

Enzymatic surface erosion of high-moduli polycarbonates based on natural phenols

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Introduction: Degradable polymeric implants undergo two distinctive pathways of resorption: bulk degradation with delayed erosion of mass or surface erosion without significant change in the bulk [1]. Interestingly, a limited set of aliphatic polycarbonates e.g. poly(trimethylene carbonate) (PTMC), exemplified quick surface erosion behavior *in vivo*, but significantly slower degradation *in vitro*. When the hydrolytic enzymes were applied *in vitro*, the degradation rate of PTMC increased dramatically, demonstrating similar surface erosion characteristics as found *in vivo*. Therefore, hydrolytic enzymes have been suggested to play a significant role in the biodegradation of PTMC [2, 3]. These aliphatic polycarbonates are also flexible, rubbery materials, making them suitable for various biomedical applications e.g. soft tissue engineering. In this work, we report on the enzymatic surface erosion behavior of a series of polycarbonates based on natural phenols tyrosol and homovanillyl alcohol. Their strong mechanical properties such as the moduli are similar to previously reported aromatic polycarbonates derived from tyrosine ester [4].

Methods: (Co)polycarbonates from tyrosol and homovanillyl alcohol (Hva) were synthesized by condensation polymerization carried out in dichloromethane and pyridine using triphosgene. The monomer composition of the copolymer was confirmed by ^1H and ^{13}C nuclear magnetic resonance spectroscopy. The molecular weights (M_n and M_w) were determined relative to polystyrene standards by gel permeation chromatography in N,N -dimethyl formamide. Thermal properties were measured using differential scanning calorimetry: the glass transition temperature (T_g) was calculated from the 2nd heating scan performed at a rate of $10^\circ\text{C min}^{-1}$. For degradation studies, compression-molded discs with thicknesses of approximately $250\ \mu\text{m}$ were conditioned in a solution of lipase from *Thermomyces lanuginosus* (activity of $5\ \text{kU/ml}$) at 37°C , and in PBS as control. Changes in specimen characteristics, i.e. specimen mass and thickness, molecular weights, surface morphology, and mechanical properties were measured over time.

Results: A series of polycarbonates was synthesized from tyrosol and Hva with molar compositions of 100/0, 90/10, 75/25, 50/50, and 0/100. The polymer M_n ranged from 120 to $230 \times 10^3\ \text{g/mol}$, and M_w/M_n values from 1.4 to 1.5. T_g in the dry state increased from 59 to 74°C as Hva content increased from 0 to 100%. This series of copolymers are hydrophobic with a static water contact angle of approximately 80° . Under physiological conditions, the equilibrium water uptake of the (co)polymers was $< 1\%$, and they remained in the glassy state with only a moderate reduction in T_g of approximately 10°C . Poly(tyrosol carbonate) discs incubated in solution containing lipase demonstrated a

linear and concomitant loss in mass ($0.16 \pm 0.04\ \text{mg cm}^{-2}\ \text{d}^{-1}$) and in thickness ($3.0 \pm 0.8\ \mu\text{m d}^{-1}$) over 9 weeks. Increased content of Hva in the compositions resulted in slower erosion rates (Fig. 1). No significant change in molecular weight was measured for all polymers. Specimens incubated in control PBS without lipase remained unchanged in mass, specimen thickness, and molecular weight.

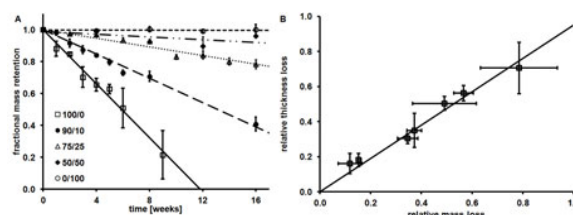


Figure 1. A) Mass retention of discs with molar compositions of 100/0, 90/10, 75/25, 50/50, 0/100 of tyrosol/homovanillyl alcohol. B) Correlation between mass loss and thickness loss of poly(tyrosol carbonate) discs. (All specimens were incubated in lipase solution).

Further, scanning electron microscopic (SEM) images revealed patterns of pits and cavities on film surfaces incubated with lipase, whereas control specimens underwent no changes in surface morphology (Fig 2.). The mechanical properties of this series of polycarbonates were strong with high moduli ranging from $0.81 \pm 0.16\ \text{GPa}$ to $1.19 \pm 0.21\ \text{GPa}$ (wet state) and increased slightly with Hva content. Remarkably, the mechanical properties were retained during the erosion process as measured for poly(tyrosol carbonate) after 18 weeks.

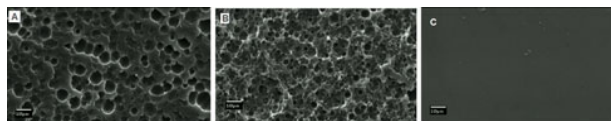


Figure 2. SEM images of the surface morphologies of poly(tyrosol carbonate) discs incubated in A) lipase solution for 1 week, B) 9 weeks, or C) PBS control for 9 weeks. (All specimens were rinsed with 70% ethanol).

Conclusions: Polycarbonates made from tyrosol and Hva have high moduli and are in the glassy state under physiological conditions. Moreover, we observed enzymatic surface erosion behavior *in vitro* in the absence of hydrolytic bulk degradation. The rate of surface erosion was tunable via polymer composition and correlated with slight changes in T_g . In summary, our polymer system possesses a unique set of properties that combine the strong mechanics of aromatic polycarbonates with the enzymatic surface erosion behavior of aliphatic polycarbonates.

References: [1] Gopferich A. *Biomater.* 1996;103-14. [2] Zhu KJ, et al. *Macromol.* 1991;24:1736-40. [3] Zhang Z, et al. *Biomater.* 2006;27:1741-8. [4] Ertel SI, Kohn J. *J Biomed Mater Res.* 1994;28:919-30.