Synthesis and characterization of a potentially non-thrombogenic polyethylene-poly(amido-amine) graft copolymer

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The synthesis of a new biocompatible graft copolymer, polyethylene–poly(amido-amine) (PE–PAA) is reported. The thermal behaviour and the mechanical properties of PE–PAA have been studied as a function of the percentage of PAA. The copolymers show a very low crystallinity and apparent enthalpy of fusion. The elastic modulus E and the yield stress σ_y of PE–PAA copolymers are lower than those of pure PE whilst the ultimate mechanical properties are comparable to those of PE. Preliminary biological tests have been also performed. The experimental results indicate that these new graft copolymers may be used as blood contact materials, or more specifically, as arterial prostheses.

INTRODUCTION

In previous research it has been found that some synthetic poly(amido-amines), when in a crosslinked form, act as powerful and selective heparin absorbers from plasma or blood[1,2].

However, their mechanical properties were not satisfactory for constructing artificial prosthesis. On the other hand, we found that block copolymers between styrene and poly(amido-amine) could be prepared. These new materials show mechanical properties similar to those of polystyrene and apparently retain the ability to absorb heparin on their surface, thus acquiring non-thrombogenic properties[3,4].

These polystyrene–poly(amido-amine) block copolymers were rigid and rather brittle materials[4]. Consequently, we decided to study the synthesis and properties of a new graft copolymer based on poly(amido-amine) with greater toughness and flexibility. To this purpose, polyethylene–poly(amido-amine) graft copolymers were prepared and characterized.

The present paper deals with the synthesis, thermal and mechanical characterization of these new polymeric materials.

EXPERIMENTAL

Synthesis of the copolymer

Chlorosulphonated polyethylene. Low density polyethylene (50 g) was dissolved in refluxing dry benzene (400 ml). To this solution, 3 g azodiisobutyronitrile and 60 ml sulphuryl chloride were added cautiously under a stream of nitrogen (some frothing occurred).

Refluxing was then continued for 1 h under an inert gas atmosphere, then most of the volatile products were eliminated by flash distillation, and the residuum was coagulated by adding an excess of dry ether.

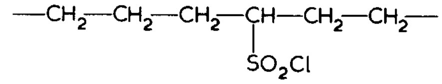
After washing with ether, the product was dried at room temperature and 0.1 mmHg. The yield was about 51 g. Analysis: S 1.2%; Cl 6.5%.

Polyethylene–poly(amido-amine) graft copolymer. Secondary amino end-capped poly(amido-amine) was prepared as previously described[5].

It has been reported elsewhere[3] that the poly(amido-amines) can be obtained predominantly end-capped with acrylamido or secondary amino groups, depending on the preparation conditions. The poly(amido-amine) used in the present work was prepared by using 1,4-bis acryloylpiperazine, and *N,N'*-dimethyl ethylene diamine molar ratio 0.98:1. The polyethylene–poly(amido-amine) graft copolymers (PE–PAA) described in this paper were prepared starting from this secondary amino end-capped poly(amido-amine) and partly chlorosulphonated polyethylene, according to the following scheme:

$—CH_2—CH_2—CH_2—CH_2— \longrightarrow$

Polyethylene



$$—CH_2—CH_2—CH_2—\underset{SO_2Cl}{\underset{|}{CH}}—CH_2—CH_2—$$

Partly chlorosulphonated polyethylene

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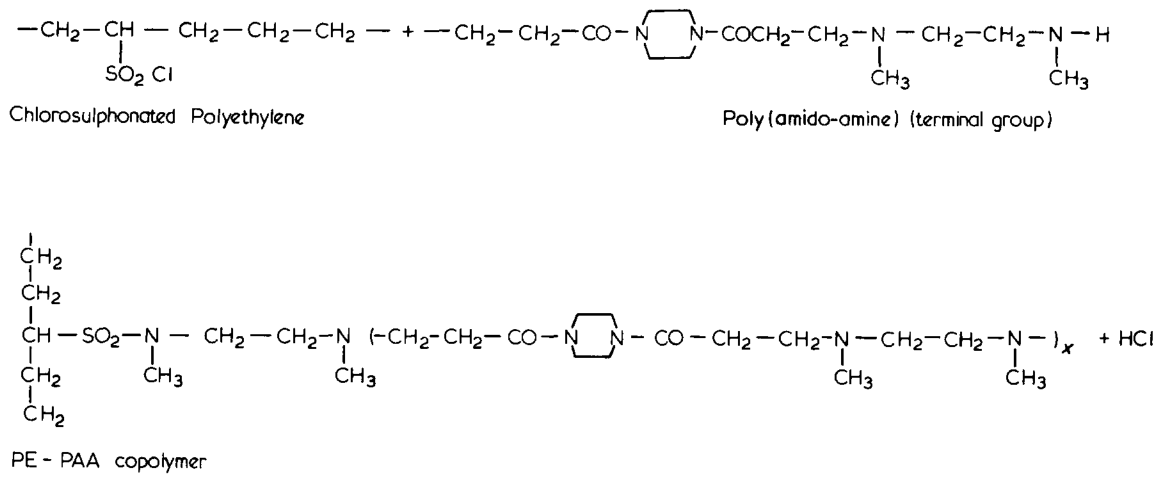

By varying the degree of chlorosulphonation of polyethylene, and the amount of poly(amido-amine) in the coupling reaction, products with different amounts of poly(amido-amine) were obtained. Any free poly(amido-amine) which might have been present at the end of the coupling reaction could be easily eliminated by extraction with methanol.

All the samples described in this paper were prepared starting from a low-density polyethylene having M_v = 80 000, and from a poly(amido-amine) having M_n = 15 000. The composition of the copolymers was determined by means of elemental analysis of nitrogen.

The following experimental procedure was used in the preparation of PE–PAA copolymer.

Chlorosulphonated polyethylene (50 g) was dissolved in dry, alcohol-free chloroform (500 ml). To this solution, a solution of 12.5 g of poly(amido-amine) in 125 ml chloroform was added at once. The reaction mixture was stirred at 60°C in a thermostatically controlled bath for 2 h.

The product was isolated by pouring the reaction mixture into 1500 ml methanol to which some 20 ml triethylamine had been added. After filtering, it was purified by dissolving in chloroform and reprecipitating with methanol. Yield 51.5 g. Analysis: N, 2.65% [13.25% by wt of poly(amido-amine) blocks].

Characterization

The apparent enthalpies of fusion and the related temperatures were determined by differential scanning calorimetry (d.s.c.). Indium (enthalpy of melting 6.8 cal/g) was used as reference substance. Measurements were performed with a Perkin–Elmer DSC-2 differential calorimeter. Wide-angle X-ray measurements were obtained either photographically with a flat camera or by the use of an X-ray diffractometer with a Geiger tube of the North American Philips Co. Inc. Nickel-filtered CuKα radiation was used throughout.

The copolymers synthesized have been tested mechanically using Instron universal testing machine Model 112.

The specimens, in dumb-bell shape, were prepared by compression moulding at P = 140 kg/cm^2 and T = 160°C and were tested at a strain rate $\dot{\epsilon} = 2$ min^{-1} and at room temperature. All the data reported are an average of at least 10 experiments.

RESULTS AND DISCUSSION

Three samples of PE–PAA copolymers containing respectively 7.06, 8.50 and 13.26% of PAA (w/w) were characterized together with a sample of the same low density polyethylene which was used in their preparation.

The d.s.c. thermograms show multiple endothermic peaks. The temperatures of the peaks and the relative values of the apparent enthalpy of fusion are reported in *Table 1* for the first and second runs.

The overall apparent enthalpy of fusion of PE–PAA copolymers is about 1/3 of that of low density polyethylene and is almost constant with the percentage of PAA, at least for the range of compositions examined.

The PE–PAA copolymer may be considered as a comb-like polymer with both the polyethylene backbone and the PAA chains able to crystallize in separate phases. This could explain the presence of the two endothermic peaks observed in the d.s.c. thermograms.

The trend in ΔH_F^* as a function of the percentage of PAA is shown in *Figure 1*.

Table 1 Thermal properties of low density PE and PE–PAA copolymers T(°C); ΔH (cal/g)

	First run					Second run				
Sample	T_I	ΔH_I^*	T_{II}	ΔH_{II}^*	ΔH_F^*	T_I	T_{II}	ΔH_I^*	ΔH_{II}^*	ΔH_F^*
PE–PAA (1) (7.06% PAA)	74	2.91	114	2.04	4.95	69	112	1.57	1.24	2.80
PE–PAA (2) (8.50% PAA)	79	4.11	113	0.25	4.35					
PE–PAA (3) (13.26% PAA)	67	1.86	115	1.81	3.67		112.8		3.30	3.30
PE Low density			112.3		16.7					

The low values of the overall apparent enthalpy of fusion of the PE–PAA copolymer are an indication of a very low degree of crystallinity. This is supported by the X-ray diffraction patterns of the copolymers in the wide-angle region as shown in *Figure 2*. The polymers were examined under identical conditions.

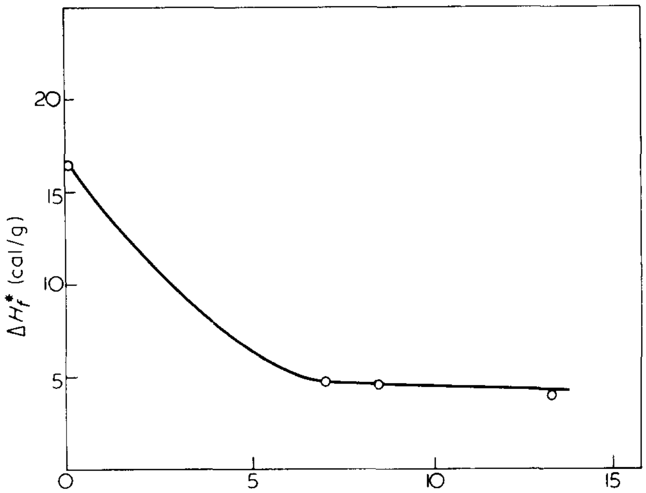

Figure 1 Overall apparent enthalpy of fusion ΔH_f^* of PE–PAA graft copolymers as function of composition

In *Figure 3* the stress–strain curves of LDPE and PE–PAA copolymer with 8.5% of PAA content are reported. A large difference in the tensile behaviour of these two materials can be noticed. In fact the elastic modulus, E, defined as:

$$\lim_{\epsilon \to 0} \; -\mathrm{d}\sigma/\mathrm{d}\epsilon$$

and the yield stress, σ_y, defined as the stress corresponding to the first point with a horizontal tangent, of LDPE is strongly decreased by the presence of the small percentage of PAA. Similar results are obtained with the other copolymers tested (*Table 2*).

The presence of PAA, also in the smallest percentage used in this work, reduces the rigidity of the material (*Figure 4*) by a factor which is almost independent of the PAA content. This result is in accordance with the d.s.c. and X-ray data reported previously (*Figures 1* and *2*) where a strong reduction of crystallinity in the PE–PAA copolymers was noticed.

In fact with only 5% of PAA the degree of crystallinity drops from the 54% of LDPE to a very small value not easily

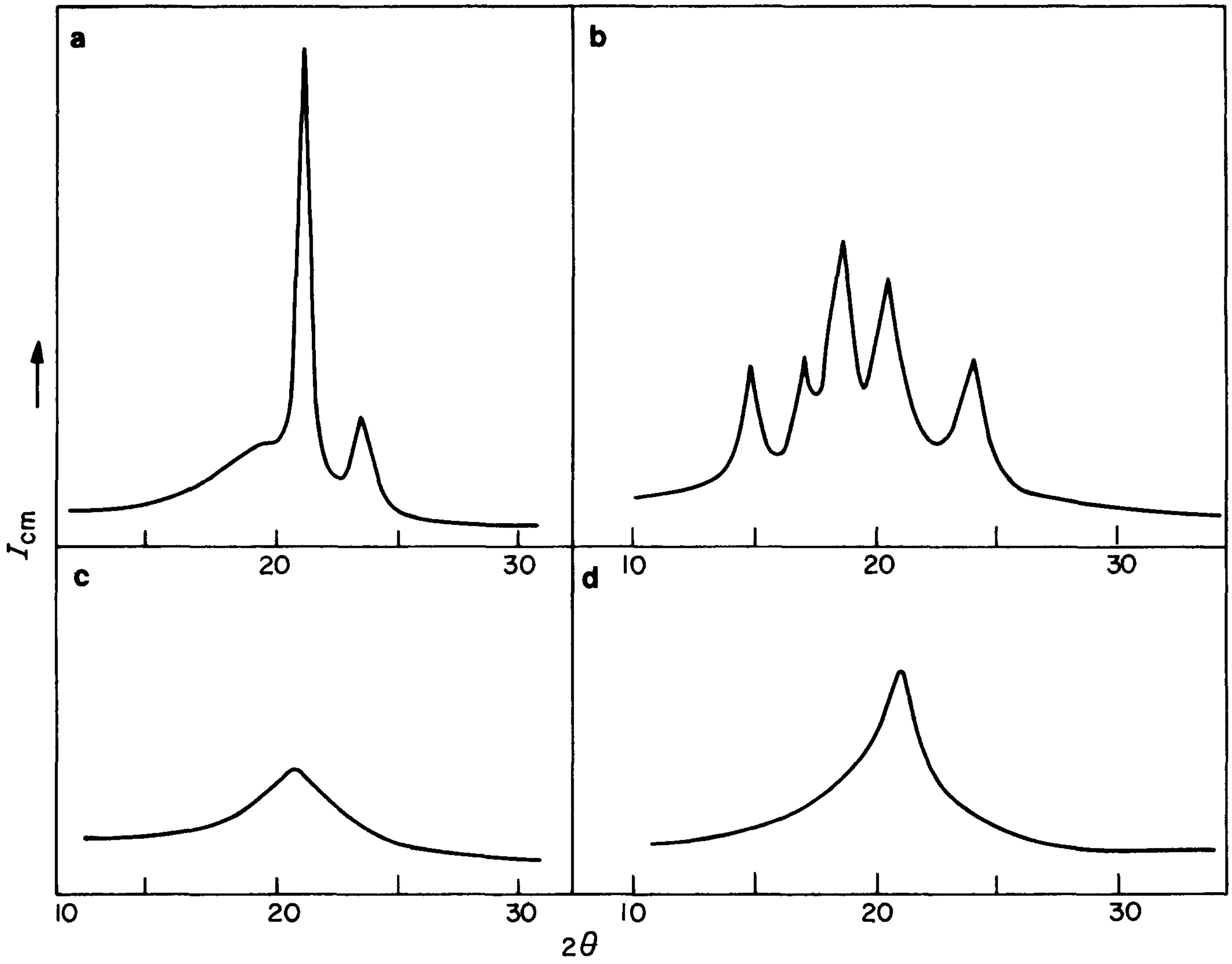

Figure 2 Wide-angle X-ray diffraction traces: A, low density polyethylene; B, poly(amido-amine) and PE–PAA graft copolymers (8.5% of PAA). C, Sample obtained by compression moulding; D, as obtained from polymerization

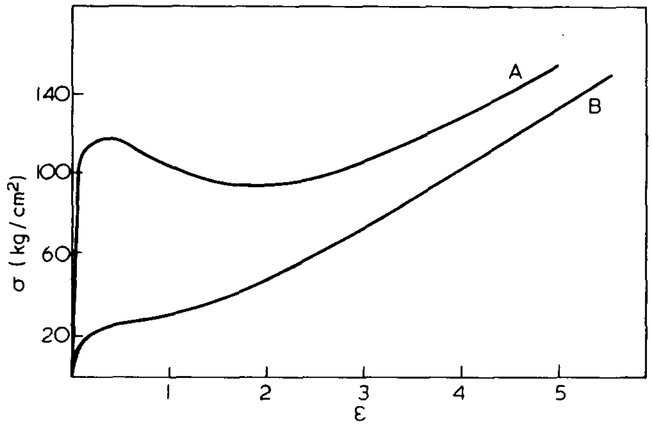

Figure 3 Stress–strain curves: (A) low density polyethylene and (B) PE–PAA copolymer (8.5% of PAA)

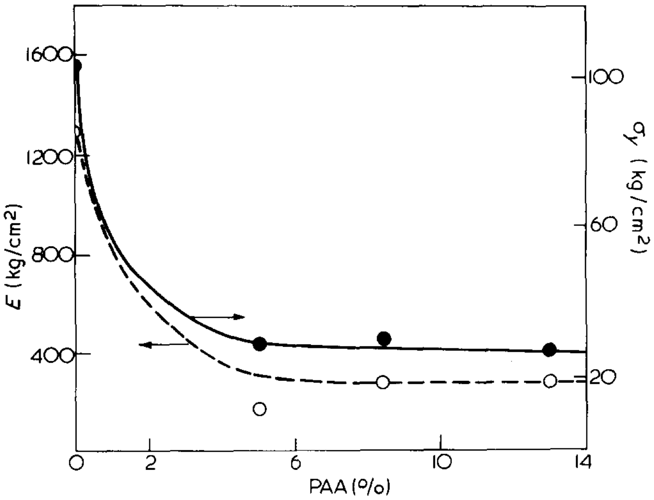

Figure 4 Elastic modulus, *E*, and yield stress, σ_y, of PE–PAA copolymers at different PAA content

Table 2 Mechanical properties of LDPE and PE–PAA copolymers

V_f (% PAA)	E (kg/cm^2)	σ_y (kg/cm^2)	ϵ_μ	σ_μ (kg/cm^2)	W (kg/cm^2)
0	1320	103.8	5.91	180.6	33.5
5.02	171	27.9	6.25	188.3	39.0
8.50	270	32.0	6.54	241.5	34.0
13.26	278	26.0	7.00	234.0	35.0

detectable for the copolymer and then remains constant.

This reduction of crystallinity produces a decrease of the elastic modulus and yield stress for all copolymers studied. Also, σ_y (*Figure 4*) is reduced by a factor of 4 in the PE–PAA copolymers and its value is then independent of the PAA content. This behaviour is in contrast with the mechanical performance of the PS–PAA copolymers previously studied[4] where the PAA was forming a second phase in the copolymers resulting in a continuous decrease of the elastic properties with PAA content. These data successfully correlated with existing equations for particulate composites supporting the hypothesis of the presence of two distinct phases in the copolymer (i.e. a PAA rubbery phase, dispersed in a PS rigid matrix). For PE–PAA copolymers the mechanical data give no evidence of a phase separation. The presence of the PAA in the PE chain reduces drastically the crystallinity, forming a copolymer which behaves as a crosslinked rubber.

The ultimate properties of these materials are almost unaffected by the presence of the PAA polymer. In fact, the ultimate strain, ϵ_μ, and the strength σ_μ are slightly increased by the PAA content, while the work to break, *W*, (defined as the area under the stress–strain curve) is almost constant (see *Table 2*).

In conclusion these new materials are very attractive both for their mechanical properties and for the easy processability. Moreover the possibility of obtaining copolymers with different PAA content but with similar mechanical properties is very interesting for practical purposes. The blend composition may be determined on the basis of medical and biological considerations without taking account of the mechanical performance of the prosthesis, provided that all material compositions under consideration meet the minimum requirements for the mechanical properties of the prosthesis. Some preliminary biological tests have also been performed on these materials.

Tough, flexible films and sheets could be prepared by slowly evaporating 10–20% chloroform solutions of PE–PAA on a flat poly(dimethyl siloxane) support, to which the films themselves do not adhere. By a similar technique, using a tubular support, small PE–PAA tubes have been prepared having the dimensions: length, 25 mm; internal diameter, 10 mm; external diameter,13 mm. These were heparinized as described elsewhere[3], and inserted into the inferior *vena cava* of test animals (dogs). The test selected is a severe one, for even materials such as silicone rubber permit complete thrombosis in 2 h. The animals were killed after 2 weeks implantation.

The results obtained so far are similar to those obtained with polystyrene–poly(amido-amine) block copolymers[3,4]. In no instances, thrombus formation took place at the interior of the tubes. Although the above results must be yet considered as preliminary, it may be concluded that the PE–PAA graft copolymers show promise as biocompatible, flexible materials designed for long term implantation in contact with blood. The results of the biocompatibility test will be published in a forthcoming paper.

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