Biodegradable NovoSorb™ Polymers: Structure/Property Relationships & In-vitro/In-vivo Degradation

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Introduction

Hydrolytically degradable synthetic polymers have found extensive use in medical implants. Of those currently used homo and co-polyesters of lactic and/or glycolic acids have largely been exploited over the years due to their excellent inherent properties. Their ability to degrade to biocompatible molecules, the ease with which these fragments are resorbed and removed by the body is seen as the major advantage. Consequently, these polymers have been used in many applications including resorbable sutures drug delivery systems, and orthopaedic fixation devices such as pins, rod and screws. We have evaluated the potential use of a family of biodegradable ester-polyurethane blends, formulated for orthopaedic applications and trademarked as NovoSorb™.[1] These pre-polymers have an injectable consistency, enabling them to be delivered to the defect site by arthroscopy and cured in-situ (in-situ cure, ISC) or on demand (cure on demand, COD), depending on the application at hand. The paper describes the polymer structure, their properties, in-vitro and in-vivo degradation studies carried out so far.

Experimental

Ten polymer formulations, five each prepared from in-situ and (ISC) cure on demand (COD) methods were included in the animal model. ISC polymers were based on pentaerythritol (PE) ethyl 2, 6-diisocyanatohexane (ELDI) and a polyol: PE and D,L-lactic acid (PEDLLA, PEGA). COD polymers were based on four-arm star copolymers of glycolic and l-lactic acid functionalized using ELDI and pentaerythritol triacrylate or directly functionalized with isocyanatoethyl methacrylate (IEM) and light cured (figure 1a). The filler used are β-tricalcium phospahate (TCP). A bi-lateral sheep model was used in the study. Six implant sites per leg (3 cortical and 3 cancellous regions) in femur were created. Untreated bone cavity, Purasorb™ and PMMA bone cements were used as controls in the study (figure 1b).

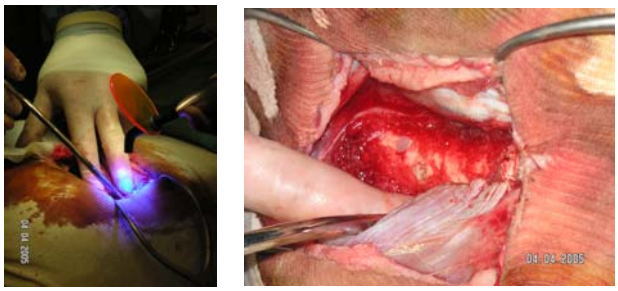

Figure 1(a & b)

Results and Discussion

ISC polymers are two part systems. The first part is designed to have isocyanate terminal groups and when mixed with a multi-arm polyol having hydroxy terminated ends triggers the formation of urethane cross links. The time for curing is controlled by the loading of the catalyst. COD polymers are designed to have (meth)acrylated terminal ends and are formulated in to one composition. The curing occurs by free radical polymerization and is triggered by light following delivery to the defect site. Typical curing times are 1-2 minutes. β-Tricalcium phosphate was included at a 20% loading in both systems for two reasons. Firstly, TCP is known to be an osteogenic promoter. Secondly, the presence of TCP at 20% loading gave the optimal mechanical properties. The increase in modulus with the increase of TCP content up to 20% with constant UCS is shown in figure 2.

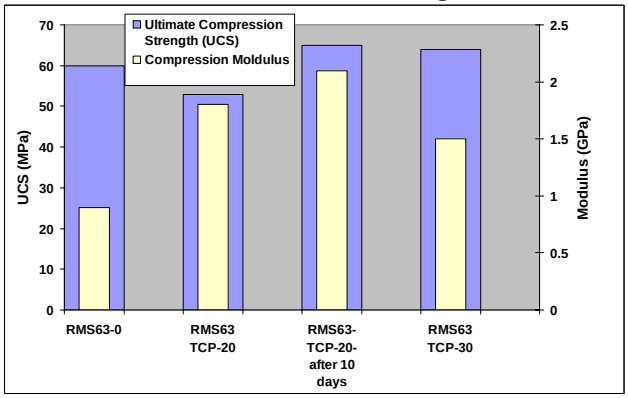

Figure 2: Effect of TCP loading

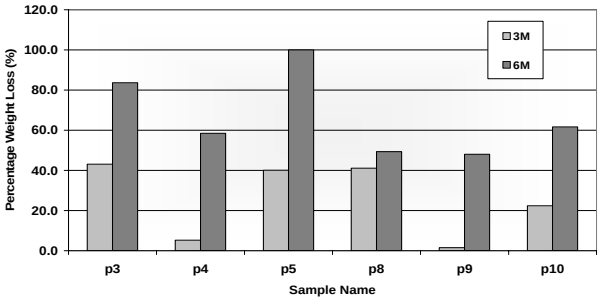

Figure 3: 3/6 month weight loss of implants (in-vitro)

Invitro degradation studies revealed varied mass loss between samples. In the first three months the samples P3, P5 and P6 degraded at a much faster rate than P4 and P9 as designed. Although all of the samples were porus, the 20% TCP in the latter two samples were expected to slow the degradation process through its inherent buffering capability and thereby reducing the local acid concentration within the sample. In 6 months most samples had lost significant mass, reduced in size, and the type of degradation, bulk/surface erosion, depended on the nature of the sample. Data for in-vitro and in-vivo studies will be presented.

References

1.(a)Gunatillake PA and Adhikari R. International PCT Application PCT/AU03/00935 (b) Mayadunne, RTA, Gunatillake PA, Adhikari R Provisional Application TW7535. (c) 7th World Biomaterial Congress, Sydney May 2004, p 703. (d) Adhikari R, Gunatillake, Mayadunne RTA, Houshyar S, Karunaratne O, Griffiths IM, , 30th Annual Meting, Society for Biomaterials, Memphis, TN. USA, p 442 (2005)