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Poly(glycerol-dodecanoate), a biodegradable polyester for medical devices and tissue engineering scaffolds

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Abstract

In this paper we describe the mechanical and biological features of a thermosetting polyester synthesized from glycerol and dodecanedioic acid named Poly-Glycerol-Dodecanoate (PGD). This polymer shows a glass transition temperature (T_g) around 32°C, and this accounts for its mechanical properties. At room temperature (21°C) PGD behaves like a stiff elastic-plastic material, while at body temperature (37°C), it shows a compliant non-linear elastic behavior. Together with biodegradability and biocompatibility PGD has distinct shape memory features. After the polymer is cured, no matter what the final configuration is, we can recover the original shape by heating PGD to temperatures of 32°C and higher. The mechanical properties together with biocompatibility/biodegradability and shape memory features make PGD an attractive polymer for biomedical applications.

1. Introduction

Biodegradable elastomeric polymers play a central role in soft tissue engineering and drug delivery. Such elastomeric polymers should exhibit a wide range of properties to address the multitude of needs in soft tissue reconstruction. It is desirable that such polymers mimic soft tissue elasticity, imparting favorable stresses on surrounding tissues, while at the same time withstanding physiologic stresses without failure. Large differentials between normal tissue stresses and device-induced stresses are associated with adverse physiologic responses, such as restenosis in blood vessel grafts.

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Furthermore, polymer devices must withstand manipulation during surgical implantation. Specifically, it would be beneficial for the device to maintain a rigid shape during implantation at room temperature, allowing the surgeon to manipulate and insert the devices in the proper anatomical position, subsequently becoming soft and compliant at body temperature to better match soft tissue elasticity. In addition, shape memory properties are highly desirable for surgical implantation, especially in minimally invasive applications. Such an implant could be folded to go through narrow passages, and once in place assume its functional shape.

For tissue engineering, scaffolds made from elastomeric polymers should also degrade slowly, allowing the necessary time for the native tissues to regenerate and substitute to the implant itself. Finally, to address regulatory and clinical needs, the polymer should be made using elements that are both inexpensive and non hazardous to the body, and be straightforward to manufacture into complex three-dimensional (3D) structures.

To date, several polymers have been synthesized, starting from a primary aliphatic chain of various lengths and a secondary compound that allows for the creation of esteric bonds. The density of the cross-link network determines the degradation time for each biopolymer, and based on this element we can design polymers with a long degradation time, well suited for implantable tissue regeneration devices. Notable work has been conducted on the fabrication [1], characterization [2] and use [3–5] of poly-glycerol sebacate (PGS), a thermoset elastomer derived from poly-condensation of glycerol and sebacic acid. PGS has mechanical properties of a tough elastomer, good biodegradability and biocompatibility with an overall low inflammatory response from the host [2]. So far, this polymer has been used to fabricate micro-patterned devices for contact guidance applications [4] and for nerve tissue engineering [5].

We designed a biopolymer for soft tissue engineering, specifically tailored for implantable medical devices. We considered the same criteria described by Wang [1]: 1) hydrolysis as mechanism of degradation, 2) ester formation as a mean to provide a hydrolyzable chemical bond, for its well characterized and versatile synthesis, 3) a degree of cross-linking to ensure low modulus and acceptable elasticity; and 4) use of non-toxic monomers.

We used glycerol as the trifunctional monomer and dodecanedioic acid (decane 1,10 dicarboxylic acid) as the acid monomer. They react to form esteric bonds that are easily hydrolyzed. By varying the molar ratio of the two compounds, we can achieve different cross-link densities. Glycerol is a precursor for synthesis of triacylglycerols and of phospholipids in the liver and adipose tissue. It also enters the gluconeogenesis and glycolysis after being converted to glyceraldehyde 3-phosphate. Dodecanedioic acid is a metabolic intermediate, synthesized from lauric acid in the omega-oxidation pathway [6]; it possesses the necessary characteristics to be used as an alternative fuel substrate in parenteral nutrition [7]. In addition to biocompatibility and desired mechanical behavior, we also considered the following implant-specific criteria: 1) slower degradation time for tissue engineering applications; 2) “dual behavior” (plastic-elastomeric transition) under specific environmental conditions to enhance surgical implantation; and 3) shape memory properties, also to enhance surgical implantation.

A slower degradation time, obtained through cross-linking and use of a 12-carbon dicarboxylic acid, would allow a longer time for host-derived cells to repopulate the implant itself. A more rigid behavior at room temperature, transitioning to a more compliant elastomeric behavior at body temperature would facilitate surgical maneuvers, as it is much easier to manipulate and to position correctly a stiff device than a soft one. Once in the body, having a more compliant material, that exhibits elastic behavior in the range of surrounding tissues, is desirable to avoid adverse physiological reactions. Furthermore, shape memory is crucial for devices that need to be implanted through narrow orifices or passages (intra uterine devices or coronary stents), whose initial shape must be smaller than the final one. Both plastic-rubber transition and memory shape are achieved by using a bulky polymeric backbone (12 C dicarboxylic acid) and modulating the degree of cross-linking so that the glass transition temperature (T_g) would be between 30 and 34°C. We obtained a polymer with modulable mechanical features, slower degradation time, and shape memory referred to as Poly-Glycerol-Dodecanoate (PGD).

2. Materials and methods

2.1 Polymer fabrication and characterization

The polymer was fabricated from glycerol (MP Biomedical, LLC, Solon OH) and dodecanedioic acid (Sigma-Aldrich, MN) in 1:1 molar ratio. Both elements were mixed together in a three-necked flask at 120°C flask under nitrogen and stirring conditions for 24 hours. After this time the mixture is placed under vacuum (100 mTorr) and continuous stirring for 24 hours. The pre-polymer, thick and viscous at this stage, can be casted in a variety of molds. Mold and pre-polymer are transferred into a vacuum oven at 90°C for 48 hrs, at the end of which the temperature is raised to 120°C and kept such for 48 hrs; vacuum is pulled and maintained at 90 mTorr for the whole duration of the curing process.

2.2 Chemo-physical properties

Molecular calculations (elemental composition and density ρ) were performed with ChemDraw software (ACDLabs, Toronto Canada). Density was also calculated experimentally with Archimedes technique. Briefly, cured samples were cut into 10 pieces in order to determine if the density was uniform across the sample, and each measurement taken in duplicate. Each sample was soaked in deionized water (reverse osmosis) for 24 hours to ensure water penetration into pores. Two measurements were obtained and used according to the equations: W_{dry} (the dry weight of the sample) and W_{sub} (the weight of the

sample submersed in water), where $Volume_{apparent} = \frac{W_{dry} - W_{sub}}{\rho_{water}}$ and

$Density_{apparent} = \frac{Mass_{dry}}{Volume_{apparent}}$. The cross-linking density (moles of active network chain per unit volume) was calculated from the following basic equation that relates the retraction stress, σ to its extension ratio

$$\alpha:\sigma = nRT \left(\alpha - \frac{1}{\alpha^2} \right) \quad (\text{Eq. 1})$$

where σ is the stress measured and $\alpha = L/L_0$ [8]. The cross-linking density n is also expressed as:

$$n = \rho / M_c \quad (\text{Eq. 2})$$

From Eq. 2 we can derive M_c (the number-average molecular weight between cross-links).

2.3 FTIR, TGA, DSC

FTIR was performed on a Spectrum BX FTIR system (Perkin Elmer Inc. Waltham, MA), equipped with an Attenuated Total Reflectance (ATR) accessory (Perkin Elmer Inc. Waltham, MA). Small slabs of fully cured and uncured polymer were tested.

Thermogravimetric analysis (TGA) was performed on a Perkin Elmer TGA (Perkin Elmer Inc. Waltham, MA) and the samples were tested in the range from 25 to 900 °C. ($n=20$). Differential Scanning Calorimetry (DSC), was performed on a Perkin Elmer DSC 7 (Perkin Elmer Inc. Waltham, MA). Specimens were tested from 25 to 60°C. ($n=20$) We analyzed data from both DSC and TGA with Pyris software (Perkin Elmer Inc. Waltham, MA).

2.4 Tensile measurements and curve fitting

We cast the pre-polymer into dog-bone shaped strips, according to the ASTM standard D 412. The specimens ($n=20$) were placed in a MTS tensile machine (MTS System Corp. Eden Prairie, MN) equipped with a 500 N load cells, a tensile grip system (MTS System Corp. Eden Prairie, MN), and a custom-built environmental chamber. The environmental chamber was equipped with two temperature probes one to measure the temperature of the chamber, the other in direct contact with the specimen. The temperature inside the chamber was regulated by means of a thermocontroller (Cole-Parmer Instrument Co. Vernon Hills IL) receiving input from the two probes and driving a heating element (Watlow, St. Louis, MO) placed inside the chamber to the desired temperature. Deflection rate was kept at 50 mm/min. The specimens were tested to failure at 21, 32, 37 and 42°C. We fit the data obtained from tensile tests (strain and stress) at 37°C to a one-term Ogden constitutive model for hyperelastic materials using Matlab software (The MathWorks, Natick, MA). The one term Ogden model is based on a strain energy function of the form:

$$W(\lambda_1, \lambda_2, \lambda_3) = \frac{\mu_1}{2} (\lambda_1^{\alpha_1} + \lambda_2^{\alpha_1} + \lambda_3^{\alpha_1}). \quad (\text{Eq. 3})$$

W is the strain energy function, λ_i denote the stretch ratios in the x_1 , x_2 and x_3 directions, and μ_1 and α_1 are constants that are fit to experimental data. The resulting 1st Piola-Kirchoff stress is calculated as:

$$T_i = -\frac{1}{\lambda_1} p + \frac{\partial W}{\partial \lambda_i}. \quad (\text{Eq. 4})$$

T_i is the 1,2 or 3 normal component of the 1st Piola-Kirchoff stress and p is the hydrostatic pressure. For the uniaxial tensile test in this study, the hydrostatic pressure p can be

calculated from the fact that stresses on the specimen face perpendicular to the test direction are zero. Assuming the specimen is tested in the x_3 direction, this leaves the final expression for the 1st Piola-Kirchoff stress as:

$$T_3 = -\frac{1}{\lambda_3 \sqrt{\lambda_3}} \mu_1 \sqrt{\frac{1}{\lambda_3}}^{\alpha_1-1} + \mu_1 \lambda_3^{\alpha_1-1}. \quad (\text{Eq. 5})$$

The 1st Piola-Kirchoff stress is calculated from the experimental tensile test by dividing the applied force by the initial specimen area. The coefficients from the model (eq. 5) are then fit in a least squares sense to the experimental stress using the unconstrained optimization routine *fminunc* from the MATLAB optimization toolbox. Coefficient of determination value (R^2) was calculated for the fit. In addition, the Baker-Eriksen inequality [9]

$$\left(\lambda_3 \frac{\partial W}{\partial \lambda_3} - \lambda_2 \frac{\partial W}{\partial \lambda_2} \right) (\lambda_3 - \lambda_2) > 0 \text{ was assessed and found to be satisfied for each fit.}$$

2.5 In-vitro degradation

Slabs of dry PGD ($n=15$) were weighted and placed in 15 ml conicles (Falcon Bedford, MA) and allowed to soak in PBS (Gibco, Carlsbad, CA) at 37°C for 20, 40 and 90 days. Samples were removed at the different time-points, dried at 40°C and weighted again. Dry weight change was thus determined. A linear regression model was fit to the data obtained.

2.6 Cell growth and WST-1 assay

To fabricate PGD-coated plates (PP), a solution of 1% PGD and tetrahydrofuran (THF) was casted on thirty-six 35 mm glass Petri dishes and after THF evaporation, the plates were cured with the same protocol described above. The culture plates were rinsed several times in 70% ethanol, sterile PBS to wash any unreacted monomer, and finally stored in PBS until their use. We used human aortic fibroblasts (Promocell, Germany) (plating density=2000 cells/cm²) We studied cell viability over time by WST-1 assay (Roche, Basel, Switzerland). WST-1 assay was assessed by withdrawing plates ($n=6$) at 6 different timepoints. WST-1 reagent (200 μ l) was added to each plate and incubated overnight. The drift in absorbance was detected at 480nm with a plate reader (Genios plus, Tecan Ltd., Switzerland) driven by Magellan software (Tecan Ltd., Switzerland). Cells from each plate were counted with a hemocytometric slide. Cell number was calculated as density, by normalizing the number of cells per each plate to the area of the plates. For the control plates (CP), we plated the same cells with the same protocol onto thirty-six 35 mm un-coated polystyrene plates. A protocol identical to PGD plates was followed. The two groups were followed under microscopy to assess confluence.

2.7 Shape memory assessment

To assess PGD shape memory properties, we used tensile test coupons ($n=10$) made according to the ASTM standard D 412, and the same set-up used for mechanical testing. The initial gauge length (L_0) was stretched, at room temperature, to three different strain levels (60, 80, 100%). All the specimens were placed in a warm tap water bath at 40°C. Within 20 seconds specimens returned to their original size, we measured them and

compared the new lengths with each pre-stretch length. This cycle was repeated three times per each coupon. We also tested PGD for shape memory after warm elongation. Briefly, we elongated tensile test coupons at 37°C by using the same set-up used for the tensile tests, and 60, 80 and 100% strains. Once achieved the final configuration the coupons were cooled down to 21°C to keep their deformed configuration. Finally, they were immersed in a warm bath at 40°C; within 20 seconds, they returned to their original length that was measured. This cycle was repeated three times per each specimen.

2.8 Statistics

We used SPSS statistical software (SPSS Inc. Chicago, IL). ANOVA with Tukey HSD was used to compare means between groups ($p < 0.05$). Degradation data was fit to a linear regression model to estimate the polymer half-life.

3. Results

3.1 Chemo-physical properties

Elemental composition of the repetitive unit is: (calculated for $C_{15}H_{28}O_6$) C=59.19%, H=9.27%, O 31.54%. Its calculated average mass is 304.37 Da. Calculated density was $1.128 \pm 0.06 \text{ g/cm}^3$, close to the experimental data of $1.131 \pm 0.010 \text{ g/cm}^3$. Cross-linking density n , calculated from Equation 1 (see materials and methods), was $1.35 \pm 0.2 \times 10^{-4} \text{ mol/cm}^3$ and M_c (the number-average molecular weight between cross-links) was $8466 \pm 1180 \text{ g/mol}$

3.2 FTIR, TGA, DSC

Reaction between glycerol and dodecanedioic acid in a 1:1 molar ratio yields an elastomer that is soft and pliable out of the oven, hardening upon cooling at room temperature. We anticipated that formation of PGD occurred by polycondensation of glycerol and dodecanedioic acid. Fourier Transformed Infra-Red (FTIR) on pre-polymer slabs confirmed a broad OH stretch, at 3331 cm^{-1} , partially masking a methyl stretch at 2927 cm^{-1} . (Fig 1a) On fully cured slabs the O-H stretch at 3331 cm^{-1} is absent unmasking the methyl stretch at 2927 cm^{-1} , and an intense C=O stretch, indicative of esteric bonds, appears at 1735 cm^{-1} (Fig 1b). Thermogravimetric analysis (TGA) shows no melting point in the range from 25 to 900°C, with PGD undergoing a complete combustion at about 700°C. Differential scanning calorimetry (DSC) confirms a glass transition temperature (T_g) of 32.1°C (31–34.2 °C).

3.3 Tensile Testing and Mechanical Properties

We found a statistically significant difference between specimens tested at 21°C and 37°C. During extension at 21°C, PGD showed the typical linear elastic stress strain response followed by necking and plastic deformation of an elastic-plastic material, while at 37°C PGD showed a non-linear elastomeric response (Fig 2a, 2b). The tangent Young modulus dropped from a maximum of 136.55 (67.2–155.7) MPa to 1.08 (0.25–2.6) MPa at 21°C and 37°C respectively; tangent modulus at 37°C was calculated at a strain level of 7.8% (5.5–9.8). Strain at break (SAB) at 21°C was 225% (192.1–243.5) dropping to 123.2% (62.9–163.6) at 37 °C. (Tab. 1) The one-term Ogden constants were $\mu_1 = 0.3 \pm 0.12 \text{ MPa}$, $\alpha_1 = 2.14$

± 0.5 with $R^2 = 0.998 \pm 0.001$ for the nonlinear elastic response at 37°C, demonstrating that PGD can be modeled using classic hyperelastic models.

3.4 In-vitro degradation

Normalized change in dry weight was negligible in the first 20 days of soaking in PBS at 37°C, at 40 days. The weight dropped to 94.2% (93.1–95.3%), progressing to 87.4% (85.7–88.4%) at 90 days. Fitting a linear regression model to the data obtained we found the function $y = -0.001x + 1$, where y is the ratio of residual biopolymer, -0.001 is the rate of degradation, x is the time in days and the coefficient 1 is the amount of polymer at time 0. This function predicted PGD in-vivo degradation behavior with a p-value less than 0.005% and R^2 of 0.978. From this formula we calculated the time at which PGD would be 50% of its original weight (half-life) and found an estimated time of 16 months.

3.5 Cell growth and WST-1

Growth study showed that the density of human fibroblasts onto PP increases slower than controls at first, however the rate increases around day 10 in culture remaining constant until day 18, when the growth rate begins to slow down. CP, on the other hand, had a fast growth rate reaching confluence (microscopy) around day 10. At this time they showed a density peak that decreased slightly and maintained a plateau until the end of the study. PP reached the same density of the controls around day 18. At this time they also reached confluence (Fig 3a) as also observed microscopically. WST-1 assay showed a pattern similar to the density curve, with a drop for CP starting at day 10, and for PP around day 18. (Fig 3b)

3.6 Shape memory features

Our preliminary study demonstrated that PGD has distinct shape memory features, every specimen, elongated to the different strains levels (60, 80 and 100%), during cold draw or warm elongation, returned exactly to its original length (L_0) within 20 seconds after immersion in warm water, every single time this cycle was repeated. PGD showed 1) a cold deformation temperature range (below 32°C) and 2) a warm deformation temperature range (37°C and above). During cold draw the polymer maintains the degree of deformation and shape we apply; during warm elongation the deformation is not maintained unless the polymer is cooled down rapidly. No matter how we achieve the deformed configuration (through cold or warm deformation) the polymer returns to its original shape when heated to 32°C and above.

4. Discussion

We have synthesized a biodegradable elastomeric polymer PGD that is biocompatible, biodegradable, exhibits linear elastic behavior at room temperature, nonlinear elastic behavior at body temperature, and has shape memory properties. These characteristics make this material especially attractive for creating surgically implantable tissue engineered scaffolds, whose mechanical behavior and degradation pattern can be both altered by varying the glycerol:dodecanedioic acid molar ratios, and curing conditions.

PGD is also soluble in a number of organic solvents (acetone, tetrahydrofuran, ethanol, 1,3 dioxolane), and its un-crosslinked, mildly viscous, pre-polymer can be shaped in a variety of structures, ranging from sheets to complex 3D shapes.

We anticipated that PGD is a polyester of glycerol and dodecanedioic acid, with esteric bonds between the glycerol OH groups and the dodecanedioic acid carboxylic groups. FTIR shows the presence of a broad stretch at 3331 cm^{-1} in the pre-polymer phase, indicating the predominance of alcohol-associated OH and therefore a rather un-reacted compound. The same peak is absent in the fully cured polymer where an intense C=O stretch, typical of esters, appears at 1735 cm^{-1} . The length of dodecanedioic acid and the number of esteric bonds it forms with glycerol are responsible for the thermomechanical characteristics of PGD.

At 21°C Strain at break was more than three times its original length, and more than twice its initial length at 37°C . The modulus also changed significantly, indicating a stiff material at room temperature, which became soft and pliable at body temperature. Therefore, PGD shows the typical features of a stiff elastic-plastic material at room temperature (with a very high elongation at break and high modulus), and the properties of a nonlinear elastomer at body temperature, at 37°C in fact PGD has approximately the same cross-linking density and mechanical characteristics of styrene-butadiene rubber [10] (synthetic rubber).

This dual behavior could be explained by the polymer T_g , at room temperature PGD backbone possess only molecular vibrational motion, and no other molecular motions are present; the polymer is in fact “frozen” in its hard and glassy state. As the temperature increases, approaching T_g (32°C), the backbone acquires rotational motion along its major axis, and as the temperature increases further, the secondary interactions between adjacent polymer chains become looser and looser and now contiguous chains are free to move with one respect to another. Since we did not observe any change in the mechanical properties from 37°C and 42°C , we conclude that at 37°C the polymer has lost its “glassy” state and is completely amorphous. This data is also confirmed by DSC showing the “step-wise” anomaly that describes the glass transition, ending at about 35°C .

The immediate clinical implication of this behavior is clear during implantation, especially for soft tissues, in which the main difficulty encountered is to re-establish the correct 3D shape of a soft implant and even more importantly re-establish the normal anatomical relationship with the surrounding host structures. Implants fabricated from PGD, being stiff and maintaining their 3D shape at room temperature, would be easier to manipulate and to place in the correct anatomical position.

We showed that PGD tensile data at 37°C can be fit to a one-term Ogden model, that is a classical model describing behavior of hyperelastic materials, we possess a valid model to predict the mechanical behavior of devices fabricated with PGD using commercially available finite element codes. We would be able to estimate and make prediction on how the material behaves, and therefore select the design, and material composition more suitable for our purposes.

Cell density study and WST-1 assay show that PGD allows cells to adhere, grow and remain metabolically active in culture. Cells seeded on a PGD substrate, compared to the control group (represented by cultured cells on polystyrene plates) appear to replicate at a slower rate first, probably due to the acclimation to a different substrate, but at day 10 the growth rate increases, reaching confluency around day 18 in culture when the density between the study group and the controls is similar. Metabolically, the cells in culture seem to follow a similar pattern.

Polymers with shape memory are characterized by a peculiar thermo-mechanical response to heat, defining three temperatures: [11]

1. Deformation temperature (T_d) is the temperature at which the polymer can be deformed into its temporary shape and it can be higher or lower than the T_g .
2. Storage temperature is the temperature below which no recovery from the deformed state occurs, it can be lower or the same of the T_d .
3. Recovery temperature (T_r) is the temperature at which the memory effect is active and the polymer returns to its original shape, and this temperature is typically around T_g .

Observations from our preliminary study of shape memory, and data from mechanical testing and thermoanalysis show that PGD possess essentially two temperatures ranges: temperature of cold deformation (T_{dc}) and temperature of warm deformation (T_{dw}). T_{dc} , below the glass transition temperature, is the temperature at which the polymer is in its glassy state, where cold draw and plastic deformation are possible. In this range of temperatures the deformation is maintained even after the external forces are removed. T_{dw} , few degrees higher than the T_g , ($\sim 37^\circ\text{C}$) is the temperature at which PGD has completed its transition to a rubber-like state as characterized by a non-linear elastic deformation of the polymer. The deformation is not maintained once the external forces are removed, unless the deformed system is cooled down below the T_g .

PGD in a deformed configuration starts recovering its original shape if heated up to the T_g , and the recovery rate becomes faster as the temperature increases, with an optimal recovery temperature around $39\text{--}40^\circ\text{C}$.

T_{dc} and T_{dw} have an important macroscopic significance: 1) PGD can undergo large plastic deformation by cold extension, and when heated to 32°C and higher returns to its initial configuration, this process is faster as the temperature increases; 2) PGD can be deformed while in its rubbery state, and maintain the deformed configuration if cooled below glass transition temperature.

Microscopically, if we deform PGD in its rubbery state and maintain the deformation we can “freeze” this shape into the glassy state; in the plastic state instead the deformation is achieved and maintained thanks to the cold draw effect [8,12]

Thermodynamically speaking, the deformed configuration, no matter how achieved, has high energy, and raising the temperature allows entropy relaxation and return to the low conformational energy state created during the curing process [13].

Shape memory would make PGD suitable for all those procedures where the device, in order to be implanted, needs access through small orifices. This is especially critical for minimally invasive surgical applications, gaining popularity due to shorter postoperative recovery time, but which impose significant limitations on the size and shape of device that may be implanted. Vascular stents for angioplasty are one prime example of an application that could benefit from shape memory behavior. PGD stents once placed inside the vessel and warmed up at the contact with blood would assume their shape, if embedded with drugs, through slow degradation, would be able to act very much like the drug-eluting stents currently used.

PGD could be successfully deployed for fabrication of an Intra-Uterine Device (IUD). Such device could be folded for an easy insertion and once placed in-situ, it would assume the correct shape. It would be soft and pliable therefore with minimal risk of perforation or discomfort for the patient; being biodegradable, it would not require a second procedure for removal. Other applications could be for spinal disc or articulating surface repair using PGD devices that are formed and then compacted at room temperature but then expand when brought in contact with tissues and heated to body temperature. PGD, either as an injectable suspension or as small devices embedded with pro-inflammatory molecules (interferon, etc), could be used for obliteration of cavities (i.e. pleurodesis) once in place the PGD device would cause a localized inflammatory reaction creating a local fibrous reaction and ultimately obliteration.

5. Conclusions

The data acquired in this study show that PGD is a versatile biopolymer. Its novelty is due to the dual behavior showed at different temperatures and the shape memory properties. The plastic-rubber transition around physiological temperature is advantageous when we design medical devices to implant. Maintaining a stiff configuration is essential during manipulation/implantation of such devices. A soft configuration is of fundamental importance once the device is working inside the body, to minimize the stress differential between the device and the host tissues. The shape memory feature is important for applications such as mini-invasive surgery, as we can pack any device in a much smaller configuration, and once placed in the appropriate position deployed to its final functional configuration.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Fourier Transformed Infra-Red spectra: uncured PGD (1a) a broad peak is visible at 3331 cm^{-1} and denotes the presence of alcohol-associated hydroxyl groups. Cured PGD (1b) the OH peak at 3331 cm^{-1} has disappeared and a C=O stretch at 1735 cm^{-1} , typical of esteric bond appears.

Figure 2. Stress vs strain plots of PGD: at 21°C (2a) and 37°C (2b). At 21°C the curve is of a tough plastic material while at 37°C it shows a non-linear elastomer

Figure 3.

3a) graph showing the density over time, controls have a faster growth rate, but as it declines, PGD plates increase their growth rate reaching the same density around day 18.

3b) WST-1 shows that fibroblasts remain viable for the duration of the study, in the PGD and control groups, following similar pattern of the growth curve.

Table 1

Synopsis of thermo-mechanical properties of PGD

T_g	Modulus (MPa)	Strain at break (%)
32.1°C	136.55 (67.2–155.7) (21°C)	225 (192.1–243.5) (21°C)
	1.08 (0.25–2.6) (37°C)	123.2 (62.9–163.6)