

In vitro Degradation of NovoSorb™ Polyurethanes Designed for Orthopaedic Applications

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Introduction

Injectable Biodegradable polymers that can be cured in-situ to form high strength porous and non porous materials have a number of advantages in orthopaedic applications. A key advantage is arthroscopic delivery with growth factors to promote bone tissue regeneration. Existing polyglycolides, polylactides and their copolymers have limitations in formulating injectable systems. We have developed¹ a family of biodegradable polyurethanes (NovoSorb™) with properties suitable for many biomedical applications. NovoSorb can be formulated as an injectable gel which cures in-situ (ISC) or on demand (COD) to high strength cross linked polymer networks. This paper describes *in-vitro* degradation of prefabricated NovoSorb™ formulated for orthopaedic applications. The mechanical properties and *in-vivo* degradation of these materials will be presented as separate papers in this conference.

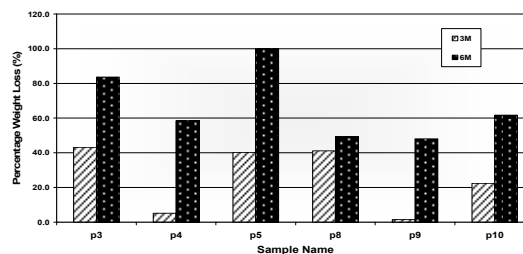
Experimental

Six polymers, three each from ISC (P3, P4, P5) and COD (P8, P9, P10) methods were investigated. ISC polymers were prepared by reacting two prepolymers (A and B). A was prepared from pentaerythritol (PE) and ethyl 2, 6-diisocyanatohexane (ELDI), and B was a mixture of polyols PE/dl-lactic (PEDLLA MW 456) and PE/glycolic acid (PEGA MW 453). The polyols PEDLLA and PEGA were prepared by acid-catalysed polycondensation. Polymers P3 and P4 were porous cylindrical solids with and without β -tricalcium phosphate (5 μ m), respectively. And P5 was based on PELLA-ELDI as prepolymer A. ISC polymers were prepared by reacting two prepolymers with stannous octoate as catalyst. The degassed polymer mixture was then injected into cylindrical cavities [6 mm (D) x 12 mm (L)] of a Teflon® mould and cured at 37°C overnight. Porous polymers were obtained by incorporating water to the prepolymer mixture. COD polymers were based on isocyanatoethylmethacrylate (IEM) functionalized four-arm star polyols prepared from glycolic acid, l-lactic acid and PE. COD polymers P8 and P9 were porous cylindrical solids with and without β -tricalcium phosphate, respectively. P10 was based on a terpolymer polyol of PE, l-lactic acid, GA and ϵ -caprolactone. COD polymers were prepared by curing acrylate functionalized polyol by exposing to 450 nm blue light source (Elipar FreeLight 2). The initiator system was camphorquinone/*N,N*-dimethyl amino ethyl methacrylate. The *in-vitro* study was carried out according to ASTM method F 1635-04 at 37°C in 0.1M PBS. The solution pH was maintained at 7.4 ± 0.2 by replenishing the PBS when the pH approached 7.2. The results reported is an average of triplicates for mass and dimension loss at 3 and 6 months. The polymer degradation was also assessed by measuring amine concentration by ninhydrin assay.

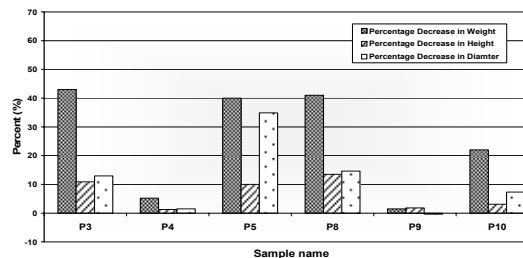
Results and Discussion

Figure 1a illustrates the mass loss of polymer samples after 3 and 6 months. P3, P5 and P8 showed similar weight loss after 3 months, whereas mass loss of P4 and P9 was

negligible. After six months P5 was completely degraded and P3 showed 80% weight loss while other samples lost 40 to 60 % of their weight. It was interesting to note that the P8 retained its specimen shape over the 3 month period, perhaps indicative of mostly surface erosion rather than bulk degradation (Fig 2). In general, the COD polymer showed lower mass loss than the ISC polymers. Tri-calcium phosphate incorporation decreased the rate of polymer degradation as illustrated by polymers in both series. By 6 months time, mass loss in ISC was between 60-100% compared to 50-60 % in COD. Polymers that contained TCP, P4 (ISC) & P9 (COD) lost very little mass in the first 3 months compared to those without TCP. In the ninhydrin assay, polymer with higher mass loss showed higher concentration of amine.



(a)



(b)

Figure 1 (a) Mass loss (wt-%) after 3 and 6 months (b) Weight loss and decrease (%) in test specimen dimensions after 3 months.

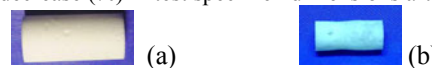


Figure 2 Test specimen P8 before (a) and after (b) 3 months in PBS buffer.

Conclusion

This study demonstrates that NovoSorb™ can be formulated to have different degradation rates depending on the application requirements. Incorporation of tri-calcium phosphate reduces the rate of degradation. The mode of degradation of these polymers resembles surface erosion rather than bulk degradation.

References 1. (a) Gunatillake PA and Adhikari R. International PCT Application PCT/AU03/00935 (b) 7th World Biomaterial Congress, Sydney May 2004, p 703. 2. Adhikari R, Gunatillake, PA, Mayadunne RTA, Houshyar S, Karunaratne O, Griffiths IM, , 30th Annual Meeting, Society for Biomaterials, Memphis, TN, USA, 2000, p 442.