# Polyglycolide-Based Blends for Drug Delivery: A Differential Scanning Calorimetry Study of the Melting Behavior

**Kirsten J. Dickers,[1] Hiep Huatan,[2] Ruth E. Cameron[1]**

[1]*Department of Materials Science and Metallurgy, University of Cambridge, New Museums Site, Pembroke Street, Cambridge, CB2 3QZ, United Kingdom*
[2]*Pharmaceutical R&D, Pfizer Global R&D, Sandwich, Kent, CT13 9NJ, United Kingdom*

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**ABSTRACT:** The melting behavior of polyglycolide (PGA) with eight other biodegradable polymers was investigated to determine whether forming a blend could be used as a method of lowering the melting point of PGA. Blends were prepared by melt processing in differential scanning calorimetry (DSC) pans and were then analyzed by DSC. In every case, a comparison of the blend DSC plot with those of the two individual components showed that the melting behavior of PGA remained unchanged by blending. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 89: 2937–2939, 2003

**Key words:** blends; blending; miscibility; differential scanning calorimetry (DSC)

## INTRODUCTION

Polyglycolide (PGA) is a semicrystalline polyester that degrades in the body over a period of several weeks. It is approved for biomedical use and has been used extensively as a suture material in surgical applications.[1] PGA is suitable for such applications not only because of its convenient timescale of degradation but also because it is nontoxic and biocompatible and degrades to products that are metabolized in the body.

There is also considerable interest in using this polymer as a controlled-release drug delivery material because its degradation and drug release are well characterized[2,3] and may be manipulated. However, the difficulty of processing PGA into drug delivery devices currently prevents its use in this field. Generally, devices are formed by solvent or melt processing, but as PGA is soluble in only a few solvents, none of which are acceptable for pharmaceutical use, and melts at a temperature (>220°C) at which most drugs are decomposed or degraded, these methods are unsuitable.

One method of overcoming the problems associated with processing would be to reduce PGA's melting point or the total crystalline fraction in the material. In theory, this could be achieved by the formation of a miscible polymer blend, which would have a lowered melting temperature through melting point depression by dilution of the crystalline phase, although this is only likely to produce a small decrease. Blending could also reduce the amount of crystallinity in the PGA fraction or result in cocrystals of lower stability. However, miscibility is generally the exception when polymers are blended. Because polymers have high molecular weights, mixing is thermodynamically unfavorable unless there is a strong, favorable interaction between the blend components.

This has been shown experimentally in several studies involving blends in which one or both components have been polyesters. In particular, Rocha et al.[4,5] investigated blends of PGA with poly(ϵ-caprolactone) (PCL), poly(D,L-lactide), and poly(3-hydroxybutyrate-*co*-3-hydroxyvalerate) (PHBHV). They found that blending did not cause the glass-transition temperature of either polymer to change, and this indicated a lack of miscibility, as predicted by thermodynamic theory.

General studies of blends involving at least one polyester component have indicated that miscibility occurs only when there is a favorable intermolecular interaction between the two polymers.[6–10] Miscibility is often determined by the ratio of methylene groups to ester groups in the polyester repeat unit, as there is a strong repulsion between them. At low $[CH_2]/[COO]$ ratios, this interaction dominates and prevents mixing. Accordingly, PGA, with a $[CH_2]/[COO]$ ratio of 1, should show extremely poor miscibility. This was shown to be the case for a blend of PGA with polycarbonate: the presence of two glass-transition tem-

*Correspondence to:* R. E. Cameron (rec11@cam.ac.uk).
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peratures, unchanged from those of the pure components, suggested that the blend was immiscible.[7]

In this study, previous work on PGA blends was extended to include a wider range of biodegradable polymers. Two-component blends were produced, and their melting behavior was then examined by differential scanning calorimetry (DSC), to determine whether it was possible to achieve a blend with a melting point low enough for use as a drug delivery material.

## EXPERIMENTAL

The polymers used in the DSC experiments were chosen after they were screened by thermogravimetric analysis (TGA) to ensure that they remained 95% undecomposed at 236°C, the melting temperature of the PGA used. The degree of decomposition was estimated from the TGA plot.

PGA was purchased from Alkermes, Inc. (Cambridge, MA) PCL, poly(D,L-lactide-*co*-caprolactone) (PCLLA; 40:60 ratio), and PHBHV (88:12 ratio) were obtained from Aldrich (Gillingham, UK), and poly(ethylene glycol) (PEG) was acquired from Sigma (Gillingham, UK). Poly(D,L-lactide-*co*-glycolide) (PLGA; 50:50 ratio) was purchased from Boehringer Ingelheim (Ingelheim, Germany), and cellulose acetate (CA) with an acetyl content of 39.8% was obtained from FMC Corp. (Philadelphia, PA). Poly(*p*-dioxanone) was obtained as PDS II clear sutures from Ethicon (Piscataway, NJ), and poly(glycolide-*co*-trimethylene carbonate) as Maxon II clear sutures were acquired from Davis & Geck (St. Louis, MO).

Experiments were performed on a pure sample of each polymer and on a blend with 80 wt % PGA. The polymers were ground, crushed, or cut, and then blends were mixed manually in larger quantities before representative samples (ca. 10 mg) were removed for analysis. In some cases, the polymers were difficult to grind or crush, so the samples used for analysis were relatively inhomogeneous. However, the inhomogeneity was removed during the melt-processing step.

DSC analysis was carried out with a PerkinElmer 7 series DSC instrument (Shelton, CT). Each sample was placed in a nonhermetically sealed aluminum pan, with an empty aluminum pan as the reference. The purge gas was nitrogen. The sample was first heated from 20 to 236°C at a rate of 50°C/min and was then held for 1 min at this temperature so that complete melting would be ensured. It was then quenched to 20°C at a rate of 80°C/min and held for 5 min so that complete solidification would be achieved. Finally, the sample was heated at a rate of 10°C/min to 240°C, and this stage was used for analysis.

The melting together of the blends in DSC was not a vigorous mixing procedure. However, there is precedent in the literature (e.g., ref. 11) for this method of melt mixing before melting point depression analysis. A further practical consideration is that the thermal degradation of PGA and many of the other polymers

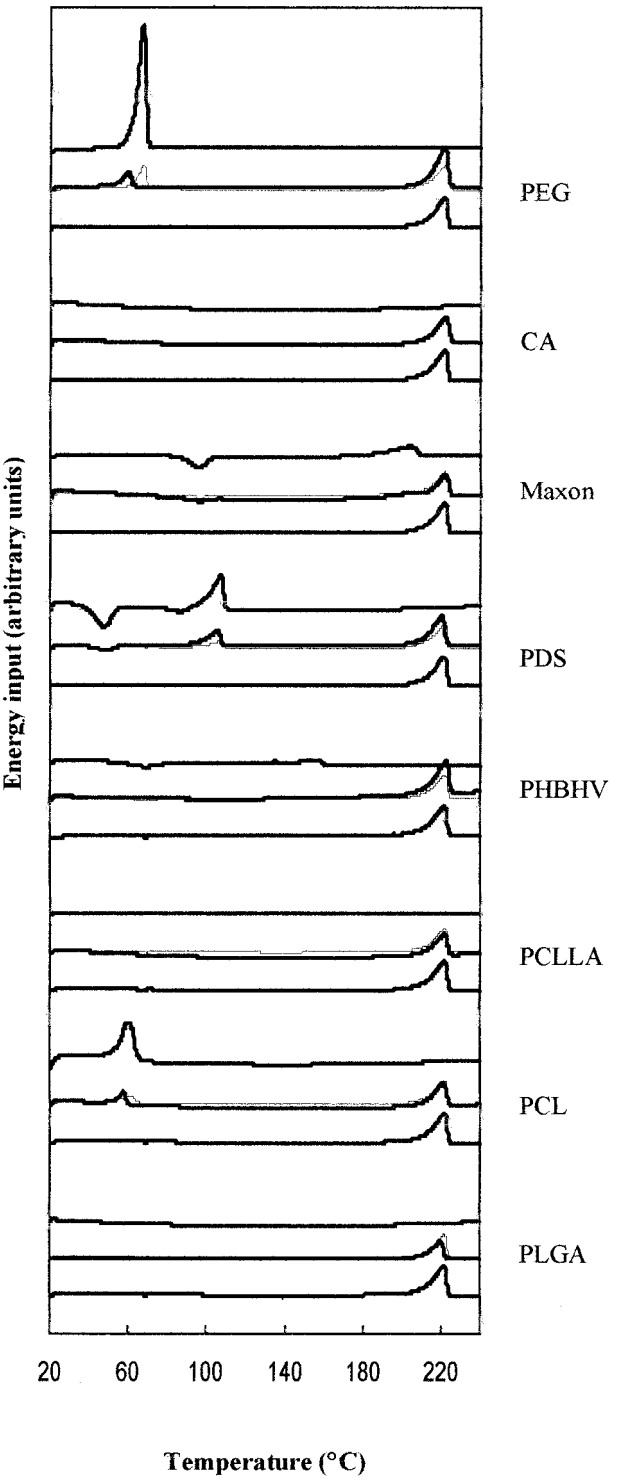


**Figure 1** DSC plots for the eight blends studied. Each set contains plots for PGA alone, an 80:20 blend, and the second blend component alone (the lower, middle, and upper bold lines, respectively) and a calculated plot for an immiscible 80:20 blend (faint line).

considered in this article was very significant at the temperature required, and so the time there needed to be kept very short. Solvent mixing was not possible because of the lack of acceptable pharmaceutical solvents for PGA. This procedure, therefore, represents a practical solution to the mixing problem, avoiding unacceptable solvents and unacceptable thermal degradation.

## RESULTS AND DISCUSSION

DSC plots for the reheating stage of the blends produced in this study are shown in Figure 1. In all cases, the blend trace is almost an exact superposition of the two individual component traces. Any deviations are only slight and can be attributed to errors in the weight fraction of the second polymer, as some were very difficult to grind and, therefore, could not easily be mixed with PGA. A calculated plot for an additive blend is shown in each example for comparison. This was calculated in the following way:

$$\Delta H_{\text{blend}} = 0.8\Delta H_{\text{PGA}} + 0.2\Delta H_X$$

where $\Delta H$ is the energy input by the DSC apparatus (J/g) and $X$ is the second blend component.

For a blend to be processed at a lower temperature, a significant fall in the melting temperature or loss in crystallinity would be required. Clearly, neither was seen in this experiment, and it is a clear that the blends discussed cannot be used to improve processability. For a more complete analysis of the polymer interactions and the resultant miscibility, a full Flory–Huggins analysis of the melting point depression could be performed.[12,13] The lack of a significant melting point depression, suggested by the additivity of the curves, would tend to suggest that there is little interaction between the polymers to encourage miscibility.

## CONCLUSIONS

Blends of PGA with several biodegradable polymers were investigated, and no change in the melting behavior of PGA was observed. The observed behavior is consistent with the theory that in blends containing polyesters, a low $[CH_2]/[COO]$ ratio is detrimental to miscibility.

The melting temperature or extent of crystallinity of PGA was not reduced in any of the blends studied. This means that the processing temperature required to produce a drug-loaded blend by melting would still be high enough to cause substantial degradation of most pharmaceutical compounds.

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