

Injectable Pastes that form Porous Scaffolds for Orthopaedic Applications

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INTRODUCTION: This paper describes a new material that changes from an injectable paste into a porous scaffold when temperature increases from room to 37°C. The scaffold system can either be sintered dry or physiologically wet forming a macroporous scaffold. The material is formed from a biodegradable polymer blend and can act as a protein and cell delivery system. This versatile method uses a single polymer processed by two separate methods to yield the components that are temperature insensitive (Type 1) and temperature sensitive (Type 2). The Type 2 components provide adhesion and strength. The Type 1 component acts as a spacer and delivery vehicle that can be blended or further modified by design prior to implantation in critical sized bone defects. Data are presented on the macrostructure, injectability, compressive mechanical properties & cellular response pertinent to clinical delivery.

METHODS: Type 1 particles of PLGA (lactide-co-glycolid 85:15 High I.V. 0.6-0.8dL/g, Alkermes) were produced using emulsification and solvent evaporation, employing dichloromethane as a solvent and 0.3% Poly(vinyl alcohol) 13-23000 molecular weight as stabilizer. These porous vesicles were further surface treated with a 70:30 blend of ethanol/sodium hydroxide (0.25M) for 20 minutes and PBS washed dried and sieved to produce particulate material in 100µm bands. Type 2 particles were produced by blending up to 15wt% PEG (Mw 400, Fluka 81172) and PLGA (85:15). Melt blends were manufactured by heating and physically mixing components on a ceramic tile. The blends were cooled, removed from the tile and ground after cooling with liquid nitrogen. Temperature triggered scaffolds (incorporating Type 2 particles) were crosslinked by heating components to 37°C for 15 minutes.

RESULTS: The addition of PEG to PLGA results in a reduced glass transition temperature that is optimized to facilitate crosslinking of the particulate scaffold under target conditions. Evaluation of the injectability by force

measurements through a 4mm orifice at 2mm/sec extrusion rate required 14 Newtons of force.

Porosity of the system evaluated by Micro CT can be controlled from 30-65%. Compressive strength data indicates Young's Modulus of 30-50MPa can be achieved by the sintered scaffold depending on conditions used.

DISCUSSION & CONCLUSIONS:

The optimization of glass transition temperature facilitates control of particle crosslinking under physiologically relevant conditions to produce a macroporous scaffold. The compression tests have also been conducted under simulated clinical conditions with our preferred Type 2 formulation. We have developed a degradable, injectable scaffold system capable of developing strength and elastic modulus in a range suitable for use in non load bearing skeletal regeneration.

REFERENCES: MM, Silva (2006) *The effect of anisotropic architecture on cell and tissue infiltration into tissue engineering scaffolds* Cyster LA, Barry JJ, Yang XB, Oreffo RO, Grant DM, Scotchford CA, Howdle SM, Shakesheff KM, Rose FR *Biomaterials*. Dec;27(35):5909-17. Epub Sep 1..

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