Mechanical Strength and Bioactivity Assessment of PEGDMA-based Injectable and Photocurable Bone Tissue Scaffolds

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Statement of Purpose: In the field of orthopedic medicine, complex bone fracture cases may require bone grafting and tissue engineering techniques to adequately heal. Tissue scaffolds create a suitable environment for grafted cells and provide mechanical support by mimicking the body's natural extracellular tissue matrix [1]. Recently, injectable tissue scaffolds are sought after extensively due to their minimally invasive nature of administration. Poly (ethylene glycol) dimethacrylate (PEGDMA) is an adequate biopolymer candidate for this purpose, due to its properties regarding strength and biodegradability/ biocompatibility [2]. PEGDMA can be photo-crosslinked using Lithium phenyl (2,4,6-trimethylbenzoyl) phosphinate (LAP), a photoinitiator reactive to blue light. Additionally, calcium-based bioceramic fillers can increase the scaffold's mechanical strength and provide essential components for mineralization during osteogenesis [3]. The objectives of this study include quick-and-easy fabrication of an injectable scaffold, followed by the analysis of the effect of five (5) different types of bioceramic fillers on the mechanical properties of the scaffolds. Also, subsequent effect on the murine preosteoblasts cell line (OB-6) attachment profile has been studied for biocompatibility of the scaffold.

Methods: Scaffolds for the control group were prepared by mixing PEGDMA (400 MW, Polysciences, Inc., USA) with 0.5% (*w/v*) LAP, dissolved in Ultrapure water in a 1:1 volume ratio. For experimental groups, powdered calcium-based bioceramic filler was added to the biopolymer solution at the desired experimental amount and vortexed until homogenous. The bioceramic fillers investigated include Calcium Zirconate (CZ), Calcium Sulfate (CS), Calcium Phosphate (CP), Calcium Carbonate (CC), and nano-Hydroxyapatite (HA). Cylindrical scaffold samples were created by injecting the scaffold solution into ASTM standard molds (L = 12 mm, d = 6 mm) using a 1 mL syringe. Scaffolds were then photo-cured using blue light for 5 minutes and removed from the molds for mechanical testing. All mechanical tests were done on an ADMET eXpert 2600 universal testing machine with an Interface S-type load cell. Scaffolds were subjected to vertical compression testing at a constant rate of 0.005 mm/sec and constrained on the static end to prevent slipping. Subsequently, cell culture studies were done with OB-6 cells at a density of 40,000 cells per scaffold. Cell attachment profile was imaged using a fluorescence set of dyes (Invitrogen LIVE/DEAD Cell Assay Kit) on days 3, 7, and 14. Analysis of variance (ANOVA) followed by Tukey's post hoc analysis was performed to test the statistical significance between the groups.

Results: Among the scaffold groups with 2% (*w/v*) filler, HA incorporated scaffolds displayed significantly higher compressive strength over CS, CC, and CZ samples, while CP had a comparable compressive strength with HA incorporated scaffolds. Taking these two groups with the highest comparative mechanical strength, the concentration of bioceramic was increased to 10% (*w/v*); beyond 10% (*w/v*) filler addition was faced with issues related to scaffold injectability. However, it was observed that 2% (*w/v*) HA had a significantly greater strength than the other groups, including the increased 10% (*w/v*) concentration, as shown in figure 1A. Further, HA filled scaffold samples were analyzed for cell attachment, as shown in figure 1B with representative fluorescent images. Enhanced cell attachment in the HA filled scaffolds was highlighted, as compared to the control.

Conclusion: Hydroxyapatite additives reinforce the mechanical strength of PEGDMA based scaffolds and remain injectable at low concentrations. 10% (*w/v*) filler amount disrupts the effective photo-crosslinking, thereby losing on mechanical strength of the scaffold. The cell attachment profile confirms the scaffold biocompatibility, and further opens a new avenue in approaching future translation studies in the preclinical and clinical setting.

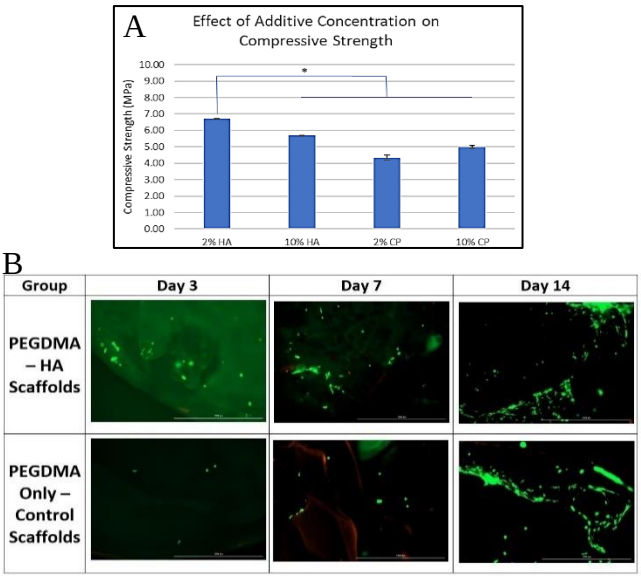

Figure 1 (A) Concentrations of CP and HA increased to 10% *w/v* and strength compared to 2% (*w/v*) concentration. * denotes *p-value* < 0.05. (B) LIVE/DEAD representative images for scaffold groups for Day 3, 7, and 14. 2% *w/v* HA added to the PEGDMA-HA scaffolds.

References:

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