Tricalcium phosphate based Resorbable Ceramics:
Influence of MgO and SrO addition on Mechanical Properties and Biocompatibility

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Statement of Purpose: Resorbable calcium phosphate (CaP) based biomaterials are important because they can significantly improve health care by shortening the time necessary for restoration of functional loading of grafted bones.[1-3] The **objective** of this work is to gain fundamental information on designing CaP based resorbable materials and scaffolds having controlled degradation behavior. Our **hypothesis** is that doping with metal ions can influence the mechanical and biological properties in resorbable calcium phosphate materials such as β-TCP. The **rationale** is once we delineate the effect of metal ions on mechanical, *in* vitro and *in* vivo biological properties, we can tailor β-TCP based bone graft for specific application such as spinal fusion, carniomaxillofacial and other bone replacements. The focus of this work is to understand the influence of dopants e.g. MgO and SrO on the physical, mechanical, and biological properties of β-TCP resorbable ceramics.

Methods: β-Tricalcium phosphate powders (β-TCP, Berkley Advanced Biomaterials Inc. Berkeley, CA, 550 nm) with three compositions (i) pure TCP, (ii) β-TCP with 1.0wt% MgO and 0.25wt% SrO (β-TCP-Mg/Sr-1), (iii) β-TCP with 1.0wt% MgO and 1.0wt% SrO TCP (β-TCP-Mg/Sr-2) were prepared by solid state method. Compact samples from the powders were prepared by uniaxially pressing and then sintering at 1250°C for 2 h. Phase analyses were carried out using X-ray diffraction (Philips PW 3040/00 X'pert MPD) and surface morphologies of sintered samples were analyzed by SEM (FEI Inc., OR, USA). The infrared spectra were recorded by a Fourier transform infrared spectrometer (FTIR, Nicolet 6700, ThermoFisher, Madison, WI). Mechanical properties of sintered samples were tested by using a Shimadzu mechanical tester (Shimadzu AG-1S, Japan) with a constant crosshead speed of 0.33 mm/min. *In* vitro human osteoblast cell culture was used to determine influence of dopants on cell-material interactions. *In* vivo study was done by implanting β-TCP samples for 16 weeks into the distal femur of male Sprague-Dawley rat model.

Results: XRD spectra of pure β-TCP sintered at 1250°C showed α-TCP peak indicating occurrence of phase transformation from β to α-TCP (JCPDS No 09-0348)(Figure 1(a)). All the peaks observed in the spectra of sintered MgO/SrO doped samples were of β-TCP (JCPDS No 09-169). The IR spectra of β-TCP showed band shift on doping with MgO and SrO. It also showed new bands at 932 and 970 presumably associated with Mg-β-TCP. The average density of pure β-TCP, β-TCP-Mg/Sr-1 and β-TCP-Mg/Sr-2 were found to be 96.2 ±1.2%, 97.1 ±1.6% and 97.3 ±1.1%, respectively. It was observed that addition of dopants resulted in slight increase in density of β-TCP. SEM micrographs of the surface for all the three compositions revealed highly dense structure. Doped β-TCP showed formation of some glassy phase as also observed in our earlier studies.[2,4] Compressive strengths of all samples sintered at 1250°C are presented in Figure 1(b). Doped β-TCP samples showed compressive strength comparable to pure β-TCP. *In* vitro study reveled that cells attached and proliferated on all the surfaces. β-TCP doped with MgO/SrO showed good cell growth and spreading.

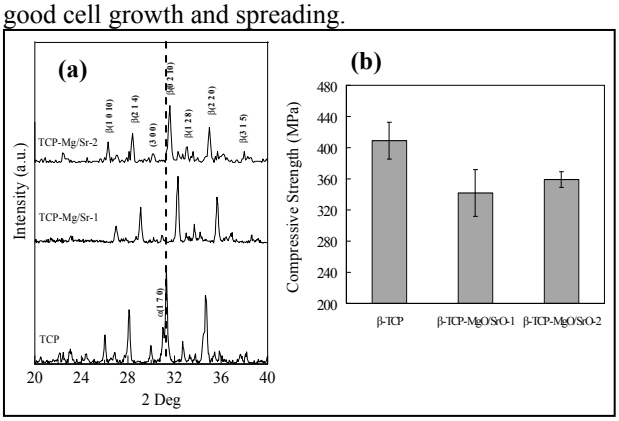

Figure 1. (a) X-ray powder diffraction patterns and (b) Compressive strength of pure β-TCP and MgO/SrO doped β-TCP samples sintered at 1250°C.

From the *in* vivo study the osteocalcin concentration in the implant and blood serum for doped implant were 0.88 ng/mL and 6.68 ng/mL, and that for β-TCP were 0.69 and 5.72 ng/mL, respectively. Low Ca^{2+} concentration was detected in urine samples of rats with doped β-TCP implant (18 μg/mL) compared to pure β-TCP implant (31.0 μg/mL) showing slow degradation property for doped β-TCP. Histology study displayed substantial integration of both doped β-TCP and pure β-TCP implants with the surrounding bone tissue.

Conclusions: Presence of MgO and SrO in β-TCP suppressed the phase transition from β to α-TCP. Doped β-TCP also showed slight increase in densification compared to pure β-TCP. The *in* vitro results revealed that doped β-TCP sample was biocompatible and non-toxic. *In* vivo study showed low Ca^{2+} concentration for doped implants confirming slow degradation of doped β-TCP. These results suggest that properties of bioresorbable doped TCP could be tailored for specific tissue engineering applications. Financial support from NIH (EBR01007351) is greatly acknowledged.

References: 1) Bandyopadhyay A, J. Am. Ceram. Soc**.** 2006; 89; 2675-2688.
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