Tunable Polyester Matrices Based On Sebacic Acid Using Crosslinking As A Strategy In Combinatorial Approach

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Statement of Purpose: For a good polymeric implant, matching of the mechanical properties of the implant with that of the native surrounding tissues is the biggest challenge. Commonly used biodegradable polyesters like poly(lactide-co-glycolide) release degradation products that are not benign. Hence, it is necessary to develop polymers in which mechanical and physical properties can independently be varied, without compromising the essential aspect of cytocompatibility.

Methods: In order to develop combinatorial methods in which mechanical properties can be tuned independently, we have used crosslinking as an effective strategy to synthesize a family of biodegradable polyesters. This is achieved using a combinatorial approach by varying monomer ratios and curing (esterification) time. Catalyst free melt-condensation technique was used to synthesize these polyesters, with citric acid and mannitol as the crosslinkers and sebacic acid as the chain extender. Ricinoleic acid, which is known to have analgesic and anti-inflammatory effects was also incorporated.

Results: Consequently, it was shown that a spectrum of mechanical properties (elastic modulus 22-327 MPa, which matches human ligament and tendon), tensile strength (0.7-12.7 MPa), contact angle (42^0-71^0) could be achieved. Importantly, we were able to show a shift in the erosion mechanism from predominant bulk to surface erosion with increase in curing, which led to the development of a theoretical model for curing in condensation polymers, which was hitherto unreported.

The C2C12 mouse myoblast cell line was used to evaluate cytocompatibility using cell viability assay (MTT) and morphological observations with scanning electron microscopy. 3-D cell culture on scaffolds made from such polyesters using an innovative adaption to the regular salt-leaching technique was done. The scaffolds were evaluated using X-ray micro-computed tomography to estimate parameters like pore volume and pore size. We investigated the release of model hydrophilic and hydrophobic dyes (Rhodamine B and Rhodamine B Base, respectively), which are almost similar in structure, as well as the release of isoniazid and 5-fluouracil (hydrophilic and hydrophobic drugs).

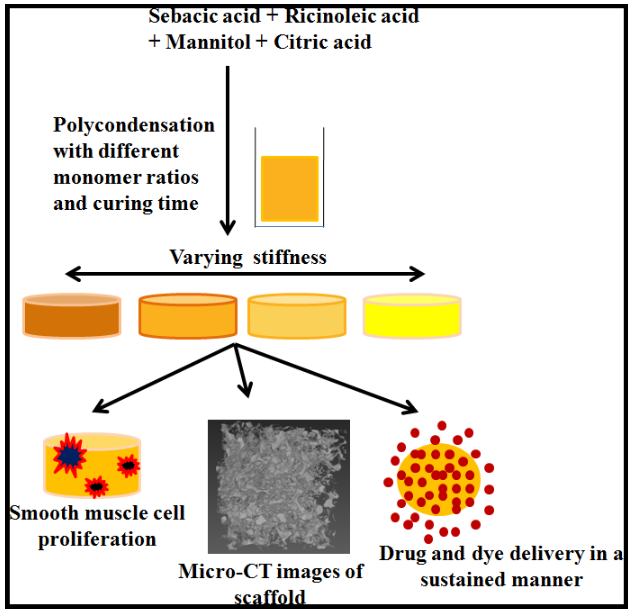

Figure 1. A schematic showing the synthesis of polyesters with varying mechanical properties.

Conclusions: The theoretical model developed for curing suggested that curing is a first order process in condensation polymerization. This predictive model allows us to assess and control properties during synthesis. Although crosslinking generally results in the formation of thermosets, we have adopted a method in which the pre-polymer formed is soluble in solvents before the curing step. Hence, contrary to most crosslinked polymers, the fabrication requirements are not so rigid. To summarize, we demonstrate the design of biodegradable, tunable, crosslinked polymer matrices and their application in scaffold fabrication and controlled release (Figure 1).

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References:

1. Wang Y et al, Nat Biotech 2002;20:602-6.
2. Chandorkar Y et al, J Mater Chem B 2013;1:865-75.