Tailoring Degradation Rate and Mechanical Properties of Poly(β-amino ester)s for Cardiovascular Therapies

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Statement of Purpose: Abdominal aortic aneurysms are the 13th leading cause of death in the United States with 15,000 people dying from aortic ruptures each year. To treat this condition, a biodegradable polymer coating has been proposed that will mechanically restrain the aneurysm growth and also deliver a drug that addresses the biological mechanisms of elastin degradation. Poly(β-amino ester)s have been chosen as a candidate material because these networks have a wide range of mechanical properties. Previous studies have focused on designing porous degradable scaffolds to promote bone growth[1], but tailoring these systems for cardiovascular applications has yet to be explored.

The objectives of this study are (1) to control the degradation rate of poly(β-amino ester)-based networks across a wide range of timescales and (2) to have the mechanical properties meet the mechanical demands of the cardiovascular environment. Independent tailoring of these key properties will facilitate the development of a novel treatment for abdominal aortic aneurysms.

Methods: Acrylate-terminated macromers were formed via a step-growth polymerization of a diol diacrylate (DDA) (198, 226, 268 g/mol) and 3-methoxypropylamine at molar ratios of 1.05:1 to 1.25:1. The reaction proceeded at 90°C for 24 hours on a rotary shaker at 200 rpm. The photoinitiator, Irgacure 2959, was added at 0.5 weight percent and the polymer solutions were photopolymerized with a UV lamp at 365nm. Methyl methacrylate (MMA) was added to select macromers at varying weight ratios prior to photopolymerization. 1 cm^2 squares cut from 1 mm thick sheets were degraded for 12 weeks. Samples were dried for 24 hours and weighed to determine the mass loss. Dynamic mechanical analysis (TA Q800, Newcastle DE) determined the thermomechanical properties from -100°C to 100°C at a rate of 3°C/min. Each point represents the mean ± standard deviation (n=3).

Results: Networks were synthesized from five molar ratios of DDA to amine, where the DDA had three molecular weights. Figure 1 shows the degradation profile over 12 weeks for every diacrylate molecular weight and each molar ratio. The mass loss increased as the diacrylate molecular weight decreased. The effect of adding MMA to the macromers is shown in Figure 2 where adding more MMA increases the storage modulus in a manner independent of the diacrylate:amine ratio. Between 0 to 45 wt% MMA the networks show distinct storage modulus values due the difference in crosslinking density. Above 45 wt% MMA, the networks have similar storage moduli due to the transition to a more glassy material.

Conclusions: The DDA based networks are more dependent upon the diacrylate molecular weight, not molar ratio, thus allowing for independent tailoring of the modulus and the degradation rate. Further tailoring may be accomplished by mixing DDA macromers of different molecular weights, such as DDA198 and DDA226 macromers to better align the degradation time with the average healing time of aneurysms (8 to 12 weeks). Mixing DDA macromers with MMA allows for a broad range of mechanical properties from rubbery to rigid. For acrylate based networks, the maximum failure strain and toughness occurs when the testing temperature is near the glass transition temperature $(T_g)^2$. The mechanical properties of the DDA networks without MMA are poor because the T_g of these materials is far below the temperature of interest, 37°C. The addition of MMA increases the T_g of the network, thus improving the overall mechanical properties. This allows for design of the mechanical properties before degradation occurs. Future work will include characterizing the degradation products and drug release profiles of these materials.

References

[1] Brey DM. Acta Biomat 2008; 4:207-217.
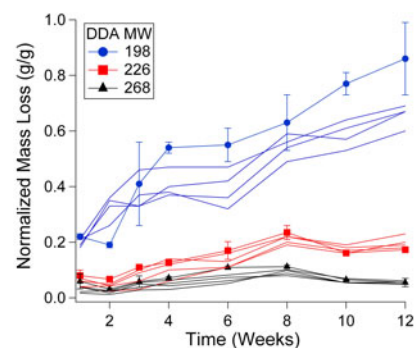[2] Yakacki CM. Adv. Eng. Mater 2008; 10:112-119.

Figure 1. Degradation profile for all DDA molecular weights and molar ratios. The molar ratio of 1.05:1 is marked and the remaining curves represent the four remaining molar ratios.
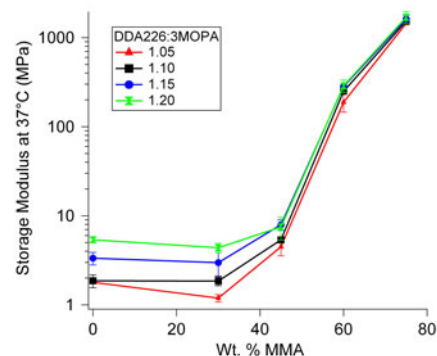

Figure 2. Storage Modulus at 37°C of networks composed of four different DDA226 macromers mixed with MMA from 0 to 75 wt%.