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# THE INFLUENCE OF WATER ON THE GLASS TRANSITION OF POLY(dl-LACTIC ACID)

U. SIEMANN

Sandoz AG, Pharmaceutical Dept., CH-4002 Basle, Switzerland

## ABSTRACT

The reduction of glass transition temperatures (Tg) in the presence of water has been investigated by differential scanning calorimetry (d.s.c.). The water absorption of Poly(dl-lactic acid) and of compositions thereof with salicylic acid caused Tg reductions up to 12 K and 28 K respectively. D.s.c. measurements of Tg changes due to the water absorption of pharmaceutically used polymers can be important to explain or to predict unexpected changes in the thermal, mechanical, and diffusive properties of polymer-drug combinations.

## INTRODUCTION

Hydrophobic polyesters such as poly(glycolic acid), poly(lactic acid) and poly(caprolactone) are known to degrade slowly in the physiological environment by hydrolysis of the main chain. These polymers have been used in many medical and pharmaceutical applications such as sutures, bone fixation, surgical dressings and depots for drug release. Poly(dl-lactic acid) is mentioned as a suitable polymer for controlled release devices with various drugs such as hormones, e.g. estradiol (ref.1), or different anti-cancer agents (ref.2).

There are few publications about experimental investigations of the Tg of hydrophobic polymers after absorption of small amounts of water. Specifically, polymers of technical interest such as nylon (ref.3) or epoxy resins (ref.4) have been studied with changing water content. It was shown that a small amount of water had a marked plasticizing effect in these systems. This can influence the mechanical properties considerably. In the following, results from d.s.c. are reported to demonstrate the influence of water on the Tg of poly(dl-lactic acid) and mixtures thereof with a drug. It is the purpose of this paper to show the significance of d.s.c. experiments under in vitro conditions similar to in vivo for polymers intended for the use in the physiological environment.

## EXPERIMENTAL PART

Poly(dl-lactic acid) was synthetized from dl-lactide by cationic polymerisation using a method described in the literature (ref.5). The intrinsic viscosity ($\eta$) in chloroform at 25°C was 56 $cm^3 \cdot g^{-1}$.

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The water absorption of the polymer was determined gravimetrically and yielded 1.2 % at 30°C. All d.s.c. measurements were performed with a Perkin Elmer DSC 4 equipped with Intracooler II. The instrument was calibrated at 10 K $min^{-1}$ against Indium. The samples were thoroughly dried for a minimum of 24 hours in a vacuum stove at about 40°C. Samples (13-20 mg polymer powder) were sealed into high-pressure steel pans. Equilibration inside the steel pans (4-5 mg water) and outside using greater amounts gave the same results. Samples were heated to about 20 K above the glass transition temperature, quench-cooled with 330 K $min^{-1}$ to 273.2 K and heated in a second run at the predetermined rate. The mid-point of the transition heat capacity increments and the onset extrapolated from the point of inflection with the standard program supplied by Perkin-Elmer was taken from the second run.

## Results

1. Adjustment of equilibrium. In a first series, the equilibrium time for the Tg reduction, starting with weighing and sealing water and polymer into the same steel pan, was studied at room temperature. After 6 hours Tg was reduced for about 12 K and remained nearly unchanged until 144 h. The reproducibility of the reduction was checked by the following procedure. After equilibration for 48 hours in water the sample was dried until constant weight. The Tg of the polymer was the same as before the treatment.

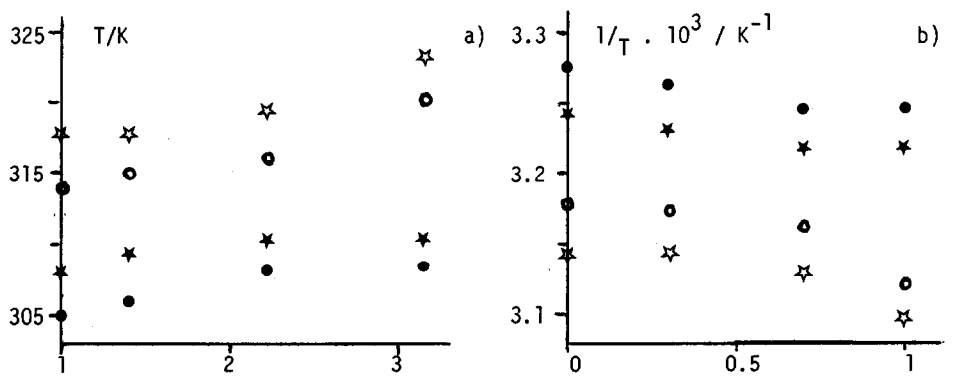


Fig. 1. Scan correction for Tg measurements of Poly(dl-lactic acid). ○, ✡ onset and mid-point of dry polymers. ●, ★ onset and mid-point after 24 h water absorption. a) Plot T vs. $v^{0.5}$; b) Plot 1/T vs. log v.

2. Influence of scan rate. At higher rates, the Tg shifts to higher temperatures due to the thermal lag of the sample and the response time of the calorimeter. A theoretical analysis has shown that the anticipated temperature shift should be dependent upon the square root of the heating rate v, heat of transi-

tion, and sample mass (ref.6). We have to take into consideration that the glass transition itself is a rate dependent parameter, apart from any thermal lag errors. Wunderlich et al. have shown that the time-dependent nature of the glass transition may adequately be described by a log v vs 1/T relation (ref.7). The effect of the scan rate on the observed Tg of poly(dl-lactic acid) in the dry and water-equilibrated state is summarized in Fig. 1 in the two different plots. Linear extrapolation to lower heating rates was possible in both plots only for the Tgs of the polymer-water system. Additionally, the theoretically predicted coincidence of onset and mid-point at low heating rates could not be verified. The further experiments were performed with the scan rate of 10 K because of the better reproducibility of Tgs.

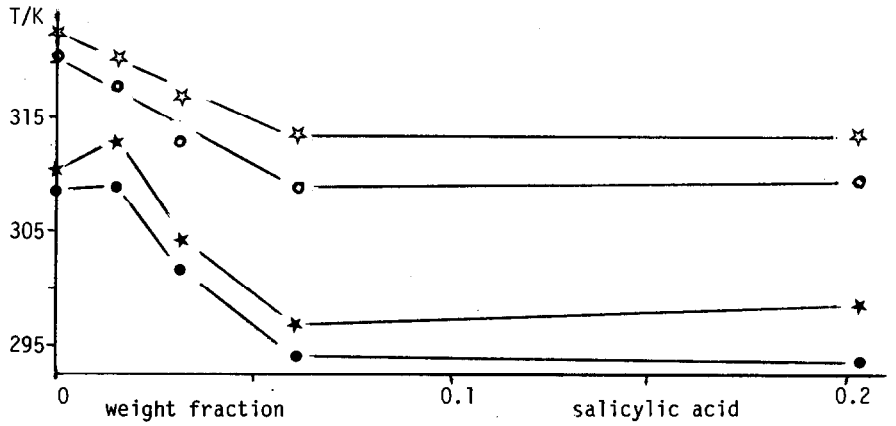


Fig. 2. Reduction of Tg in mixtures of Poly(dl-lactic acid) with salicylic acid. ○, ☆ onset and mid-point of the dry mixtures. ●, ★ (onset and mid-point after 24 h water absorption. Scan rate 10 K $min^{-1}$.

3. Influence of salicylic acid. The Tg of the polymer was reduced to a maximum difference of about 10 K with a 6 % loading with salicylic acid. Between 0% and 6%, the Tg depends proportionally upon drug contents (Fig.2). Above 6% loading the Tg remains unchanged; it is presumed that the solubility of the drug in the polymer is exceeded. After equilibration in water, the effect of both, water and drug led to a maximum reduction of about 28 K at 6 % drug contents, which is greater than the sum of the single Tg reductions caused by water and the drug.

## DISCUSSION

The Couchman-Karasz theory based on a classical thermodynamic analysis treating the glass transition as an Ehrenfest second-order transition, was previously applied to calculate the effects of small amounts of water on Tg

reduction (ref.4). The equation (1) requires the transition heat capacity increments $\Delta Cp$ to be considered as temperature independent (ref.8).

$$\ln (T_g/T_{g,1}) = \frac{m_2 \Delta C_{p,2} \ln (T_{g,2} / T_{g,1})}{m_1 \Delta C_{p,1} + m_2 \Delta C_{p,2}} \quad (1)$$

with $m_1$ and $m_2$ for the mass fractions, $T_{g,1}$ and $T_{g,2}$ for the pure components and $T_g$ for the mixture. If $T_{g,1}/T_{g,2}$ is not greatly different from unity, the approximation gives the Wood-equation (ref.9). Further simplification with the empirical rule $\Delta C_{p,i} \cdot T_{g,i} \approx$ const. gives the familiar Fox-equation. The calculation by means of the Tgs of water 134 K (ref.4), Poly(dl-lactide) 323.1 K, the transition heat increments of water 1.94 J $g^{-1}K^{-1}$ (ref.4), and the polymer 0.55 J $g^{-1}K^{-1}$ measured at 10 K $min^{-1}$ yielded 311.6 K with equation (1), 315.6 K and 317.7 K by means of the Wood and Fox-equations respectively. The experimental value was 310.6 K.

As was to be expected in this case, characterized by large differences in Tg and $\Delta Cp$ of the two components, the Couchman-Karasz equation gave the best prediction of the Tg reduction compared to the empirical rules.

## CONCLUSION

Great care has to be paid to prevent the influence of moisture when characterizing the thermal properties of apparently hydrophobic polyesters. Equilibration of poly(dl-lactic acid) in an atmosphere of about 50% r.h. can cause Tg reductions of about 5 K as calculated by means of equation (1). On the other hand, these polyesters should be studied at conditions similar to those of the in vivo situation because the water induced reduction of Tg below the body temperature can change diffusion coefficients, release of drugs and mechanical properties considerably.

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