polymer report

Block/segmented polymers: 3. Biodegradability of (amide-ester)–ester copolymer – a preliminary study

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A new aliphatic block/segmented poly(amide-ester) has been prepared from lactones, diamines and dicarboxylic acids through oligomerization. In *in vitro* studies the polymer degrades depending on the size and nature of the blocks. *In vivo* studies indicate that the polymer is biocompatible and degrades to some extent. Mechanical properties, namely tensile strength and elongation at break, and X-ray crystallinity are observed to vary during the study.

(Keywords: block/segment; oligomer; biocompatible; tensile strength)

INTRODUCTION

Interest in bioabsorbable implant materials is shifting from inert natural systems to synthetic degradables[1]. Amongst these, poly(amide-ester) is one of the latest, showing great promise in surgical sutures, ligatures and drug delivery systems[2,3]. The first synthetic degradable polymer to be implanted in the human body was marketed under the trade name DEXON plus in 1970; it was based on poly(glycolic acid) homopolymer and poly(lactic acid)–ester copolymer. The degradation products are natural metabolites with a little toxicity[4].

Recently, Bera and co-workers[5–7] have prepared a series of (amide-ester) copolymers starting from lactones, diamines and dicarboxylic acids via a two-step reaction scheme, involving first oligomerization and then polymerization. In the first step, hard crystalline oligomers, namely oligo(amide-ester) (A) and soft amorphous oligo-ester (B) were prepared separately; in the second step the two oligomers were transesterified into a block/segmented (amide-ester)–ester copolymer (*Figure 1*). Physicochemical and thermomechanical properties of this type of polymer showed them to have two glass transition temperatures, one well above and one below room temperature, and to be suitable for application over a broad temperature range. The polymer could be processed into rigid fibre or elastic film, depending on the ratio and size of the blocks.

This communication reports the biological properties of the copolymer from *in vitro* and *in vivo* studies; it shows some possibilities in biomedical applications, e.g. surgical suture materials.

EXPERIMENTAL

Materials

Poly(amide-ester), namely POLEA 3612 ($m=3$, $n=6$, $q=10$), and POLEA 366/26 ($m=3$, $n=6$, $q=4$, $p=2$, as shown in *Figure 1*) have been prepared by the method described previously[8]. Poly(glycolic ester) in the form of suture (DEXON plus) was supplied by Ethicon, UK.

Casting of film

The polymer solution (7–8 wt%) in hot dimethylformamide was cast on a glass Petri dish and the solvent was allowed to evaporate in an oven controlled at 90°C over 30 min and held overnight under vacuum (5–6 mmHg). The light-cream-coloured film was removed from the Petri dish and checked by t.g.a. for any traces of solvent present. The thickness of the film varied from 0.5 to 0.15 mm.

The film was cut for mechanical testing using the Instron Universal Machine-1195; the dimensions were: width, 10.00 mm; gauge length, 40.00 mm; crosshead speed, 40.00 mm min^{-1}.

X-ray diffraction of the film was carried out before and after *in vitro* testing using the Phillips PW 1730 (Cu) X-ray unit.

Spinning of fibre

The fibre was hand drawn from the polymer melt at 190 ± 5°C under a nitrogen atmosphere, and cooled in air. No cold drawing/annealing was applied.

Sterilization of film

The films from POLEA 3612 and 366/26 were sterilized in an autoclave at 120°C under a steam pressure of 96.5 kPa before the *in vivo* test.

Preparation of Ringer solution[9]

The solution for biodegradation studies was prepared with the following recipe in a 1 l flask: NaCl, 9.0 g l^{-1}; KCl, 0.42 g l^{-1}; $CaCl_2$, 0.24 g l^{-1}; $NaHCO_3$, 0.50 g l^{-1}; and distilled water, 1000 ml.

The clear solution thus prepared was placed in a series

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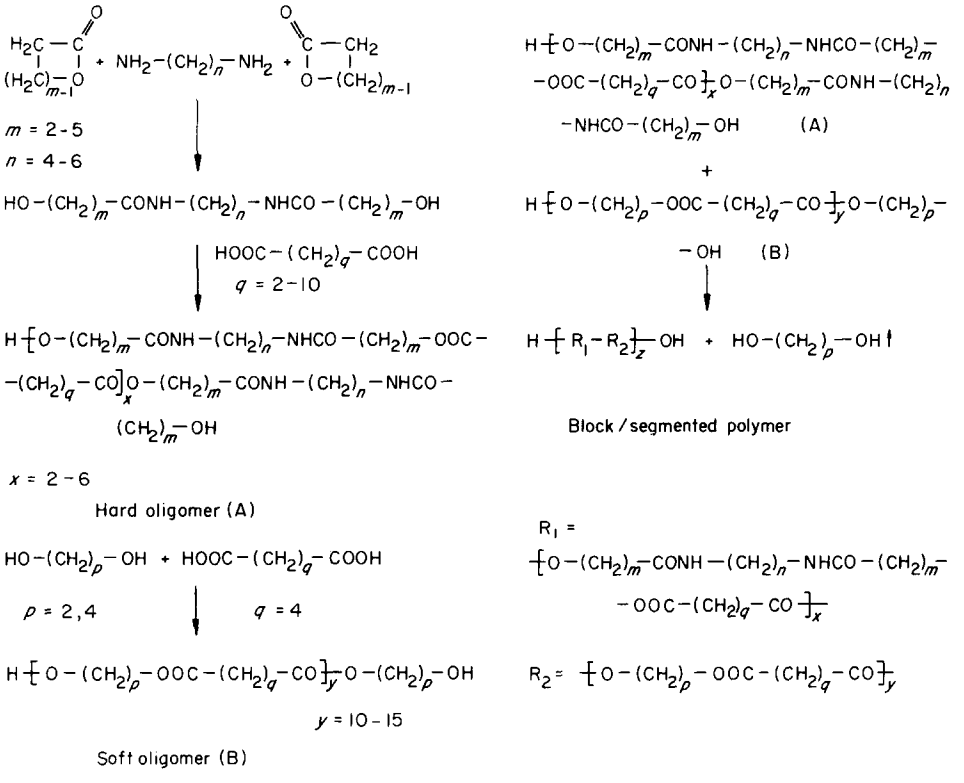

Figure 1 Preparative scheme for (amide-ester)–ester copolymer starting from lactone

of corked test tubes. The fibres (~50 mm long; five per test tube) were kept in an incubator at 37±0.5°C. Samples were taken out at regular intervals, their cross-sectional area was measured under an optical microscope and their mechanical strength was tested. The X-ray crystallinity of the films was tested in the same way.

RESULTS AND DISCUSSION

Prior to this study, monomer amido diol was tested on albino mice[3] by intravenous administration of isotonic 1% saline solution (max. dosage 40 ml/kg body weight); it was found to be non-toxic with no mortality or morbidity. This led us to investigate the degradability of the polymer in the form of fibre as well as film, in the presence of a hydrolysing medium, e.g. Ringer solution. Mechanical strength is considered as a preliminary indicator during biodegradation. Three polymers, namely poly(glycolic ester) (DEXON Plus), POLEA 3612 and POLEA 366/26, were studied in the form of film. DEXON plus degraded much faster than POLEA 3612, disintegrating into powder, whereas POLEA 366/26 swelled. In similar conditions but in fibre form (diameter 10–15 μm), DEXON plus degraded completely after 12 days, POLEA 3612 after 30 days (*Figure 2*) whereas POLEA 366/26 remained as a fibre with erosion to its surface even after 35 days. A further study is in progress with variation in block length and ratio of soft and hard blocks.

The X-ray diffraction studies of POLEA 3612 and 366/26 film did not show much differences in the early stages of degradation, but they differed as degradation proceeded. It is well known that amorphous regions degrade first, causing an increase in crystallinity in the early stages of biodegradation, and in the later stages crystalline regions are attacked, resulting in a decrease

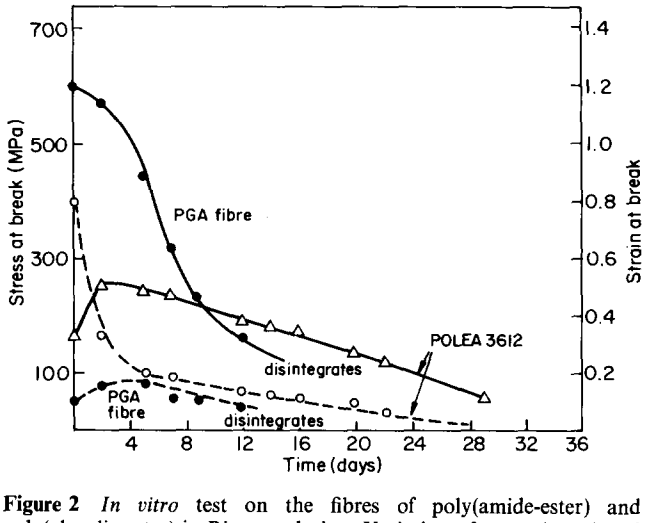

Figure 2 *In vitro* test on the fibres of poly(amide-ester) and poly(glycolic ester) in Ringer solution. Variation of stress (——) and strain (– – –) with time

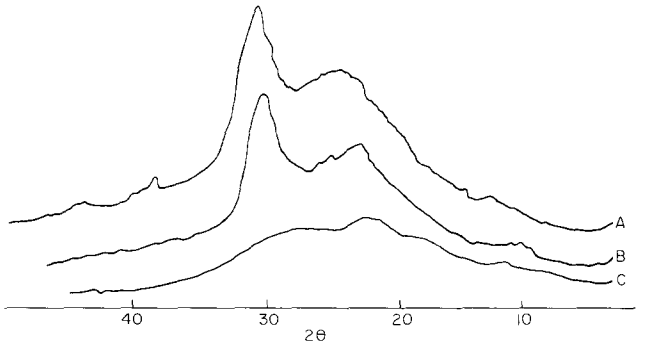

Figure 3 X-ray diffraction diagrams for poly(amide-ester) film POLEA 366/26: A, before *in vitro* test; B, after 10 days; C, after 30 days

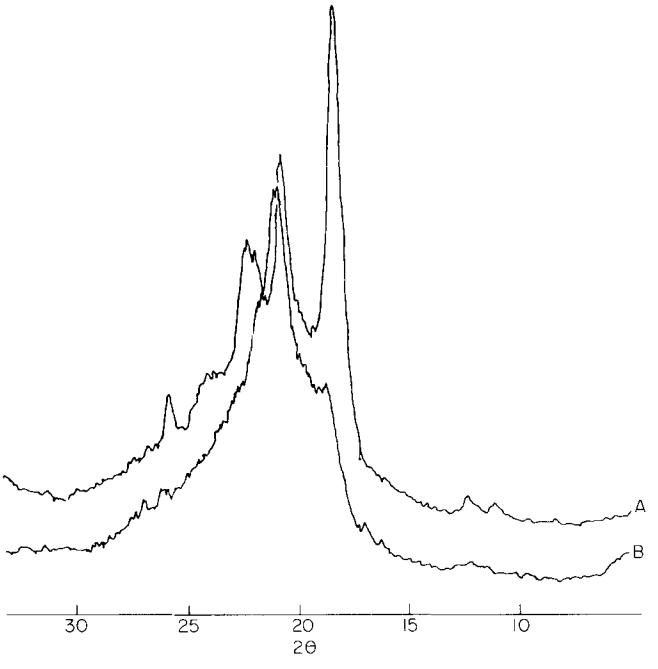

Figure 4 X-ray diffraction diagrams for poly(amide-ester) film POLEA 3612: A, after degradation; B, before degradation

in crystallinity. Surprisingly, this phenomenon was not exhibited by POLEA 366/26 up to 35 days in the present investigation (*Figure 3*) whereas POLEA 3612 behaved as expected (*Figure 4*). The other (amide-ester)–ester copolymers, namely POLEA 3612/26, POLEA 3610/26, are currently under study.

In vivo tests, involving the subcutaneous implantation of the film on a rat, showed that POLEA 3612 was completely fragmented after 30 days whereas POLEA 366/26 formed a capsule initially; both were eventually absorbed after 3 months. Analysis of histopathological tissue is under way to show how the films were absorbed. As a whole, the polymer fulfils the requirements of non-toxicity and biocompatibility. Further study on monofilaments spun from other poly(amide-ester)s with various molecular sizes is under way and will be communicated later.

CONCLUSION

The new poly(amide-ester) has potential as a perfectly bioabsorbable suture material with controlled biodegradability.

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