The effect of SiO_2 and ZnO doping on the mechanical and biological properties of β-TCP scaffolds fabricated using three-dimensional (3-D) printing

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Statement of Purpose: β-tricalcium phosphate (β-TCP) makes an ideal choice of material for orthopedic scaffolds due to its excellent biocompatibility and bioactivity, but it exhibits poor mechanical strength in porous form. There have been many studies showing that the addition of sintering additives to calcium phosphate, in the form of trace elements commonly found in bone, affect the strength and cell-material interaction of dense ceramics (1). Other studies have shown that scaffolds with controlled porosity lead to better tissue ingrowth and biological fixation (2). The objective of this study is to understand the effect of dopant chemistry and microstructure on mechanical property and bioactivity of β-TCP scaffolds processed with 3-D printing technology. Our working hypothesis is optimal presence of dopants and designed microstructure can produce bone scaffolds with better mechanical and biological properties. 3-D printing method can fabricate ceramic parts with controlled microstructure. The rationale for this study is if we can optimize the amount and chemistry of dopants in TCP, along with microstructure, we will be able to produce scaffolds with desired properties.

Methods: Powders were made in batches of 100g and doped with 0.25 wt % ZnO and 0.5 wt % SiO_2 as a binary dopant system, ball milling in ethanol for 6 hr and then dried. Cylindrical scaffold CAD files (diameter 7 mm and height 10.5 mm) were created with interconnected channels of 1000µm, 750µm, and 500µm. Scaffolds were fabricated using a 3-D printer (R-1 R&D printer by ProMetal, Irwin, Pa). Once finished, parts were dried at 150°C for 2 hr. Scaffolds were then gently brushed clean and then remaining powder was removed by air blowing. After cleaning, green scaffolds were sintered in a muffle furnace at 1250° C for 2 hr. Cell-materials interactions using established human fetal osteoblast (hFOB) cells (hFOB 1.19, ATCC, Manassas, VA) were studied for MTT assay and cell proliferation.

Results: XRD data showed significant α-phase retardation in doped samples sintered at 1250 °C when compared to pure β-TCP samples. Compressive strength comparisons between doped and pure scaffolds are presented in **Table 1**. Average compressive strengths of the doped samples were substantially greater than that of the undoped samples. Samples with 500µm channels showed the highest strength; 10.21 ± 0.11 MPa when doped with SiO_2/ZnO and 5.48 ± 0.04 MPa for pure scaffolds. **Figure 1** shows cellular proliferation by the MTT assay. The doped scaffolds consistently showed higher proliferation rates and cellular viability than did their pure counterparts. **Figure 2** shows cellular morphology after 3 days of incubation on **(a)** pure scaffolds and **(b)** doped scaffolds. The pure scaffolds seemed to have more apatite formation as shown in the SEM micrograph, but due to slower proliferation rates, there was no evidence of formation complex cellular networks. The doped samples exhibited many clusters of cells with complex filopodial interactions, suggesting formation of communication networks.

Pore Size	Pure β-TCP	Si/Zn Doped β-TCP
1000 µm	1.75 ± 0.15 MPa	4.34 ± 0.31 MPa
750 µm	2.68 ± 0.16 MPa	8.20 ± 0.41 MPa
500 µm	5.48 ± 0.21 MPa	10.21 ± 0.33 MPa

Table 1. Average compressive strength of scaffolds

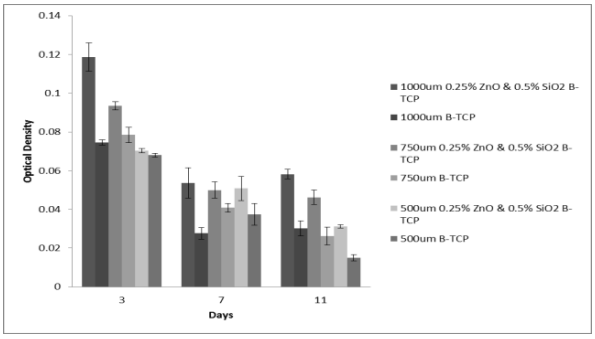

Figure 1. Cellular proliferation by MTT assay

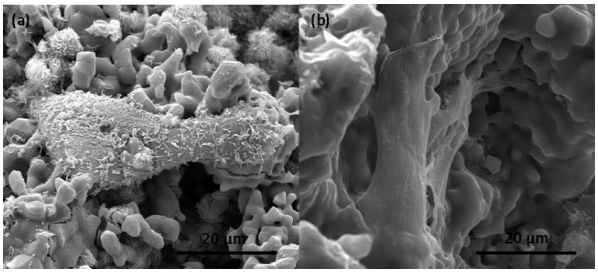

Figure 2. Cellular morphology on (a) pure scaffolds and (b) doped scaffolds

Conclusions: The addition of SiO_2 and ZnO dopants into β-TCP scaffolds resulted in an average of 2.5 fold increase in maximum compressive strength when compared to pure scaffolds. This is likely due to a reduction in grain growth during sintering of doped samples as a result of reduced β to α phase transformation. The scaffolds with 500µm interconnected channel pathway showed the highest strengths due to decreased total volume porosity. The MTT assay shows that for each day point and pore size pair, the doped samples seem to be proliferating at a significantly greater rate. While there is a slight trend showing that scaffolds with larger channel size appear to be more favorable to cellular attachment, *in-vivo* models should be considered for future study to optimize for tissue ingrowth. Authors like to acknowledge the financial support from the NIH (NBIB grant # NIH-R01-EB-0073510).

References: **1**. Bandyopadhyay, A**.** J. Am. Ceram. Soc. 2006;89:2675-88; **2**. Will **J.** J Mater Sci: Mater med. 2008;19:2781-90.