

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M_2 are the mass (weight) fractions. Since the glass transition temperature (T_{g2}) of polyethylene glycol increases with molecular weight, by *Equation* 2, the glass transition temperature (T_g) of cellulose acetate plasticized by higher molecular weight of polyethylene glycol will be higher than that of cellulose acetate plasticized by lower molecular weight of polyethylene glycol. The results shown in *Figure* 4 are consistent with *Equation* 2.

Since creep compliance is the ratio of the relative extension to the applied stress, it is not surprising that the creep compliance, shown in *Figure* 5, increased with temperature. Williams, Landel and Ferry (25) related the time and temperature interdependence of the viscoelastic properties of polymers by an equation of the form

$$\log a_T = \frac{-C_1 (T - T_s)}{C_2 + (T - T_s)} \qquad (3)$$

where a_T is the time shift factor, C_1 and C_2 are constants, T is the experimental temperature, and the T_s is the reference temperature. *Equation* 3 is normally called the WLF equation, and it gives the relative increase in time for the same viscoelastic behavior to occur at the temperature T is reduced below that of the reference temperature T_s. The three master curves of cellulose acetate films with different plasticizer levels in *Figure* 7 were obtained by using the time-temperature equivalence concept of the WLF equation.

The result of *Figure* 7 was very consistent with that of Kim et al. (15); the antiplasticization effect was more pronounced at lower temperature, and it can be explained that when the temperature is raised above the glass transition temperature of the polymer films, the polymer films contain enough energy to overcome the interaction between the polymer molecules and the plasticizer, which cause the antiplasticization effect. Hence, when the temperature is raised above the glass transition of polymer, the antiplasticization phenomenon certainly will disappear. That the glass transition temperature of cellulose acetate films always decreased with increasing plasticizer, shown in *Figure* 4, is further proof of the disappearance of the antiplasticization effect at high temperature.

REFERENCES

1. R.C. Rowe and S.F. Forse. J. Pharm. Pharmacol. 33: 174-175 (1981).
2. R.C. Rowe. Int. J. Pharm. Tech. & Prod. Mfr. 3:3-8 (1982).
3. R.R. Crawford and O.K. Esmerian. J. Pharm. Sci. 60:312-314 (1971).
4. S.C. Porter. Int. J. Pharm. Tech. & Prod. Mfr. 3:21-25 (1982).
5. S.C. Porter and K. Ridgway. J. Pharm. Pharmacol. 34:5-8 (1982).
6. G.S. Banker, A.Y. Gore and J. Swarbrick. J. Pharm. Pharmacol. 18:457-466 (1966).
7. R.S. Okor. Int. J. Pharm. 11:1-9 (1982).
8. R.C. Rowe, A.D. Kotaras and E.F.T. White. Int. J. Pharm. 22:57-62 (1984).
9. P. Sakellariou, R.C. Rowe and E.F.T. White. Int. J. Pharm. 31:55-64 (1986).
10. L. Lachman and A. Drubulis. J. Pharm. Sci. 53:639-643 (1964).
11. S.L. Brous and W.L. Semon. Ind. Eng. Chem. 27:667-672 (1935).
12. N. Kinjo and T. Nakagawa. Polymer J. 4:143-153 (1973).
13. A.T. Walter. J. Polym. Sci. 13:207-228 (1954).
14. W.J. Jackson Jr. and J.R. Caldwell. Plasticization and Plasticizer Processes, 1965, edited by R. F. Gould (Adv. in Chemical Series, No. 48), Washington, D. C., American Chemical Society, Chapter 10.
15. K.U. Kim, S.M. Hong and B.C. Kim. J. Korean Soc. Text. Eng. Chem. 24:29-34 (1987).
16. J.K. Sears and J.R. Darby. The Technology of Plasticizers. Wiley-Interscience, New York, 1982.

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17. W.J. Jackson Jr. and J.R. Caldwell. Advan. Chem. Ser. 48:185-195 (1965).

18. W.J. Jackson Jr. and J.R. Caldwell. J. Appl. Polymer Sci. 11:221-226 (1967).

19. W.J. Jackson Jr. and J.R. Caldwell. J. Appl. Polymer Sci. 11:227-241 (1967).

20. R.E. Robertson and C.W. Joynson. J. Appl. Polymer Sci. 16:733-738 (1972).

21. P.R. Couchman and F.E. Karasz. Macromolecules. 11:117-119 (1978).

22. P.R. Couchman. Macromolecules. 11:1156-1161 (1978).

23. P.R. Couchman. J. Mater. Sci. 15:1680-1683 (1980).

24. P.R. Couchman. Polym. Eng. Sci. 21:377-380 (1981).

25. M.L. Williams, R.F. Landel and J.D. Ferry. J. Am. Chem. Soc. 77:3701-3707 (1955).

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