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# Letter to the Editor

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Dear Editor,

In our previous paper entitled 'The effects of storage on the physicochemical properties and release characteristics of progesterone-loaded poly(*l*-lactide) microspheres', we reported that the drug release rate of the microspheres correlated with the glass transition temperature ($T_g$) (Aso et al., 1993). The detailed mechanism, however, was not fully discussed, since we did not measure the $T_g$ of the microspheres in the dissolution medium. We have recently found that the $T_g$ of microspheres in dissolution medium is a better parameter for representing the physicochemical properties of the microsphere matrices and for correlation with the drug release rate than the $T_g$ measured before the release study, as shown in Fig. 1. The $T_g$ measured prior to the release study was increased for the microspheres stored at 0% RH for 7 months, but the drug release rate of the microspheres was not changed. The difference in the $T_g$ between the microspheres before storage and those stored at 0% RH became negligible in the dissolution medium, as shown by plots 1 and 2. Similar results were obtained for the microspheres stored at 25°C and 96% RH for 3 days, where hydrolysis of polymers did not take place. The $T_g$ measured prior to the release study was decreased by 4°C due to absorption of water, but the drug release rate of the microspheres was not changed. This could also be ascribed to the fact that the $T_g$ of the microspheres in the dissolution medium was similar to that of microspheres before storage. In contrast, the drug release rate was increased for the microspheres stored under humid conditions for a longer time. The $T_g$ values of the microspheres measured prior to the release study and measured in the dissolution medium were lower than those of microspheres prior to storage (plots 1 and 4 or 5 in Fig. 1). Long-term storage under humid conditions caused hydrolysis of polymers, resulting in the lowered $T_g$ of microspheres in the dissolution medium. Thus, the decrease in the rigidity of the matrices increased the drug release rate of the microspheres (Aso et al., 1993).

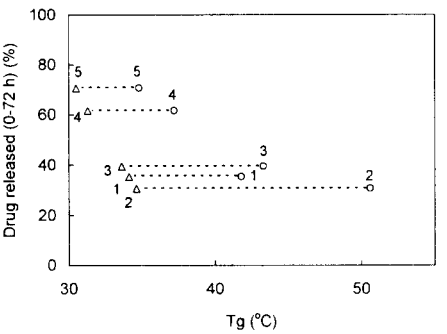


Fig. 1. Relationship between drug release (0–72 h) and $T_g$ of amorphous microspheres: (○) $T_g$ measured prior to release study, (△) $T_g$ in the dissolution medium; (1) before storage, (2) stored at 30°C and 0% RH for 7 months, (3) stored at 30°C and 50% RH for 7 months, (4) stored at 30°C and 75% RH for 5 months, (5) stored at 30°C and 75% RH for 7 months.

The present results indicate that the $T_g$ of microsphere matrices in the dissolution medium can be used as a parameter for assessment of the


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release characteristics of poly(lactide) microspheres (Aso et al., 1994).

Sincerely,

Yukio Aso, Ph.D.
Sumie Yoshioka, Ph.D.
Tadao Terao, Ph.D.

National Institute of Hygienic Sciences,
1-18-1 Kamiyoga, Setagaya-ku,
Tokyo 158, Japan

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