

## 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 developed<sup>1</sup> 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.

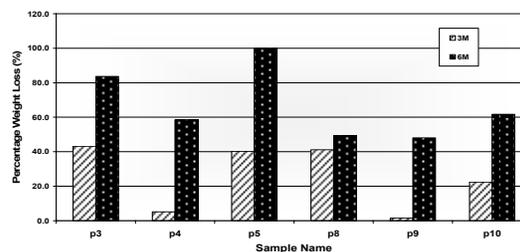
### Experimental

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  $\beta$ -tricalcium phosphate (5  $\mu$ 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  $\beta$ -tricalcium phosphate, respectively. P10 was based on a terpolymer polyol of PE, l-lactic acid, GA and  $\epsilon$ -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  $7.4 \pm 0.2$  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.

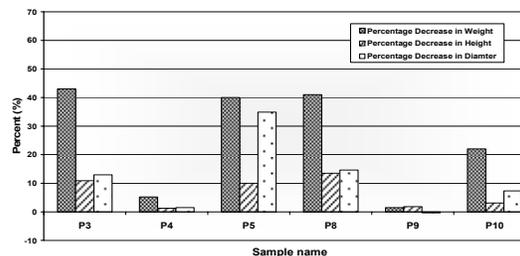
### Results and Discussion

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.

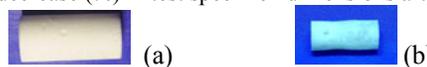


(a)



(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) 7<sup>th</sup> World Biomaterial Congress, Sydney May 2004, p 703. 2. Adhikari R, Gunatillake, PA, Mayadunne RTA, Houshyar S, Karunaratne O, Griffiths IM, , 30<sup>th</sup> Annual Meeting, Society for Biomaterials, Memphis, TN, USA, 2000, p 442.